An overview of Multiple Systems Atrophy and its management

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March 19th, 2022

Penn Medicine

Disclosures (last 12 months)

Clinical trial funding

TeVa Pharmaceuticals

Prevail Therapeutics

Cerevel Therapeutics

Addex Therapeutics

Biohaven Pharmaceuticals

Dystonia Coalition

CME activities

Amneal Pharmaceuticals

Royalties

UpToDate

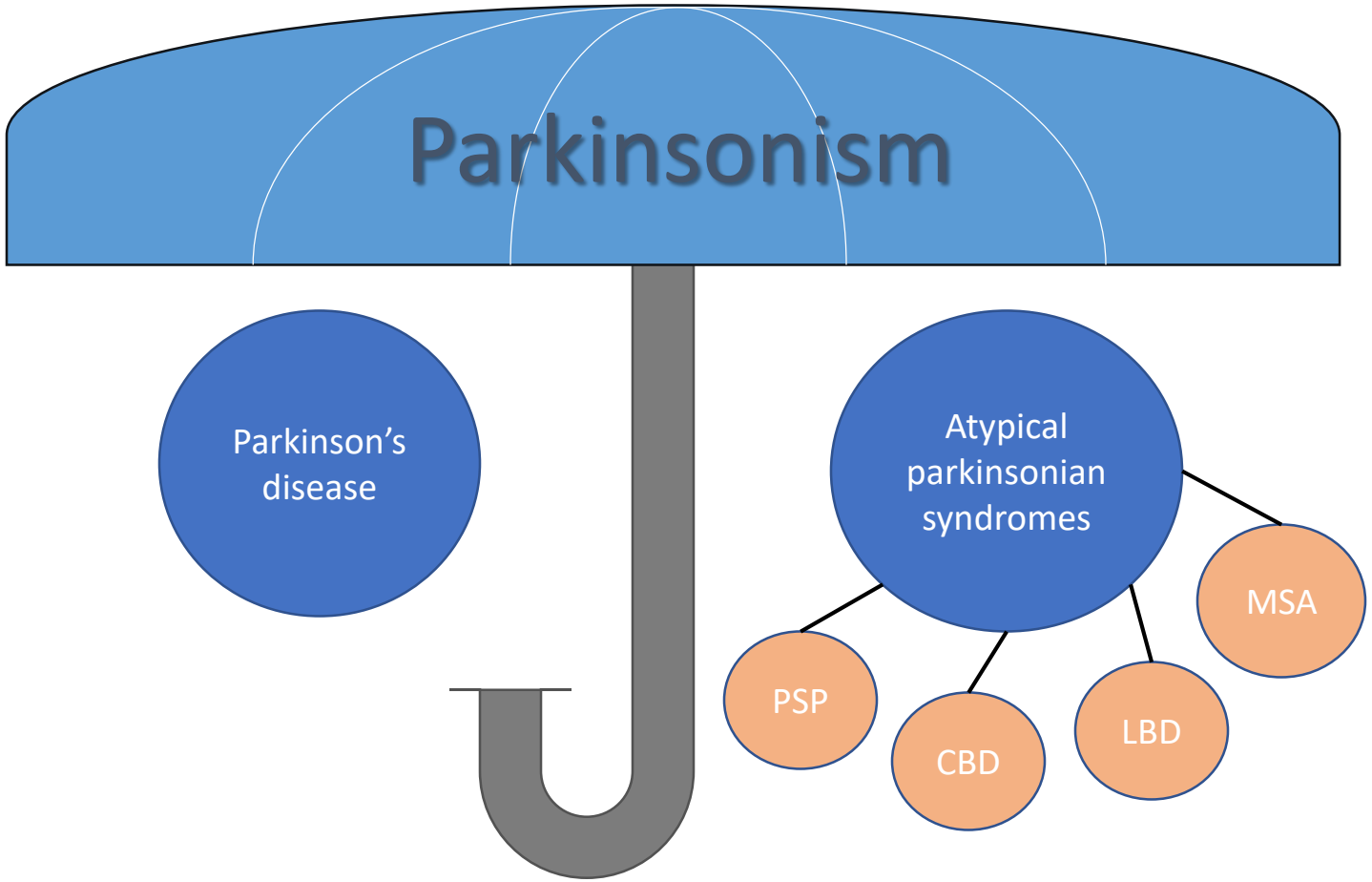
Elsevier ClinicalKey

Outline

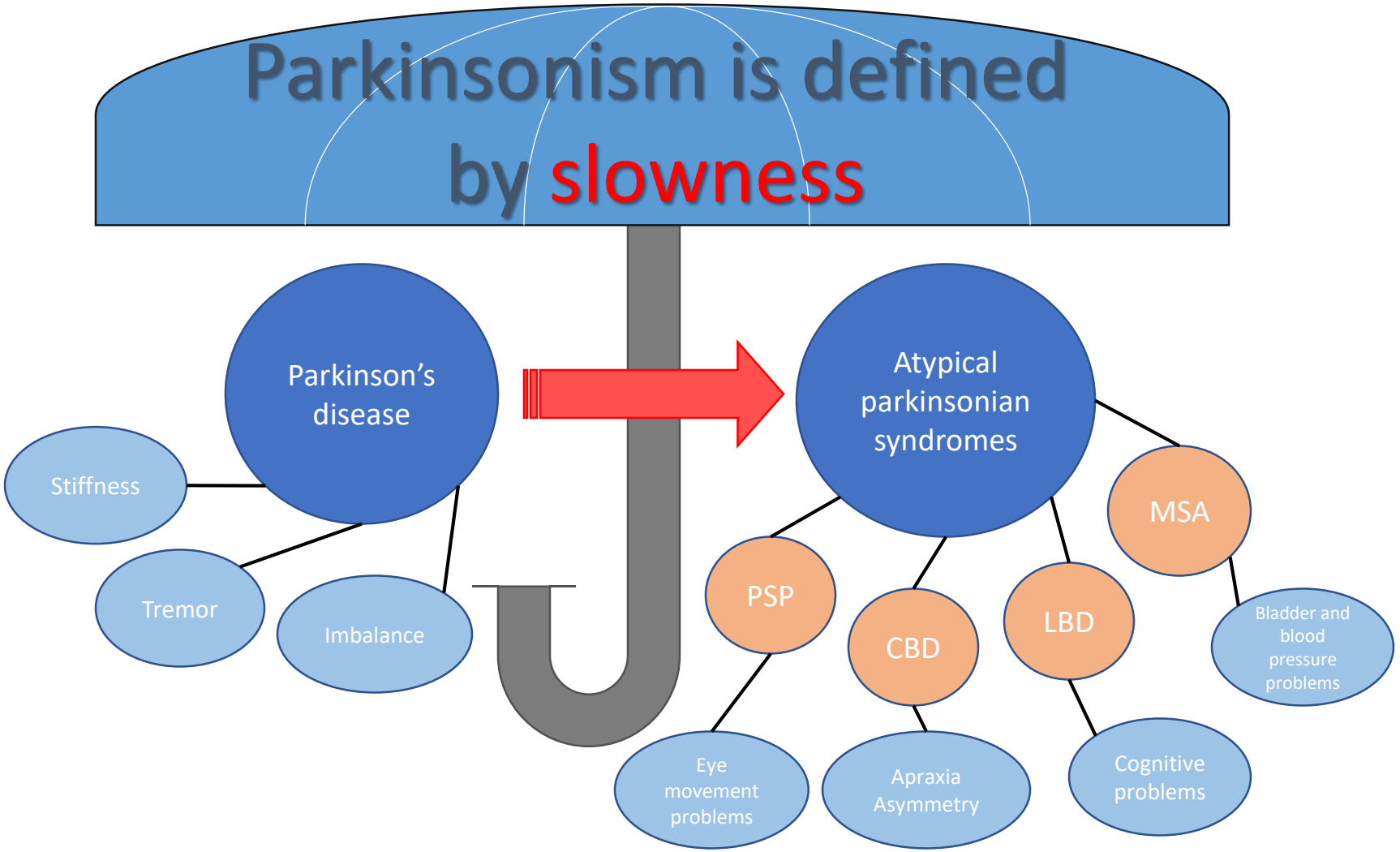
- Parkinsonism and MSA
- Treatable MSA symptoms
- Multidisciplinary care at Penn
- Clinical trials for MSA
- Closing remarks

Parkinsonism and MSA

What is parkinsonism?

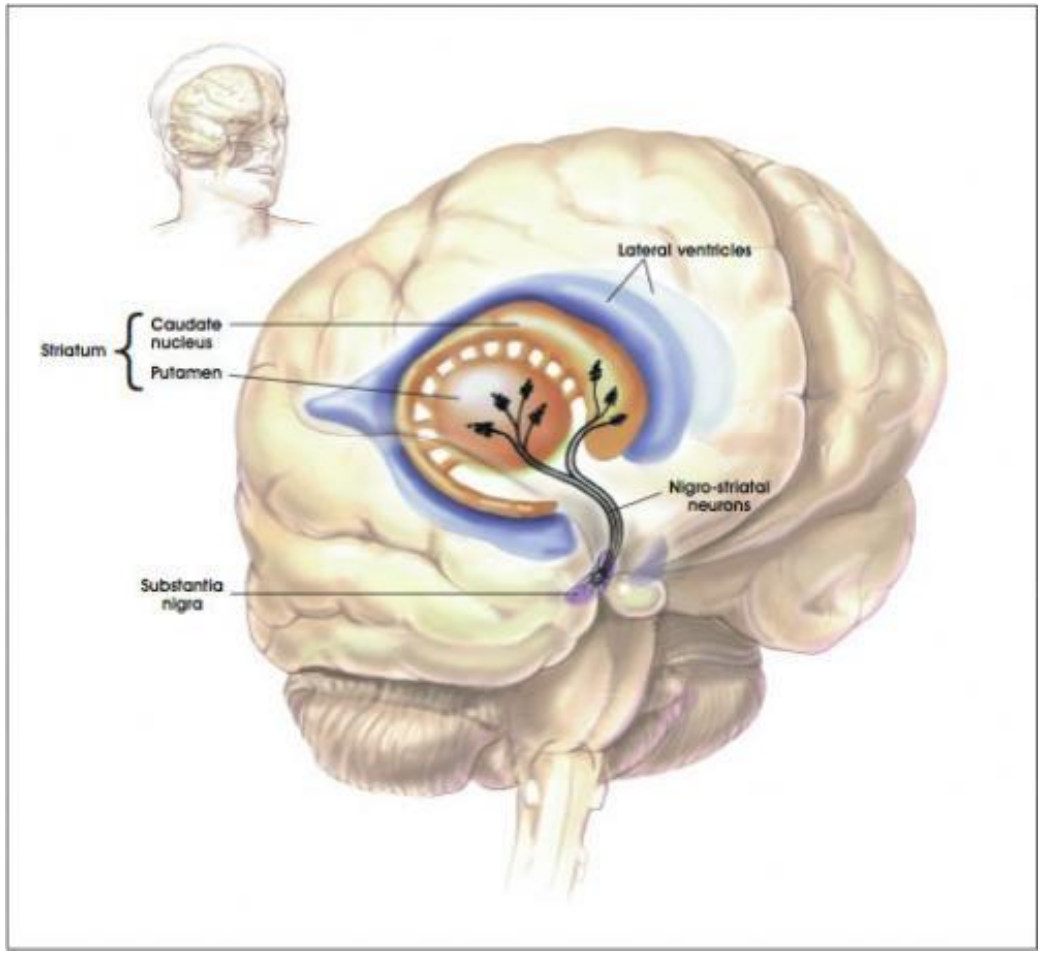


What defines parkinsonism?



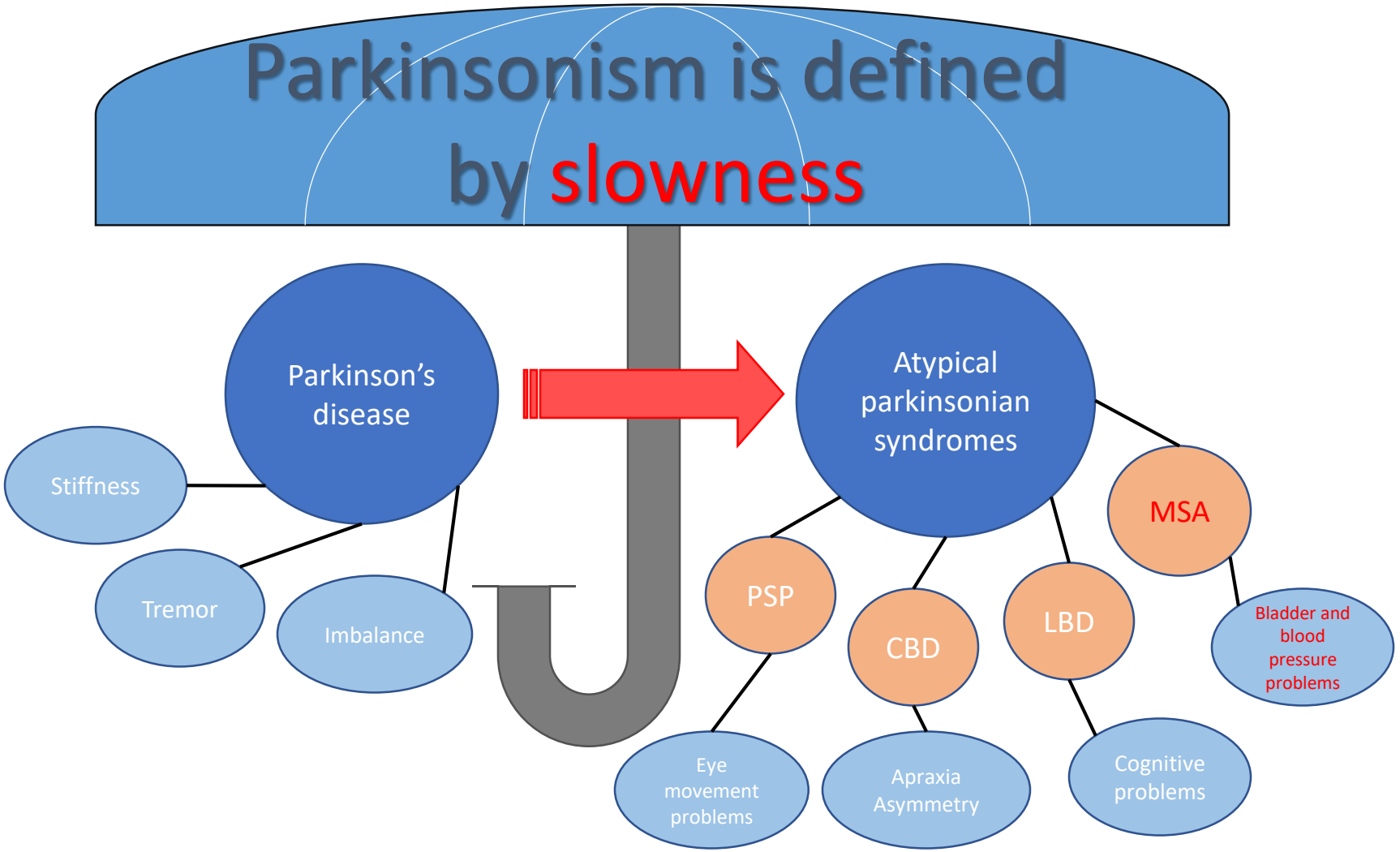
What causes parkinsonism?

- Parkinsonism is a sign of low dopamine levels in the brain
- Dopamine is a neurotransmitter created in the substantia nigra
- *In general*, degree of dopaminergic transmission is directly proportional to movement
- Dopamine levels drop when there is accumulation of toxic proteins in the brain cells



http://www.dls.ym.edu.tw/lesson2/0318.htm

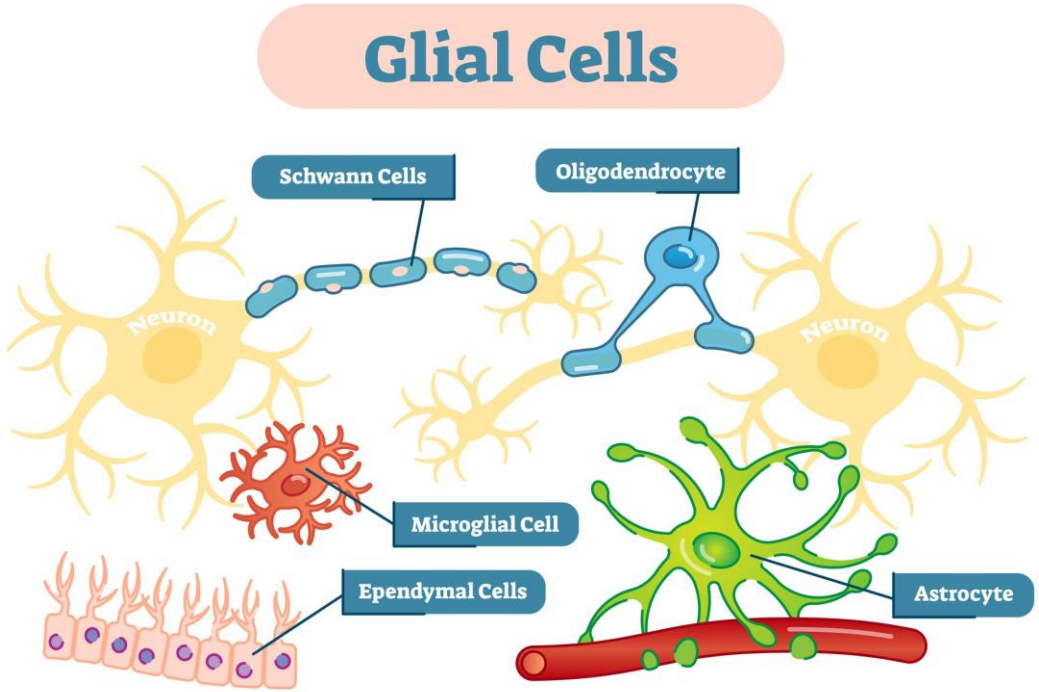
Now, let's focus on MSA

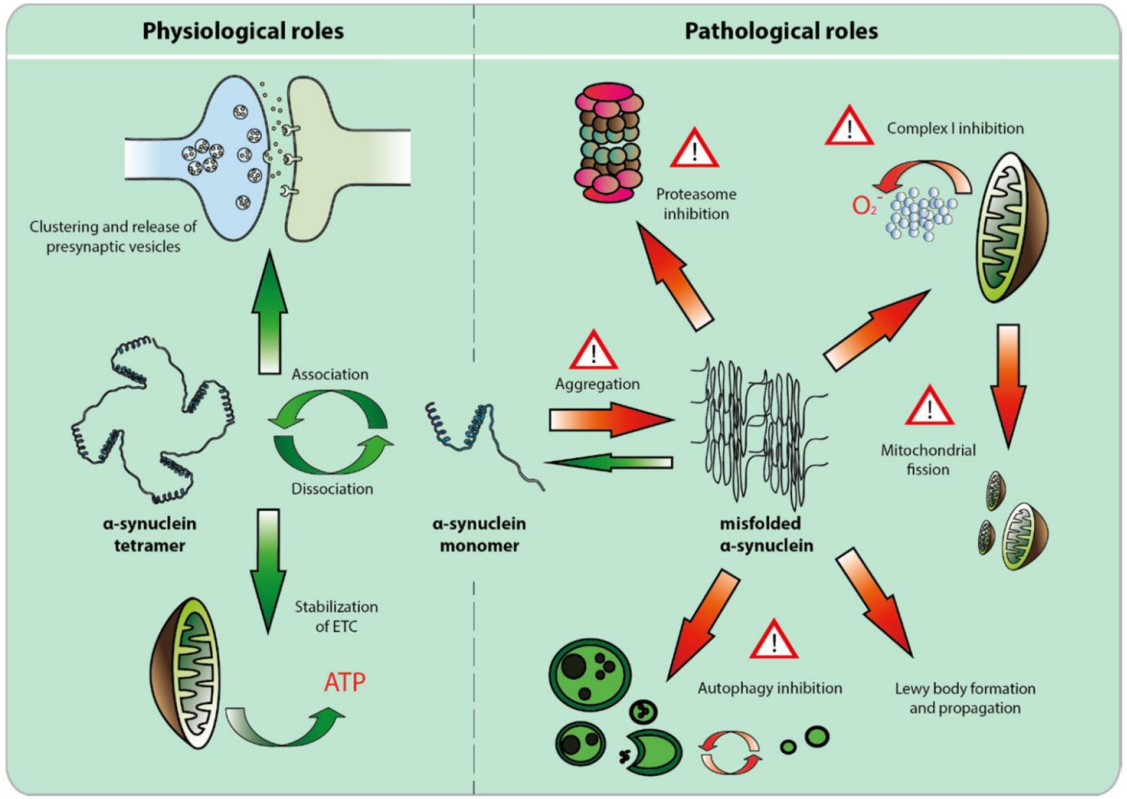


Now, let's focus on MSA

MSA

- Prevalence is 2-5/100,000 (prevalence of PD is 1-2/1,000)
- Caused by toxic accumulation of alpha-synuclein in *glial cells*

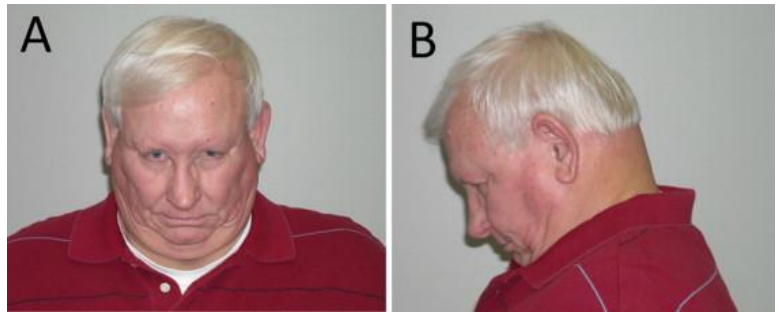




http://www.mdpi.com/biomolecules/biomolecules-05-02675/article_deploy/html/images/biomolecules-05-02675-g001.png
https://www.verywellhealth.com/what-are-glial-cells-and-what-do-they-do-4159734

How to distinguish PD from MSA, clinically

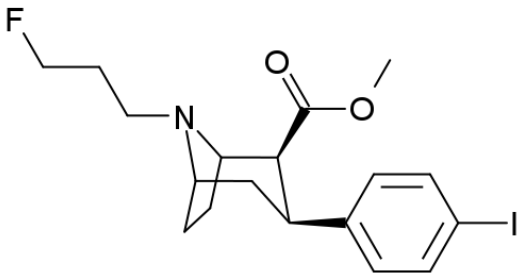
- Motor red flags
  - Balance changes and falls
  - Early difficulty with speech and swallow
  - Suboptimal response to levodopa
  - Development of prominent oral and neck dyskinesias
  - Truncal dystonia
  - Polyminimyoclonus
  - Anterocollis



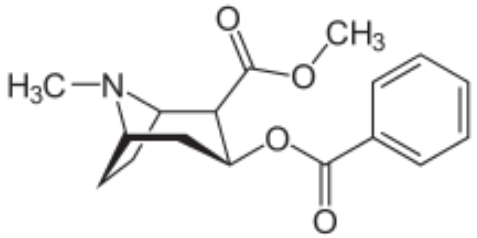
- Non-motor red flags
  - Autonomic failure (dysautonomia)
    - Orthostatic hypotension
    - Urinary dysfunction
    - Constipation
  - Stridor

https://www.sciencedirect.com/science/article/abs/pii/S0303846714003825

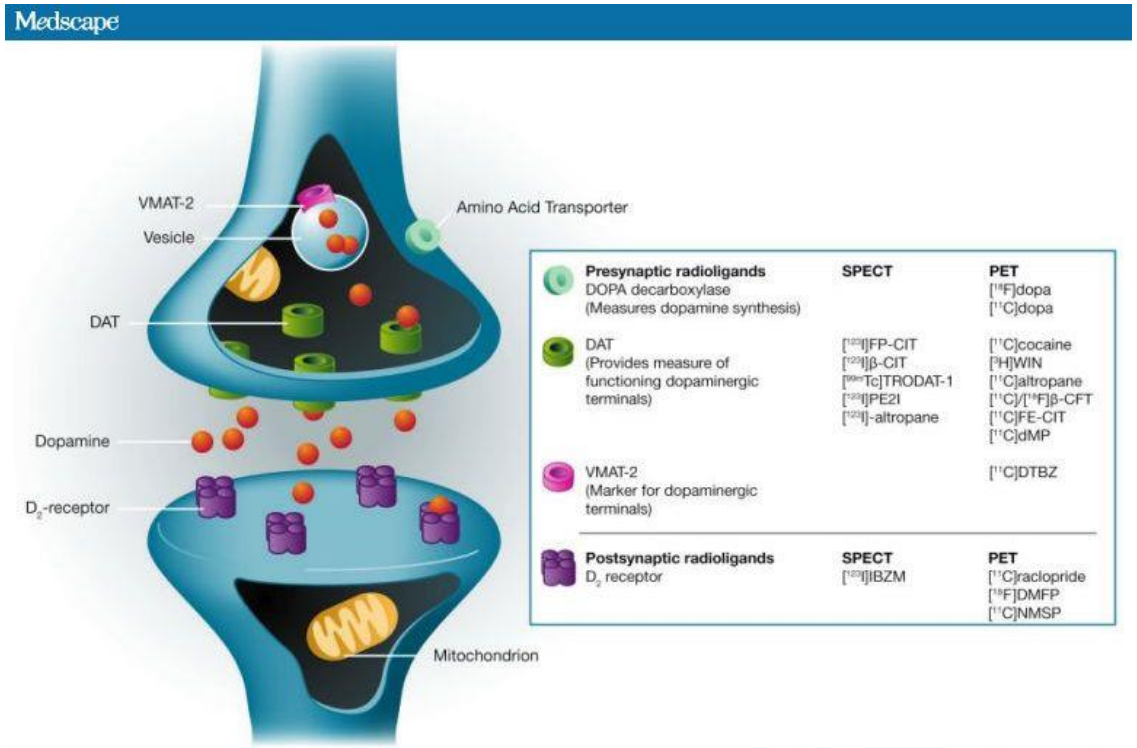
DaTscan

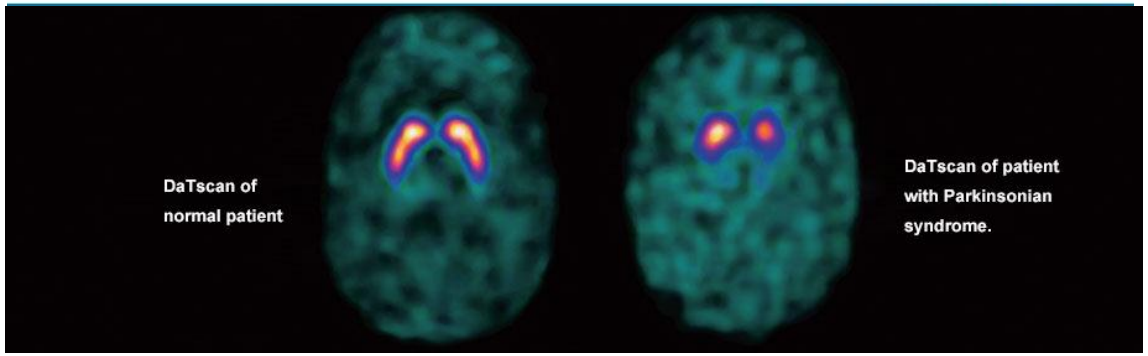


DaTscan™ II
Ioflupane I 123 Injection



Cocaine





https://www.google.com/search?q=datscan&biw=1242&bih=557&source=lnms&tbm=isch&sa=X&ved=0ahUKEwjq35qL2s7PAhUGND4KHTLJBf8Q_AUIBigB#imgrc=LN9dpkGsSjt77M%3A

The role of DAT-SPECT in movement disorders

G Kägi, K P Bhatia, E Tolosa

J Neurol Neurosurg Psychiatry 2010;**81**:5–12. doi:10.1136/jnnp.2008.157370

Minor* effect on DAT-SPECT	To be stopped prior to DAT-SPECT	Significant† effect on DAT-SPECT	To be stopped prior to DAT-SPECT
Citalopram	8 days	Cocaine	2 days
Fluoxetine	45 days	Amfetamine	7 days
Paroxetine	5 days	Methylamfetamine	3 days
Venlafaxine	3 days	Methylphenidate	1 days
Duloxetine	3 days	Methylphenidate	2 days
Escitalopram	8 days	Dexamfetamine	7 days
Fluvoxamine	5 days	Mazindol	3 days
Sertraline	6 days	Phentermine	14 days
Imipramine	5 days	Modafinil	3 days
Clomipramine	21 days	Bupropion or amfebutamone	8 days
Pimozide	28 days	Benzatropine	5 days
Ziprasidone	2 days		
Memantine	5 days		
Amantadine	6 days		
Budipine	6 days		
Ephedrine, epinephrine	6–10 h		
Phenylephrine			
Pseudoephedrine			
Xylometazoline			

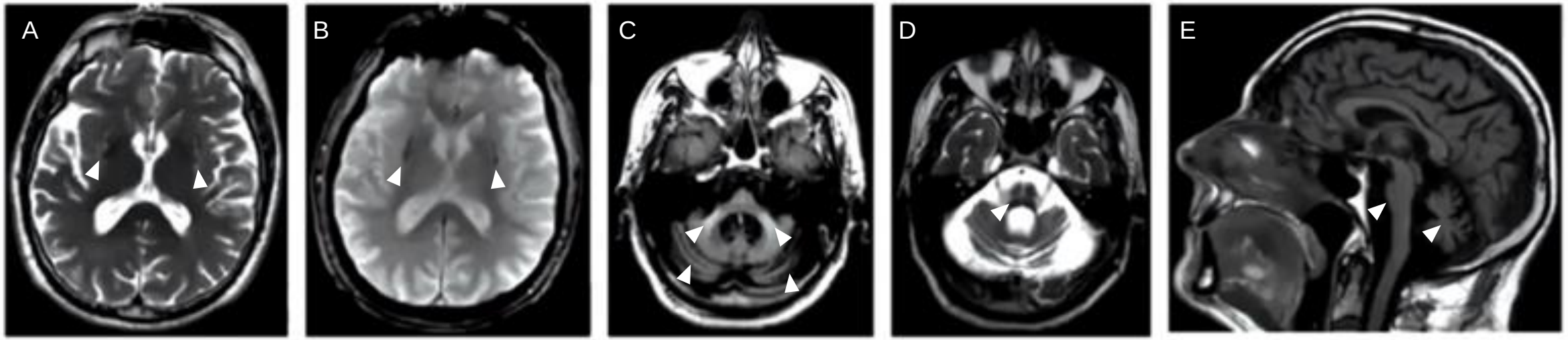
About MSA

- Onset age 55 years (33-76)
- Men : women = 1.3 : 1
- Symptoms can affect different areas of the brain

Basal ganglia (A&B)
Dysfunction causes Parkinson-like symptoms

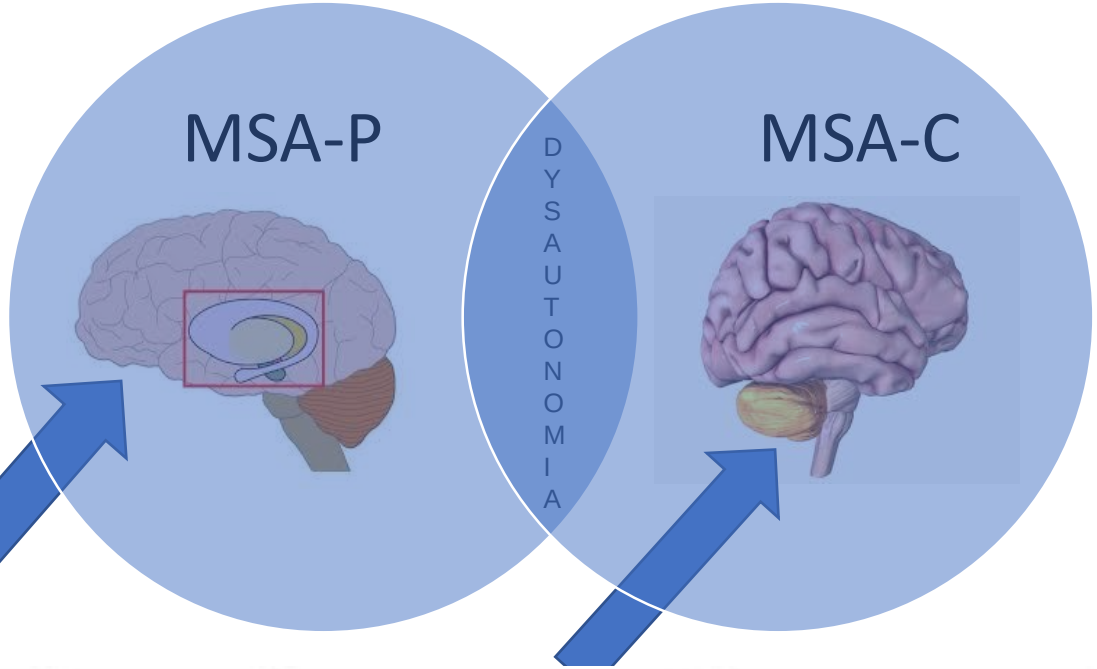
Cerebellum (C)
Dysfunction causes imbalance and incoordination

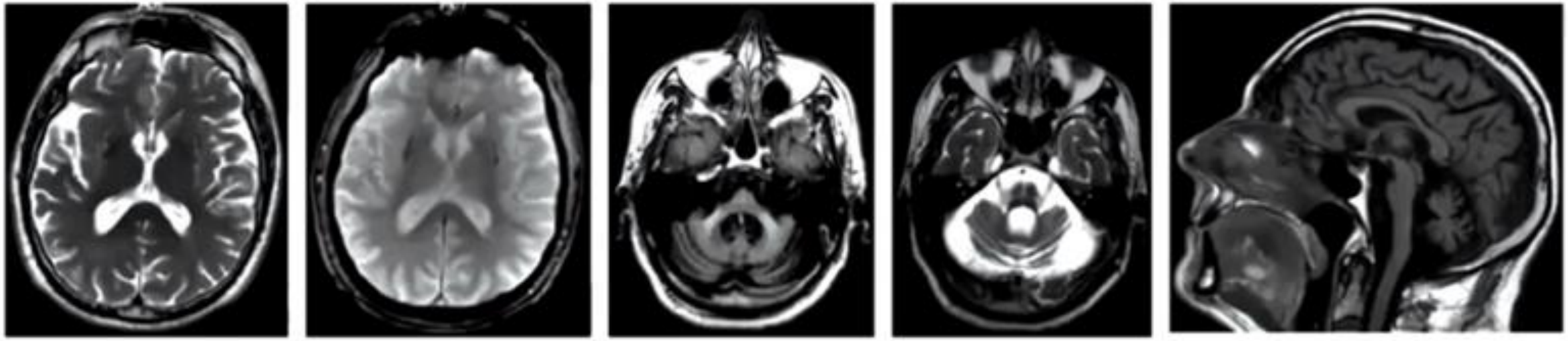
Brainstem (D&E)
Dysfunction causes autonomic dysfunction



https://radiopaedia.org/articles/multiple-system-atrophy
https://www.hkcr.org/CaseOfMonth/2012/05/05a.html

Types of MSA





https://www.neuroscientificallychallenged.com/blog/what-are-basal-ganglia
https://www.medicalnewstoday.com/articles/313265

Treatable MSA symptoms

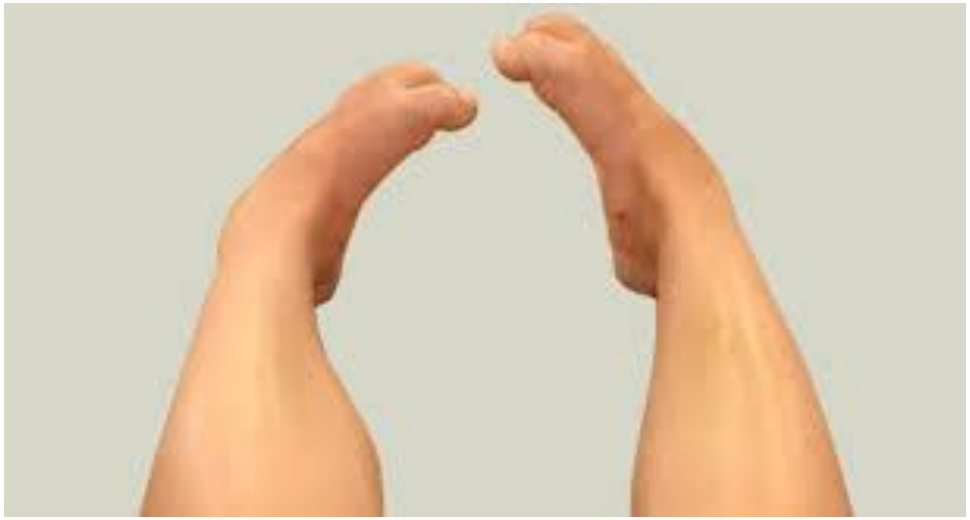
Motor symptoms

Slowness/stiffness

- Levodopa, in all its presentations
  - Immediate release: Sinemet 10/100, 25/100, 25/250
  - Extended release: Sinemet CR 25/100, 50/200, Rytary
  - On demand: Inbrija
- Response is unpredictable
- Side effects
  - Fogginess
  - Sleepiness
  - Worsening orthostatism
  - Confusion
  - Hallucinations
  - Dyskinesias/dystonia

Tremor/dystonia

- Levodopa
- Trihexyphenidyl (Artane®)
- Amantadine
  - Short-acting: Symmetrel®
  - Long-acting: Gocovri®, Osmolex®
- Botulinum toxin injections
  - Botox®
  - Xeomin®
  - Dysport®
  - Myobloc®



Gait dysfunction/falls

The most important step is to try to understand the cause

- Orthostatic hypotension → hydration, compression stockings, medication
- Parkinsonism → dopaminergic medication and refer to physical therapy
- Ataxia → refer to physical therapy
- Orthopedic (back, hip, knees) → refer to orthopedics or pain management as appropriate
- Deconditioning → refer to physical therapy
- Visual → refer to ophthalmology

Treatable MSA symptoms

Non-motor symptoms

Orthostatic hypotension

- Drop in blood pressure upon standing
- Leads to lightheadedness, syncope, falls

<u>Medication management</u>

- Pyridostigmine (Mestinon®)
  - Three times daily medication
- Midodrine (Proamatine®)
  - Three times daily medication
- Fludrocortisone (Florinef®)
  - Once daily medication
- Droxidopa (Northera®)
  - Three times daily medication

Urinary incontinence

- Pelvic floor therapy
- Scheduled bathroom breaks
- Catheterization

<u>Medications</u>

- Tolterodine (Vesicare®)
- Oxybutynin (Ditropan®)
- Mirabegron (Myrbetriq®) – only incontinence medication that does not cause confusion or hallucinations

REM-sleep behavior disorder

- Can precede motor onset by decades
- ~40% of patients will develop Parkinsonism in 5 years
- ~80% of patients after ~10 years
- Can be treated with:
  - Melatonin
  - Clonazepam (Klonopin®)

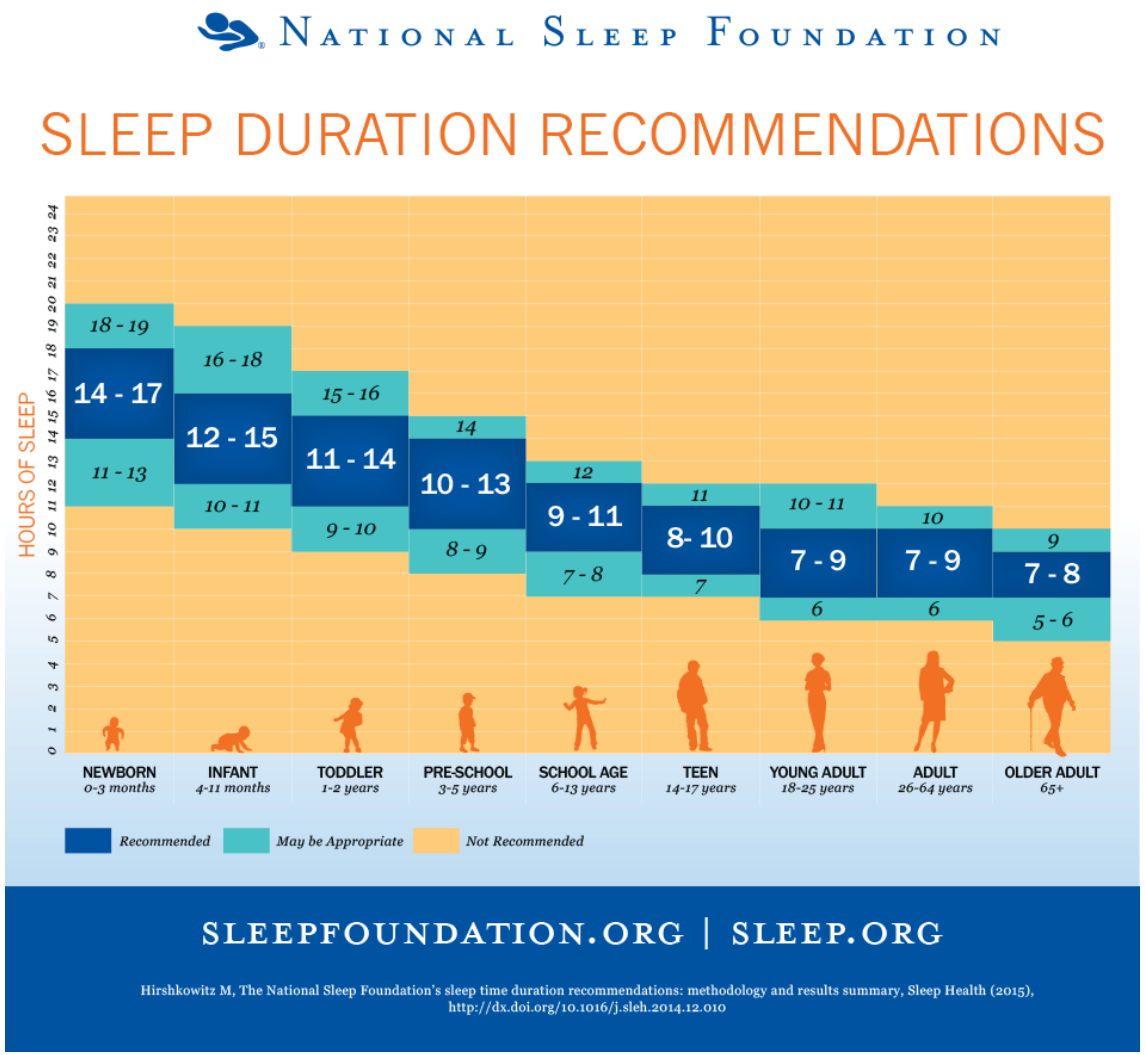
https://www.apdaparkinson.org/what-is-parkinsons/symptoms/sleep-problems/
Goldman J, et al. Curr Opin Neurol. 2014

REM-sleep behavior disorder

Padded Bed rail

Body pillow

Insomnia


NATIONAL SLEEP FOUNDATION
SLEEP DURATION RECOMMENDATIONS
HOURS OF SLEEP
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24
NEWBORN 0-3 months: 18 - 19 | 14 - 17 | 11 - 13
INFANT 4-11 months: 16 - 18 | 12 - 15 | 10 - 11
TODDLER 1-2 years: 15 - 16 | 11 - 14 | 9 - 10
PRE-SCHOOL 3-5 years: 14 | 10 - 13 | 8 - 9
SCHOOL AGE 6-13 years: 12 | 9 - 11 | 7 - 8
TEEN 14-17 years: 11 | 8- 10 | 7
YOUNG ADULT 18-25 years: 10 - 11 | 7 - 9 | 6
ADULT 26-64 years: 10 | 7 - 9 | 6
OLDER ADULT 65+: 9 | 7 - 8 | 5 - 6
Recommended
May be Appropriate
Not Recommended
SLEEPFOUNDATION.ORG | SLEEP.ORG
Hirshkowitz M, The National Sleep Foundation's sleep time duration recommendations: methodology and results summary, Sleep Health (2015), http://dx.doi.org/10.1016/j.sleh.2014.12.010

Insomnia

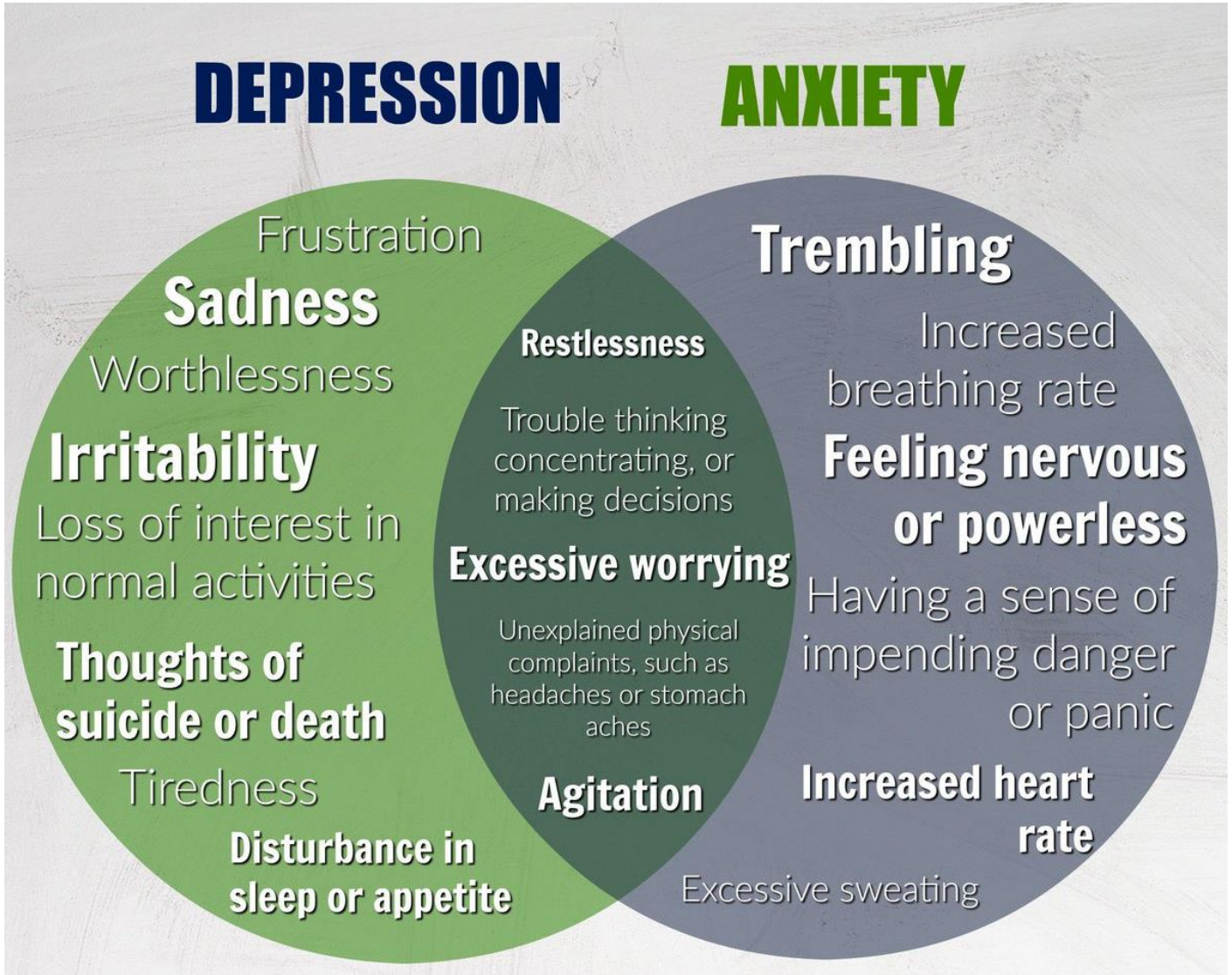
- Sleep fragmentation
- Early wakening
- Reversal of sleep-wake cycle
- Daytime napping
- *Undiagnosed sleep apnea may be a contributor!!*

Insomnia

Treatment of insomnia

- Exercise
- Melatonin (IR vs ER)
- Gabapentin (Neurontin®)
- Trazodone (Desyrel®)
- Clonazepam (Klonopin®)
- Zolpidem (Ambien®)
  - Common side effects include:
    - Excessive somnolence
    - Sleep-walking
    - Drugged feeling

Depression and anxiety



Depression and anxiety

Treatment of depression and anxiety

- Exercise/Yoga/Biofeedback
- Benzodiazepines
  - Long-acting: Clonazepam (Klonopin®)
  - Short-acting: Alprazolam (Xanax®), Lorazepam (Ativan®)
- Antidepressants:
  - Non-sedating: Escitalopram (Lexapro®)
  - Calming: Escitalopram (Lexapro®), Sertraline (Zoloft®)
  - Energizing: Venlafaxine (Effexor®)
  - Sedating: Trazodone (Desyrel®), Duloxetine (Cymbalta®)
  - Analgesic: Duloxetine (Cymbalta®), Amitriptyline (Elavil®)

(215) 829-6688

Constipation

- Exercise
- Hydration!!!
- Fiber
  - Fruits (prunes)
  - Vegetables
  - Psyllium (Metamucil®)
- Stool softners
  - Docusate (Colace®)
- Prokinetics
  - Senokot (Senna®)
- Osmotic laxatives
  - Polyethylene glycol (MiraLax®)

Anosmia

I lost my sense of smell…

Anosmia

Anosmia

Managing anosmia

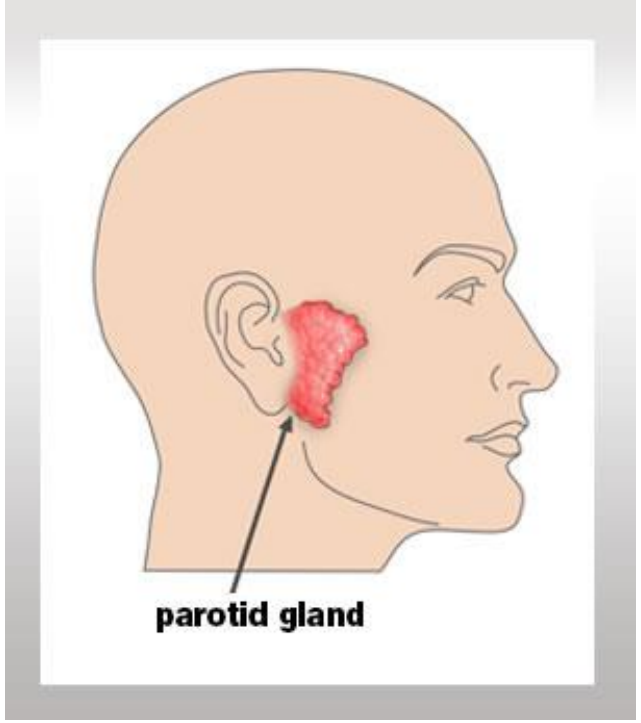
Fatigue

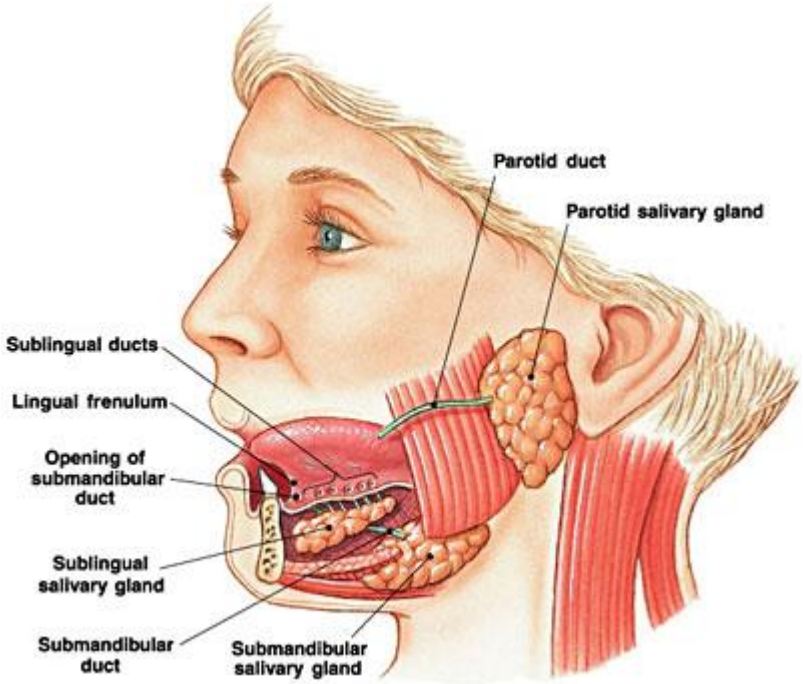
- Sleep hygiene
- Exercise
- Dopaminergics
- Caffeine
- Stimulants
  - Modafinil (Provigil®) and Armodafinil (Nuvigil®)
  - Methylphenidate (Ritalin®)
  - Dextroamphetamine (Adderall®)
  - Must be used with caution in patients with cognitive impairment or heart disease
  - These patients can cause dependence/abuse

Sialorrhea

- Atropine *ophthalmic* drops 1%
  - Anticholinegic
  - 1 drop under the tongue every 12 hours
  - Higher doses can cause systemic anticholinergic effects
- Scopolamine patches
- Dopaminergics

Sialorrhea





- Botulinum toxin
  - Injections to the parotids and/or submandibular glands
  - Toxin may spread to the eyes and cause eye dryness, or to the masseters and cause chewing difficulties
  - Xeomin® is the only FDA-approved toxin for sialorrhea

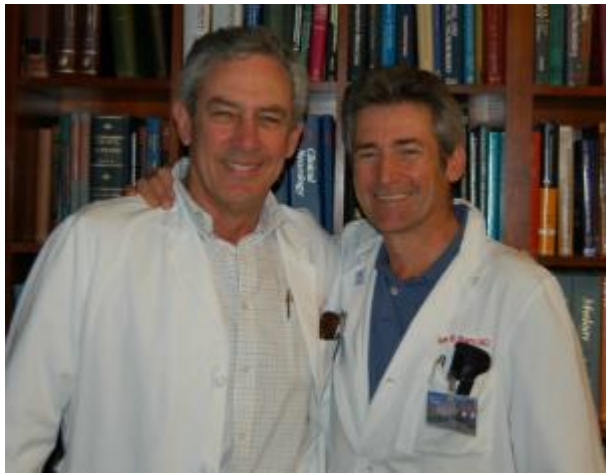
Multidisciplinary care at Penn

The COPE Clinic

The Movement Disorders Center at Penn

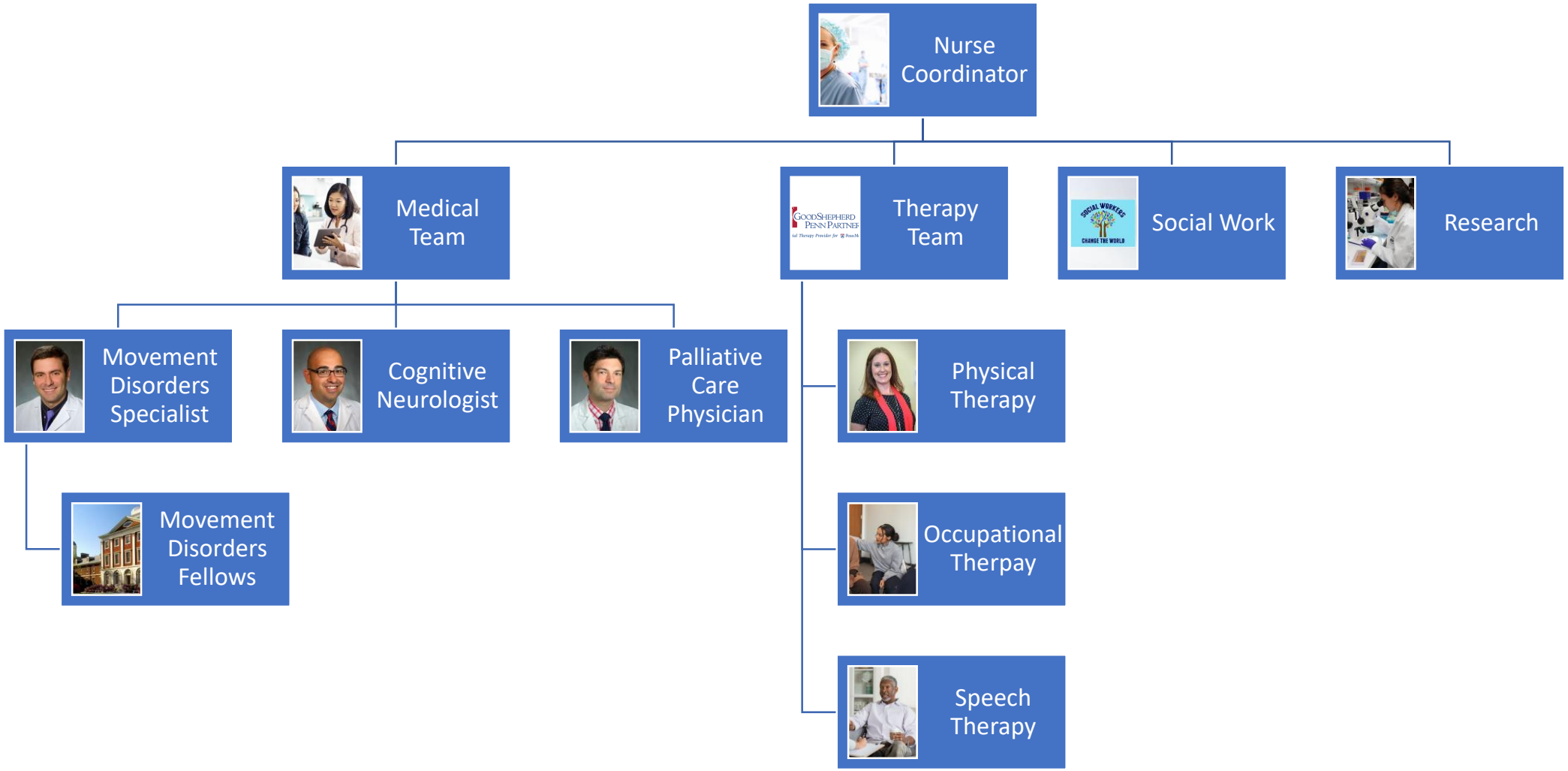
- 7 physicians
- 2 nurses
- 1 nurse practitioner
- 2 social workers
- 10 research coordinators
- 2 counselors
- The center shares a building with Good Shepherd Penn Partners Rehab Services (PT, OT, ST)
- Among the different services offered, is the **COPE** Clinic

https://www.med.upenn.edu/pdmdc/



Founded in 1982 by Drs. Matthew Stern and Howard Hurtig

COmprehensive **P**arkinsonism **E**valuation Clinic



What is a day at the COPE clinic like?

Check-in
- Pre-COVID: Front desk at PD&MDC
- During COVID: Log in to BlueJeans app

COPE (3-4 hrs)
- All teams have 25-30 minutes with each patient seen

Immediately after COPE
- Wrap-up session: all teams meet and review each case

Follow up (<7 days)
- Nurse coordinator reaches out to each patient with final recommendations

COPE Clinic workflow

Medical referrals

- Cardiology
- Gastroenterology
- Urology
- ENT
- Palliative care
- Cognitive neurology
- Neurogenetics
- Neuroophthalmology

Research

COPE

Psych referrals

- Psychiatry
- Psychology
- Neuropsychology
- Counseling service

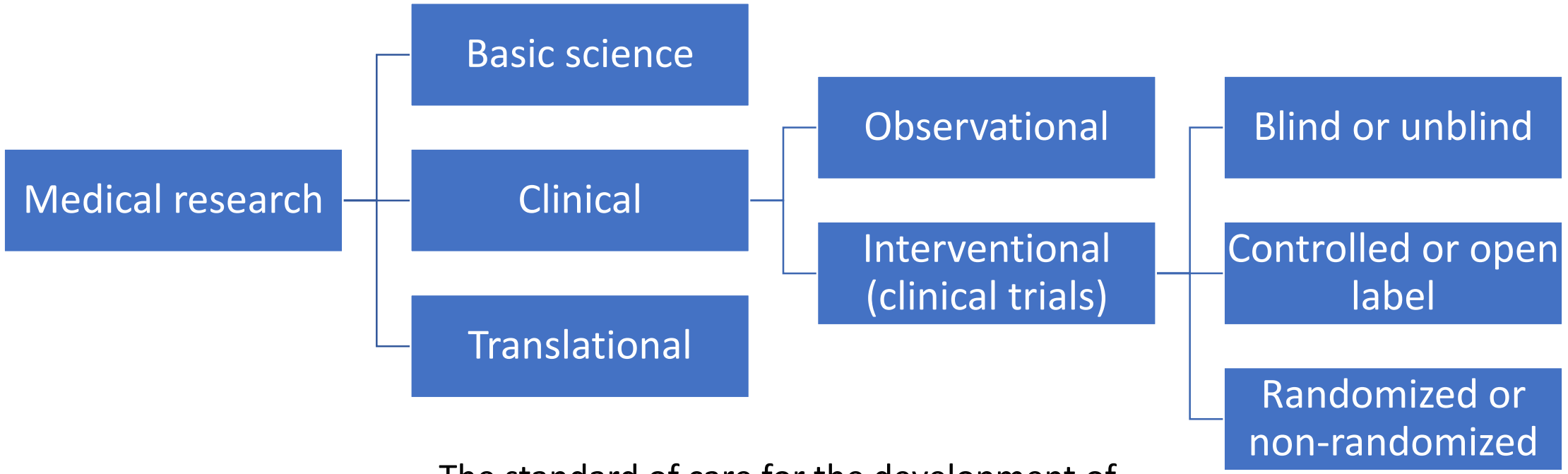
- Regional (PA, NY, NJ, DE)
  - *National??*
  - *International???*

Therapy referral

- Physical
- Occupational
- Speech
- Vestibular
- Swallow studies

Clinical trials for MSA

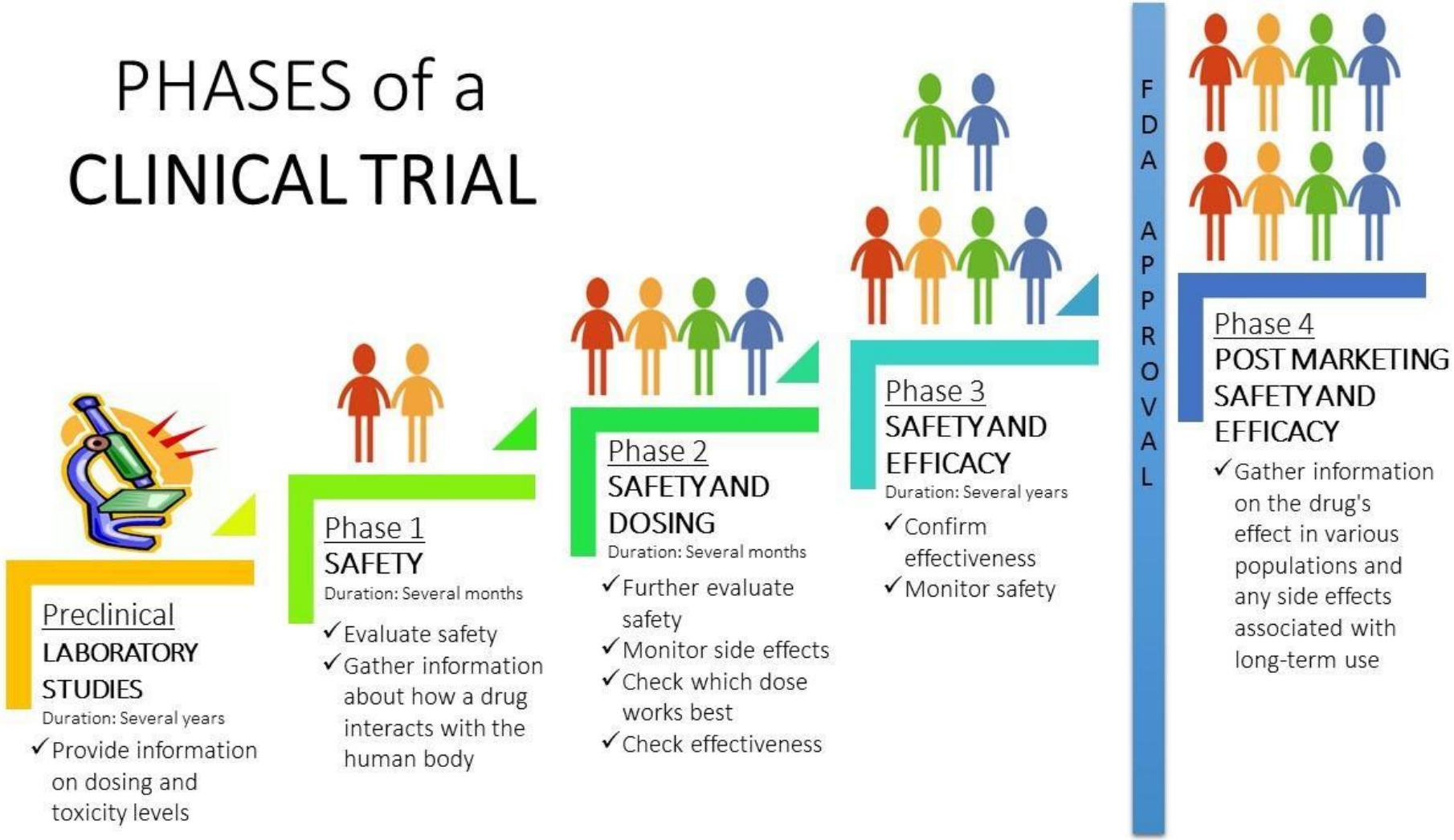
Definitions



The standard of care for the development of new medications are trials that are:

- Randomized
- Double blind
- Controlled

The drug development process

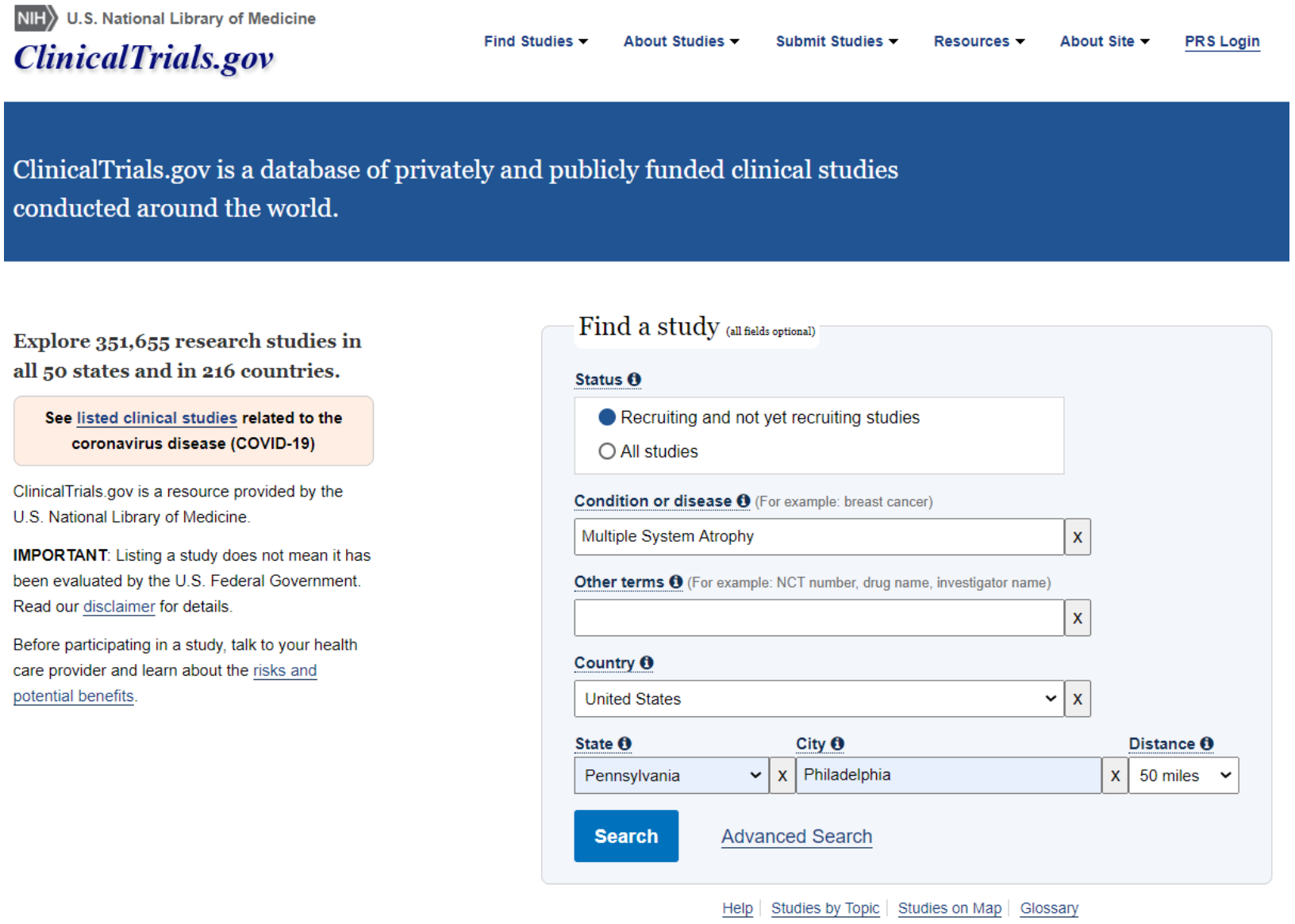


https://cead.cumc.columbia.edu/content/research-clinical-trials

Why participate in research?

- Clinical trials are the gateway to drug development.
- There is the possibility of having access to an efficacious medication sooner than the general population.
- While participating in a clinical trial, you may get access to additional medical care.
- Participation in a clinical trial often does not preclude eventual participation in another one.

clinicaltrials.gov



Study Type ICMJE	Interventional
Study Phase ICMJE	Phase 2
Study Design ICMJE	Allocation: Randomized Intervention Model: Parallel Assignment Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor) Primary Purpose: Treatment
Condition ICMJE	**Multiple System Atrophy**
Intervention ICMJE	• Drug: rasagiline mesylate rasagiline 1 mg tablet/day for 48 weeks Other Names: ◦ Azilect ◦ TVP-1012 • Drug: placebo placebo tablet for 48 weeks
Study Arms ICMJE	• Experimental: rasagiline mesylate rasagiline tablet, 1 mg/day for up to 48 weeks. Intervention: Drug: rasagiline mesylate • Placebo Comparator: placebo placebo tablet for up to 48 weeks. Intervention: Drug: placebo

Efficacy of rasagiline in patients with the parkinsonian variant of multiple system atrophy: a randomised, placebo-controlled trial

Prof Werner Poewe, MD • Prof Klaus Seppi, MD • Cheryl J Fitzer-Attas, PhD • Prof Gregor K Wenning, MD • Sid Gilman, MD • Prof Phillip A Low, MD • et al.

ARTICLES | VOLUME 14, ISSUE 2, P145-152, FEBRUARY 01, 2015

Rasagiline group (n=84) → 21 patients withdrew
Placebo group (n=90) → 15 patients withdrew

At week 48

- Rasagiline group:
  - UMSARS progressed by 7.2 units
- Placebo group:
  - UMSARS progressed by 7.8 units

Official Title ICMJE	A Phase 3, 4-week, Multicenter, Randomized, Double-blind, Placebo-controlled, Parallel-group Study of TD-9855 in Treating Symptomatic Neurogenic Orthostatic Hypotension in Subjects With Primary Autonomic Failure
Brief Summary	A Phase 3 study to evaluate efficacy, safety, and tolerability of ampreloxetine (TD-9855) in subjects with primary autonomic failures (MSA, PD, or PAF) and snOH with up to 4 weeks of treatment.
Detailed Description	A Phase 3, randomized, double-blind, placebo-controlled, parallel-group, multicenter study to evaluate efficacy, safety, and tolerability of ampreloxetine (TD-9855) in subjects with primary autonomic failures (MSA, PD, or PAF) and snOH. The study consists of 3 periods: (i) 4-week screening, (ii) 4-week randomized treatment, and (iii) 2-week follow up.

Study Type ICMJE	Interventional
Study Phase ICMJE	Phase 3
Study Design ICMJE	Allocation: Randomized Intervention Model: Parallel Assignment Intervention Model Description: Parallel assignment Masking: Quadruple (Participant, Care Provider, Investigator, Outcomes Assessor) Primary Purpose: Treatment
Condition ICMJE	Symptomatic Neurogenic Orthostatic Hypotension
Intervention ICMJE	• Drug: ampreloxetine Oral tablet, QD Other Name: TD-9855 • Drug: Placebo Oral tablet, QD

Theravance Biopharma

Theravance Biopharma

Medicines That Make a Difference®

Theravance Biopharma, Inc. Announces Top-line Results from a Phase 3 Study of Ampreloxetine in Patients with Symptomatic Neurogenic Orthostatic Hypotension

September 15, 2021

- Randomized, double-blind, placebo-controlled study did not meet the primary endpoint: improvement in OHSA #1 in patients receiving ampreloxetine for four weeks compared to placebo

DUBLIN and SOUTH SAN FRANCISCO, Calif., Sept, 15, 2021 /PRNewswire/ -- Theravance Biopharma, Inc. ("Theravance Biopharma" or the "Company") (NASDAQ: TBPH), a diversified biopharmaceutical company primarily focused on the discovery, development, and commercialization of organ-selective medicines, today announced top-line results from a Phase 3 randomized, double-blind, placebo-controlled multi-center Phase 3 study assessing the safety and efficacy of ampreloxetine compared to placebo for the treatment of symptomatic neurogenic orthostatic hypotension (nOH).

The study did not meet its primary endpoint. The majority of treatment-related adverse events were mild or moderate in severity. Serious adverse events occurred in two patients on placebo and four on ampreloxetine and none were considered related to the study drug; no deaths were reported. There was no signal for supine hypertension. The Company plans to present the results at a future scientific forum.

"These are not the results we had hoped to achieve, especially given the clear unmet need for patients suffering from symptomatic nOH and the positive top-line four-week results from the Phase 2 study announced in 2018. We will continue to analyze the data to better understand the findings," said Rick E Winningham, Chief Executive Officer, Theravance Biopharma. *"We are grateful to all those who dedicated their time and efforts to progress this study, especially during the challenges of the pandemic. We are hopeful that insights from this study may inform future drug development to help those with this debilitating condition."*

In light of these results, the Company will be determining the appropriate next steps for Study 0170 (NCT03829657; more than 75% enrolled) and Study 0171 (NCT04095793); clinical trial sites will be notified accordingly.

Brief Title ICMJE	Study of BHV-3241 in Subjects With **Multiple System Atrophy**
Official Title ICMJE	A Randomized, Double-Blind, Placebo-Controlled, Parallel- Group Study to Evaluate the Efficacy and Safety of BHV-3241 in Subjects With **Multiple System Atrophy** (M-STAR Study)
Brief Summary	The purpose of this study is to compare the efficacy of BHV-3241 versus placebo in subjects with Multiple System Atrophy
Study Type ICMJE	Interventional
Study Phase ICMJE	Phase 3
Study Design ICMJE	Allocation: Randomized Intervention Model: Parallel Assignment Masking: Triple (Participant, Care Provider, Investigator) Masking Description: Double-blind to Sponsor, Investigator and Subject Primary Purpose: Treatment
Condition ICMJE	**Multiple System Atrophy**
Intervention ICMJE	• Drug: Verdiperstat 300mg 2 -oral- capsules, BID • Drug: Placebo Matching placebo
Study Arms ICMJE	• Experimental: Arm 1: BHV-3241- Experimental Intervention: Drug: Verdiperstat • Placebo Comparator: Arm 2: Placebo Comparator Intervention: Drug: Placebo

Verdiperstat Overview

DESCRIPTION

First-in-class, brain-penetrant, irreversible inhibitor of MPO

- Has the potential to be developed in a number of disease indications associated with oxidative stress, inflammation, and neurodegeneration.
- Potential to be a first-in-class and best-in-class agent.
- Licensed from AstraZeneca in September 2018, where it was known as AZD3241.

biohaven pharmaceuticals

Biohaven Provides Update On Phase 3 Trial And Multiple System Atrophy (MSA) Program

NEWS PROVIDED BY
Biohaven Pharmaceutical Holding Company Ltd. ⇢
Sep 27, 2021, 07:00 ET

NEW HAVEN, Conn., Sept. 27, 2021 /PRNewswire/ -- Biohaven Pharmaceutical Holding Company Ltd. (NYSE: BHVN) today announced results from a focused analysis of a clinical trial of verdiperstat in multiple system atrophy (MSA). Verdiperstat did not statistically differentiate from placebo on the prespecified primary efficacy measure, nor on the key secondary efficacy measures. Initial analysis of safety data was consistent with the overall profile of verdiperstat from prior clinical trial experience. Additional analyses are still pending, and full study results will be presented at an upcoming scientific meeting.

Irfan Qureshi, M.D., Vice President of Neurology at Biohaven commented, "While we are disappointed that verdiperstat did not demonstrate efficacy for the treatment of MSA, Biohaven remains committed to fighting on behalf of people living with neurodegenerative diseases. There are currently no approved disease modifying therapies for MSA and we must continue to advance the science to improve treatment outcomes for patients suffering from this disease. We are extremely grateful to the international MSA community – especially the patients and their families, investigators and their teams, and patient advocacy groups – who made the trial possible."

Verdiperstat is an investigational first-in-class, potent, selective, brain-penetrant, and irreversible myeloperoxidase (MPO) enzyme inhibitor that Biohaven is developing for the treatment of neurodegenerative diseases. Verdiperstat may help preserve neurons through inhibition of MPO-induced pathological oxidative stress and further inflammation that contribute to cellular injury in neurodegenerative disease.

Although the mechanism of action for verdiperstat, myeloperoxidase inhibition, was shown not to be effective for MSA, the rationale of targeting brain inflammation remains strong in other disease states. An ongoing clinical trial evaluating the efficacy of verdiperstat in amyotrophic lateral sclerosis (ALS) is being conducted in collaboration with the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital and is expected to complete enrollment in the fourth quarter of 2021.

About MSA

MSA is a rare, rapidly progressive, severely debilitating, and fatal neurodegenerative disease that leads to death within a median of 6-10 years after the onset of symptoms. Manifestations of MSA can include urinary and sexual dysfunction, dizziness and fainting due to low blood pressure (orthostatic hypotension), and motor impairments such as tremor,

NEW HAVEN, Conn., Sept. 27, 2021 /PRNewswire/ -- Biohaven Pharmaceutical Holding Company Ltd. (NYSE: BHVN) today announced results from a focused analysis of a clinical trial of verdiperstat in multiple system atrophy (MSA). Verdiperstat did not statistically differentiate from placebo on the prespecified primary efficacy measure, nor on the key secondary efficacy measures. Initial analysis of safety data was consistent with the overall profile of verdiperstat from prior clinical trial experience. Additional analyses are still pending, and full study results will be presented at an upcoming scientific meeting.

Now recruiting at Penn

Brief Title ICMJE	A Study of Lu AF82422 in Participants With Multiple System Atrophy
Official Title ICMJE	Interventional, Randomized, Double-blind, Parallel-group, Placebo-controlled Study to Assess the Efficacy, Safety and Tolerability of Lu AF82422 in Patients With Multiple System Atrophy
Brief Summary	To find out the effect of Lu AF82422 on disease progression in participants with multiple system atrophy.
Detailed Description	The participants will be randomized to Lu AF82422 or placebo (2:1).
Study Type ICMJE	Interventional
Study Phase ICMJE	Phase 2
Study Design ICMJE	Allocation: Randomized Intervention Model: Parallel Assignment Masking: Triple (Participant, Care Provider, Investigator) Primary Purpose: Treatment
Condition ICMJE	Multiple System Atrophy
Intervention ICMJE	• Drug: Lu AF82422 Solution for infusion • Drug: Placebo Solution for infusion
Study Arms ICMJE	• Experimental: Lu AF82422 Participants will receive Lu AF82422 intravenous (IV) infusion every 4 weeks (Q4W) from Baseline for a minimum 48 weeks up to a maximum 72 weeks. Intervention: Drug: Lu AF82422 • Experimental: Placebo Participants will receive Lu AF82422 matching placebo IV infusion Q4W from Baseline for a minimum 48 weeks up to a maximum 72 weeks. Intervention: Drug: Placebo

Now recruiting at Penn

Eligibility Criteria ICMJE	Key Inclusion Criteria: • The participant is diagnosed with possible or probable MSA of the multiple system atrophy parkinsonian type (MSA-P) or multiple system atrophy cerebellar type (MSA-C) sub-type at the Screening Visit. • The participant had onset of motor and/or autonomic (orthostatic or urinary) MSA symptoms within 5 years prior to the Screening Visit in the judgement of the investigator. • The participant has an UMSARS Part I score ≤16 (omitting item 11 on sexual function) at the Screening Visit. • The participant has a cognitive performance evaluated by the Montreal Cognitive Assessment (MoCA) with a score ≥22 at the Screening Visit. Key Exclusion Criteria: • The participant has been treated with an anti-α-synuclein monoclonal antibody, mesenchymal stem cells or an inhibitor of α-synuclein aggregation within the last 12 months. • The participant has any past or current treatment with an active vaccine targeting α-synuclein. • The participant has 2 or more blood relatives with a history of MSA. • The participant has evidence (clinically or on MRI) and/or history of any clinically significant disease or condition other than MSA (for example, serious neurological disorder, other intracranial disease, or systemic disease). • The participant has a current diagnosis of movement disorders that could mimic MSA (for example, Parkinson' disease, dementia with Lewy bodies, essential tremor, progressive supranuclear palsy, spinocerebellar ataxia, spastic paraparesis, corticobasal degeneration, or vascular, pharmacological, or post-encephalitic parkinsonism), per investigator discretion. Other inclusion and exclusion criteria may apply.
Sex/Gender ICMJE	Sexes Eligible for Study: All
Ages ICMJE	40 Years to 75 Years (Adult, Older Adult)

Interested in learning more about this trial?

Ellen Indik

Clinical Research Coordinator

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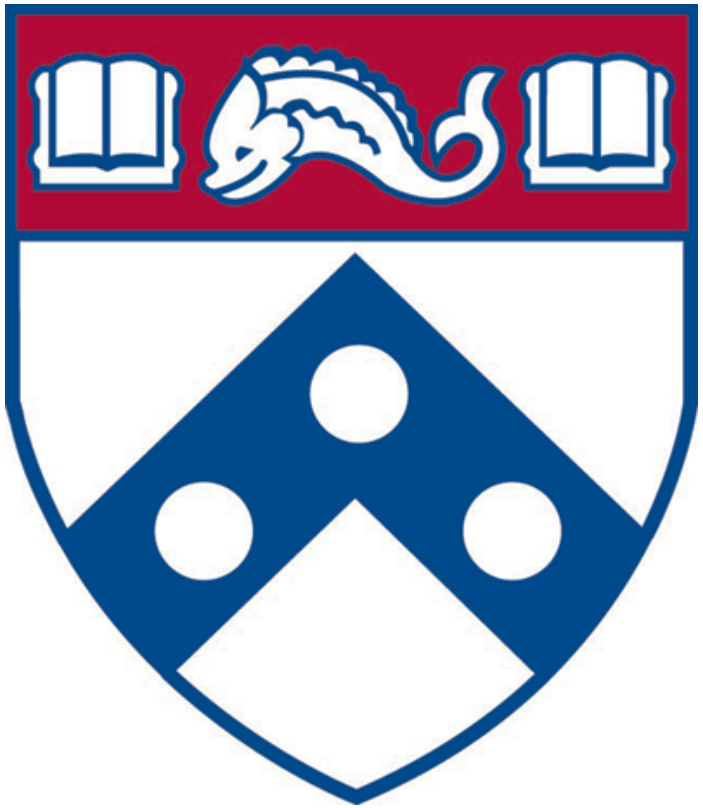
Closing remarks

- Parkinsonism is a non-specific term that refers to any patient with symptoms of Parkinson's disease
- MSA is a parkinsonian syndrome featuring dysautonomia and cerebellar symptoms
- The diagnosis is clinical
- Diagnostic accuracy is crucial for clinical trials, but not as important for clinical management
- Participation in clinical trials may allow the development of disease modifying therapies for MSA



Thank you