MULTI SYSTEM ATROPHY

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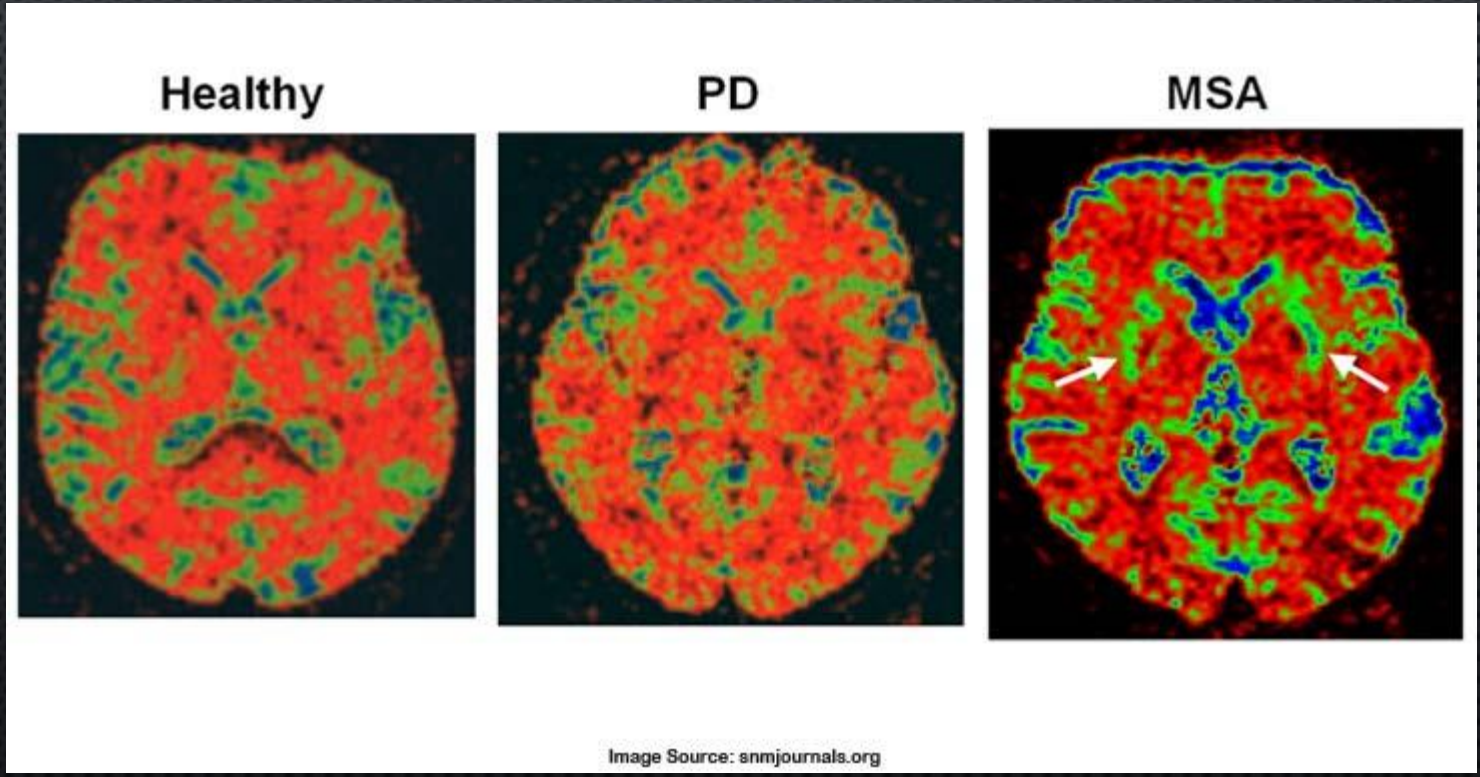
NEUROLOGY PRESENTATION

CASE

- 69 year old male
- CC: Presents following recurrent syncopal episodes for 1 ½ years
- HPI:
  - Syncopal episodes 1-3xs/week with LOC, no aura
  - 12month h/o balance and gait disturbances
  - sudden onset of intention tremors that improve with alcohol use
  - jerking motions during sleep
  - Decline in memory, anosmia
- PM/SH:
  - Cardiac arrythmia
  - Atrial flutter with plans for radiofrequency ablation
  - Right translabrynthine
- SH:
  - 3-4drinks/day
  - Retired, lives with family

- Review of medications:
  - Eliquis, Metoprolol, Digoxin, amiodarone, citalopram
- Vitals
  - All WNL except BP 162/92mmHg
- Pertinent PE
  - Gait ataxia, broad based gait
  - Slurred speech
  - Noticeable tremor with movement

DIAGNOSIS?



Definitive diagnosis

- Only way to definitely diagnose MSA is postmortem showing alpha-synuclein-positive glial cytoplasmic inclusions with neurodegenerative changes in striatonigral or olivopontocerebellar structures

Clinical Diagnosis – Probable MSA

- Sporadic, progressive, adult onset (>30 years old)
- Autonomic failure involving either urinary incontinence or an orthostatic blood pressure decrease within three minutes of standing by ≥30 mmHg systolic or ≥15 mmHg diastolic
- Poor response to levodopa (bradykinesia with rigidity, tremor, or postural instability) **or** a cerebellar syndrome (gait ataxia with cerebellar dysarthria, limb ataxia, or cerebellar oculomotor dysfunction)

Possible MSA		
	One criterion	2 features from separate domains
Probable MSA		
	Autonomic failure/urinary dysfunction criterion	poorly levodopa responsive parkinsonism or cerebellar dysfunction
Definite MSA		
	Pathologically confirmed by the presence of a high density of glial cytoplasmic inclusions	degenerative changes in the nigrostriatal and olivopontocerebellar pathways.

	Autonomic and urinary dysfunction	Parkinsonism	Cerebellar Dysfunction	Corticospinal Tract Dysfunction
Feature – characteristic of the disease	Orthostatic Hypotension	Bradykinesia	Gait ataxia	Extensor plantar responses with hyperreflexia
		Postural Instability	Ataxic dysarthria	
	Urinary incontinence or incomplete bladder emptying	Tremor	Limb ataxia	
		Rigidity	Sustained gaze – evoked nystagmus	
Criterion - features required for diagnosis	Orthostatic fall in blood pressure	Bradykinesia	Gait ataxia	no CST features are used in diagnosis of MSA
	OR Urinary incontinence	PLUS At least 1	PLUS at least 1	

	MSA – P	MSA – C
	Neuronal loss and gliosis in the substantia nigra, putamen, caudate, and globus pallidus	Degeneration of the cerebellar Purkinje cells, middle cerebellar peduncles, inferior olivary nuclei, basis pontis, and pontine nuclei
urinary incontinence and retention	Detrusor hyperreflexia from loss of inhibitory input to the pontine micturition center	Bladder atonia primarily from severe damage to Onuf's nucleus in the sacral spinal cord;
Respiratory stridor	Nucleus ambiguus	
REM sleep abnormalities	Loss of cholinergic mesopontine neurons	Loss of locus ceruleus neurons

SITE OF LESION

Preganglionic damage of intermediolateral cell columns	Pyramidal tract lesion	Pontine nuclei	Nucleus Ambiguus
Orthostatic hypotension	Extensor plantar response	Nystagmus	Stridor
Urinary incontinence	Hyperreflexia	Dysarthria	
Urinary retention	Pyramidal signs	Ataxia	

- Levodopa responsiveness – lack of response over 3 months
  - Levodopa-induced unilateral facial dystonic spasms
- progressive supranuclear palsy - Vertical eye movement abnormalities

Associated conditions

- Nocturnal or diurnal laryngeal stridor occurs in approximately one-third of patients with MSA - risk factor for sudden death

- RBD – REM Sleep Behavior Disorder
- 2/3 of patients have rapid eye movement (REM) sleep behavior disorder
  - Dream enactment during REM sleep (sleep-related memory consolidation)
  - Gestures, thrashing, punching, kicking
  - Prodromal alpha-synuclein degeneration
  - multiple system atrophy (80 – 95%)

	MSA	PD	Autonomic Failure
Levodopa response	Poor or unsustained response	Good response	
Cytoplasmic inclusions	Oligodendroglia inclusions	Lewy bodies in substantia nigra	Lewy bodies
Nigrostriatal transmission	Pre and post synaptic, reduced DA-R	Pre synaptic	
Symmetry of MD	Usually Asymmetric	Asymmetric	
Symptom onset and progression	Rapid progression, early onset	Slow progression, late onset	Slow progression,
DA uptake (PET)	Decrease in Putamen & caudate	Putamen, smaller decrease in caudate	
Clonidine stimulation test	Dysfunction of HP pathway	Intact function, release of GH	Intact function, release of GH

MSA VS PSP VS PD?

- 3 HAVE GLIAL CYTOPLASMIC INCLUSIONS WITH ALPHA SYNUCLEIN AS A MAJOR COMPONENT: SPECTRUM OF THE SAME DISEASE

EXCLUSION CRITERIA

History	PE	Lab
Symptomatic <30yo	DSM criteria for dementia	Diagnosis of exclusion
FH	Prominent slowing of vertical saccades or vertical supranuclear gaze palsy	
Systemic disease	Evidence of focal cortical dysfunction such as aphasia, alien limb syndrome, and parietal dysfunction	

- Cognitive function in MSA tends to be relatively well preserved compared with idiopathic Parkinson disease
- PBA
- olfactory dysfunction in MSA is less severe than that seen in Parkinson disease
- Raynaud phenomenon

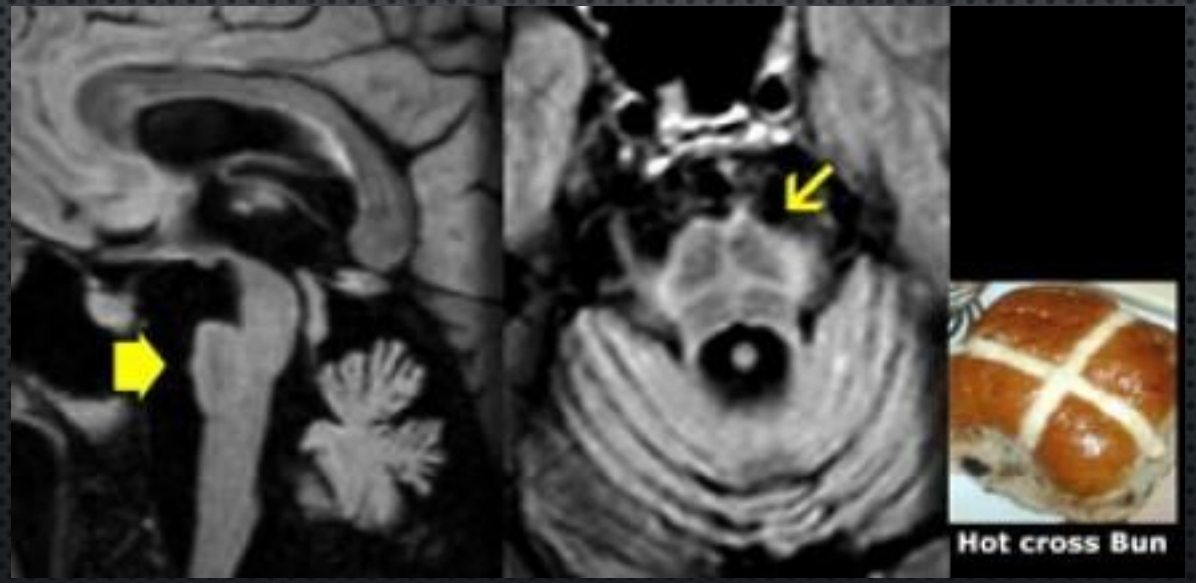
Autonomic dysfunction?

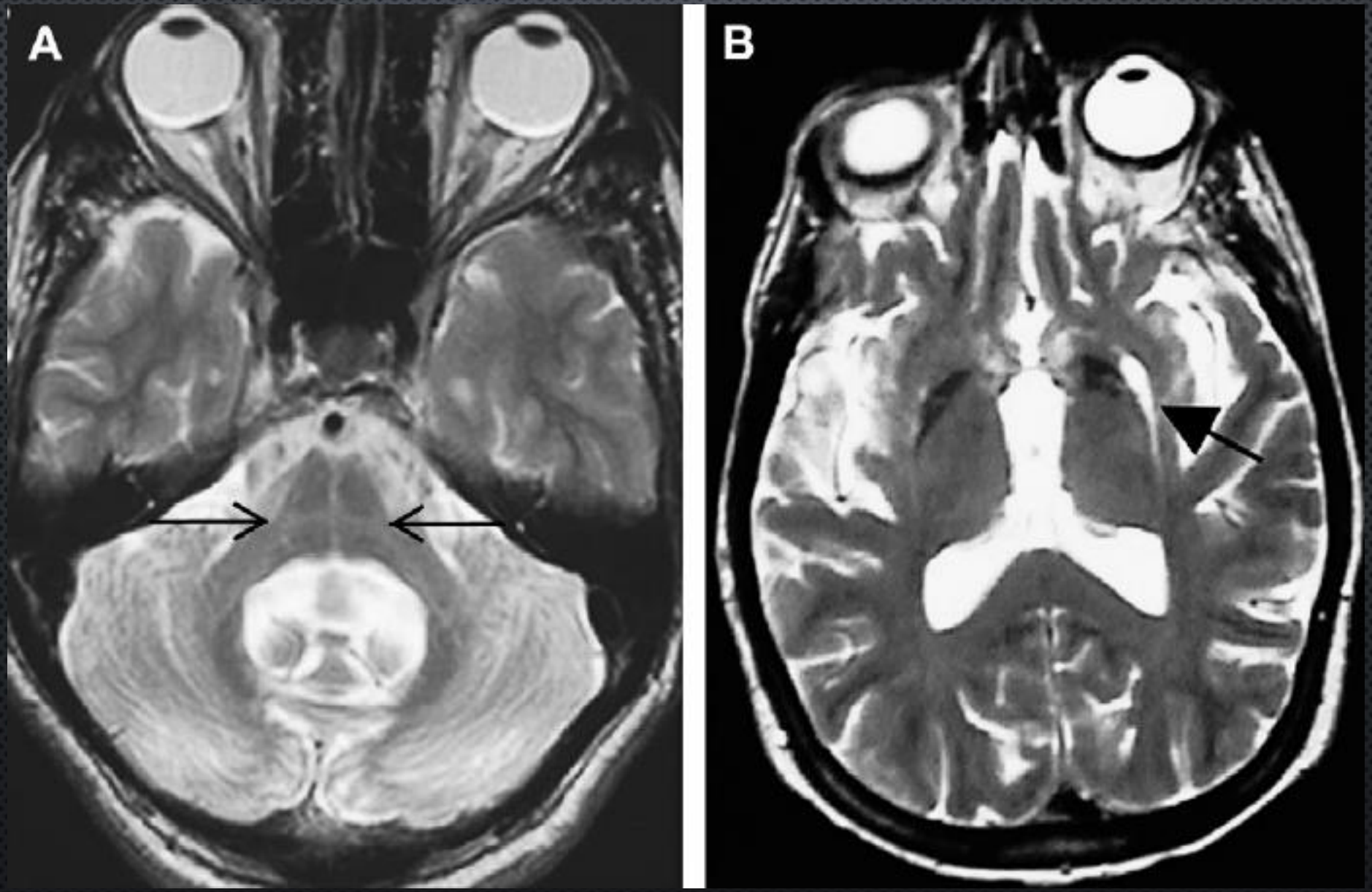
- Postural hypotension
- GU dysfunction
- GI dysfunction
- Temperature regulation
- Paresthesias

Further testing?

- Striatal dopamine transporter imaging using SPECT (DaTscan)
- Cannot differentiate Parkinson disease and the parkinsonian syndromes from one another

HOT CROSS BUNS SIGN

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MANAGEMENT

- MOTOR – RESISTANT TO TREATMENT ☹
- PHYSICAL, SPEECH, OCCUPATIONAL THERAPY
  - PHYSICAL – AMBULATION, MAINTAIN MOBILITY, PREVENT FALLS,
  - SPEECH – DYSPHAGIA PROGRESSION
  - OCCUPATIONAL – MAINTAIN INDEPENDENCE

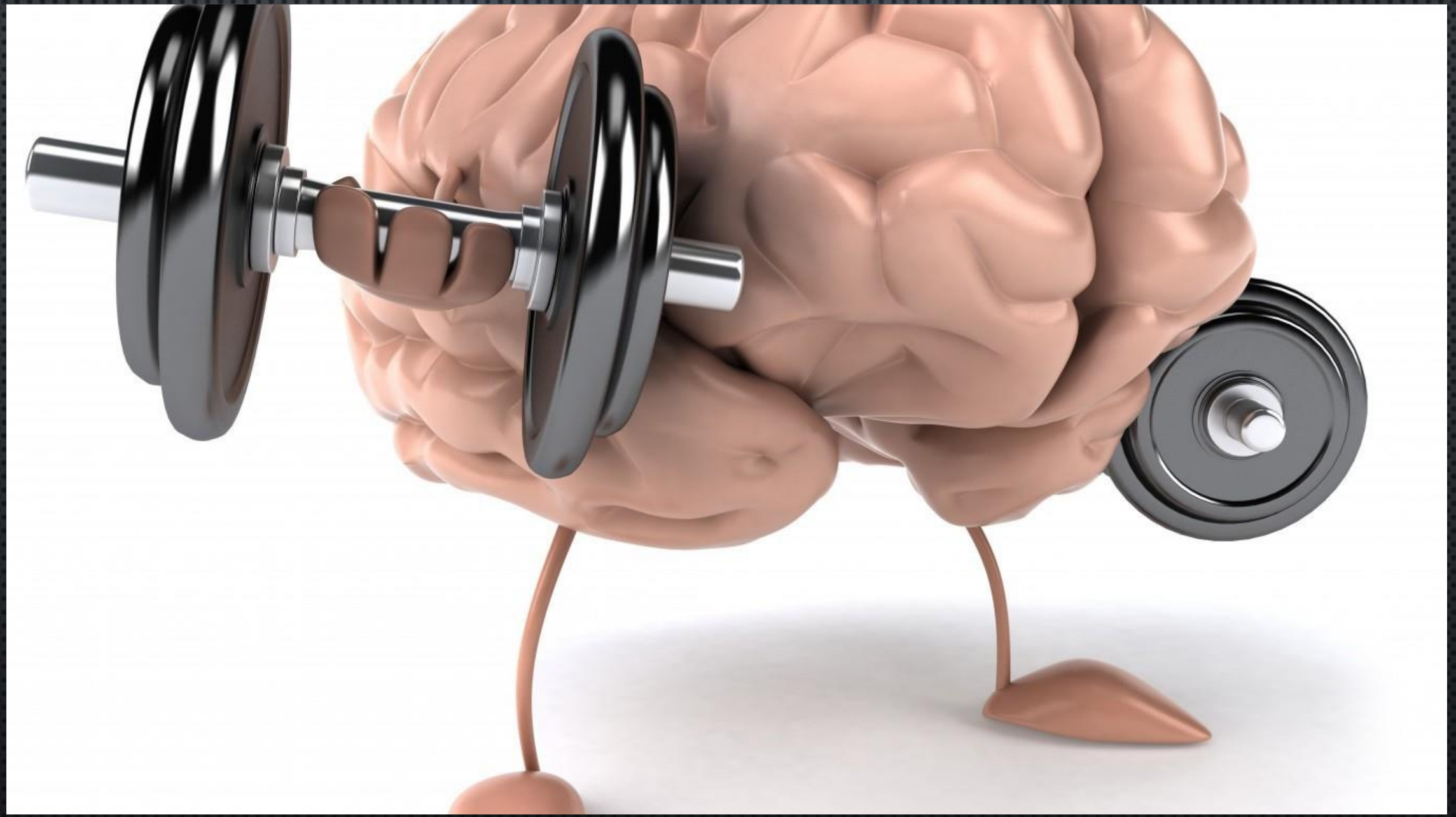
- Autonomic – responsive
  - Stridor – cpap, bipap, tracheostomy
  - Orthostatic Hypotension:
    - fludrocortisone (+ K supplementation), Droxidopa (NE precursor, short term)
    - a1 adrenergic R (2nd line)
    - Physical maneuvers, lifestyle changes, elastic stockings
  - GU
    - Detrusor hyperreflexia – tolterodine or Oxybutynin (M-Ach-R anta)
    - Bladder atony - intermittent self-catheterization
  - REM-sleep behavior disorder - clonazepam, TCAs

Prognosis

- From onset until:
  - Development of autonomic dysfunction - 2.5 years
  - Need for walking aid, 3 years
  - Wheelchair confinement, 3.5 to 5 years
  - Bedridden state, 5 to 8 years
- death is 6 to 10 years

Improvements

- Recognition of need for additional treatment (depression, ED)
- Therapy – social, support (national parkinson disease association, national parkinson foundation, multiple system atrophy coalition)
- Research on genetic linakge
  - CoQ2 gene in japanese study
- In progress
  - Sertraline (SSRIs) - (-) alpha-synuclein aggregation
  - IVIGs – (-) neuroinflammation
  - NCT02270489 – phase I study of active vaccination against an epitope similar to alpha-synuclein
  - NCT02008721 – phase III study of neuroprotective agent that inhibits alpha-synuclein protein aggregation as possible disease modification in MSA



TOO LONG DIDN'T READ

- MSA: autonomic failure, jerky postural tremor, ataxia (in MSA-C), and pyramidal tract signs

QUESTIONS

- DDx idiopathic PDv s MSA?

THANK YOU