SCOREBUILDERS

SPOTLIGHT *Series*

Review of Degenerative Neurologic Conditions

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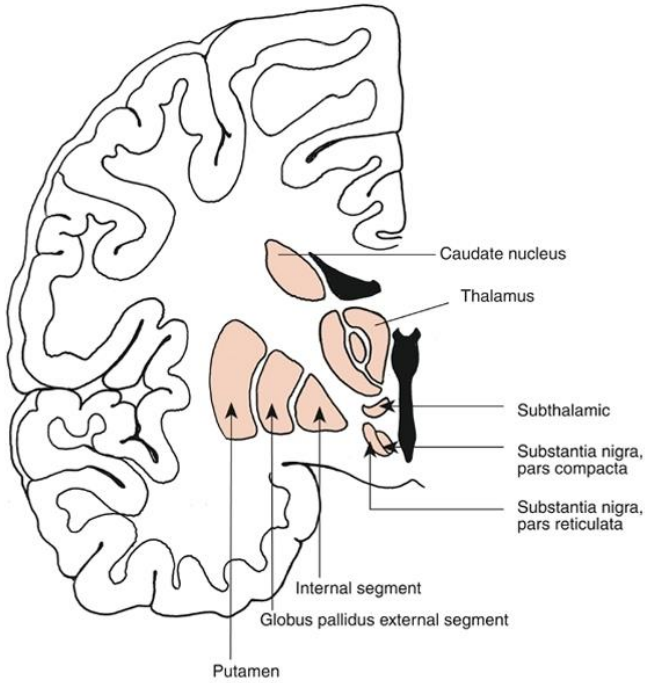
Brief Review of Parkinson Disease (PD)

Role of Basal Ganglia and PD

- **Automaticity** of movement (initiation/execution)
- regulate muscle contraction, muscle force, multi-joint movements an movements
- Critical role in functional loops (oculomotor loop, executive loop, behavioral flexibility and control loop, limbic loop)

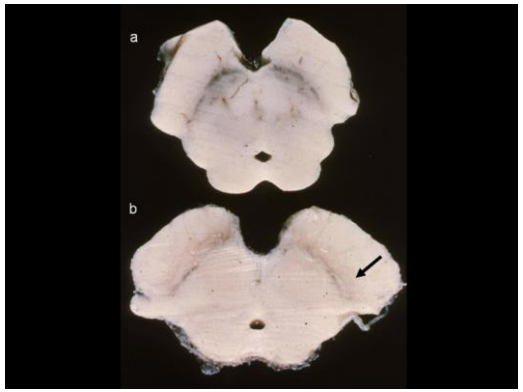


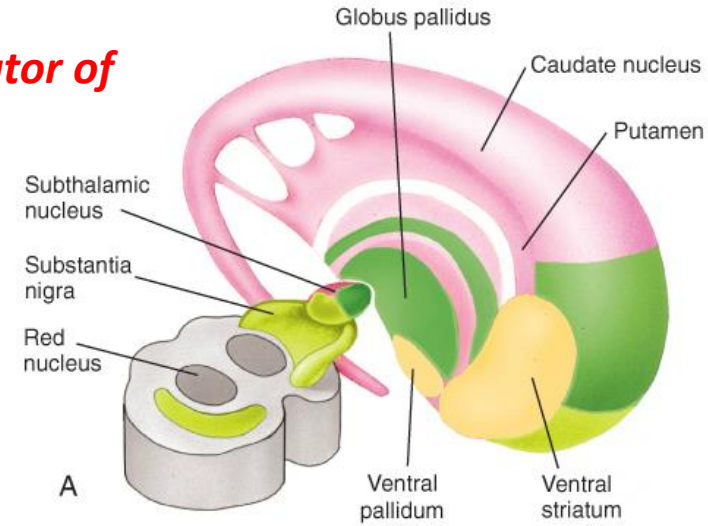
PD= Degeneration of dopaminergic neurons in substantia nigra

Loss of Dopamine→ LOSS OF MODULATION OF DIRECT AND INDIRECT LOOPS

= NET Decreased excitation of the motor cortex

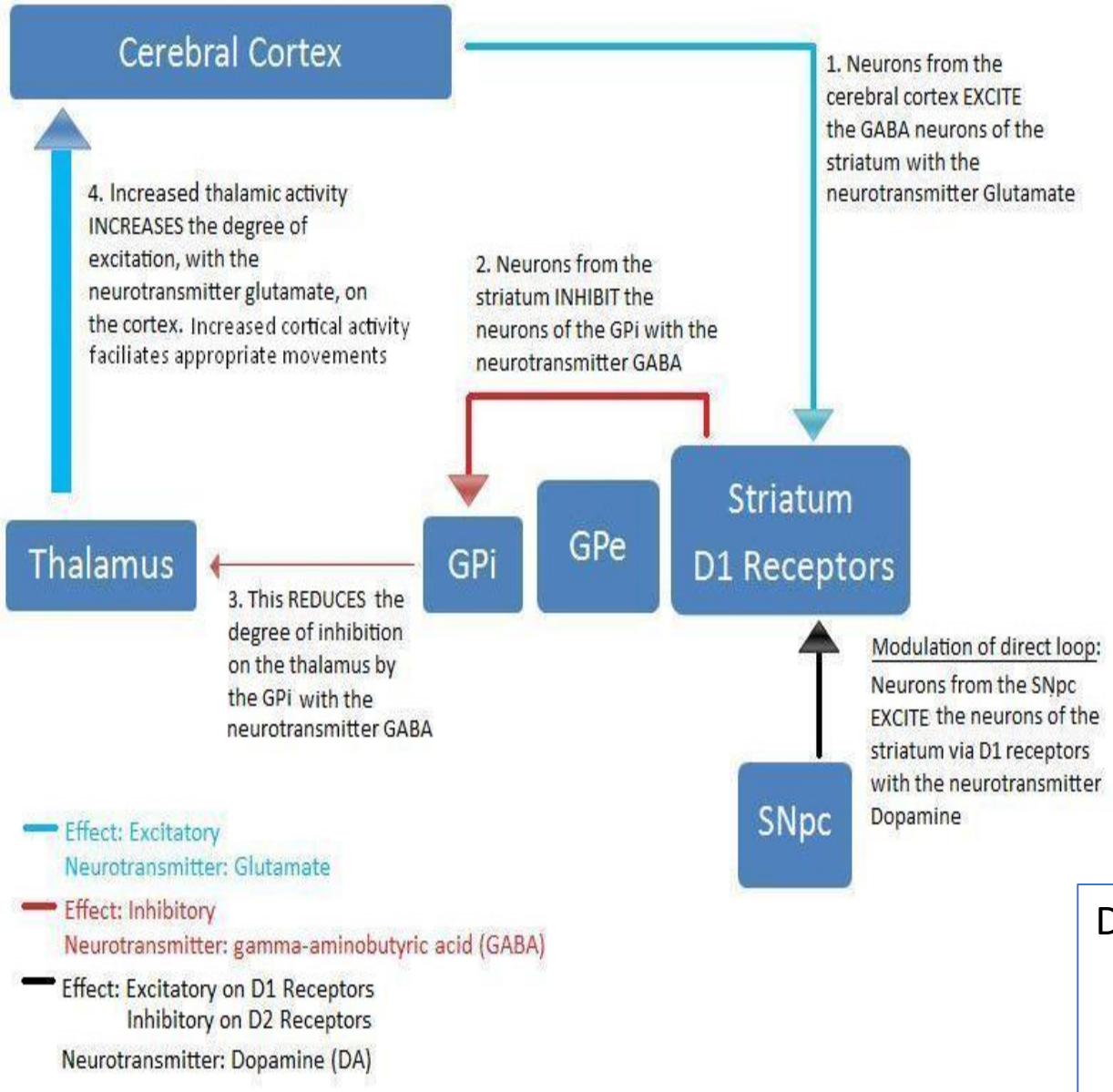
❑ Substantia nigra- ***modulator of Basal Ganglia***



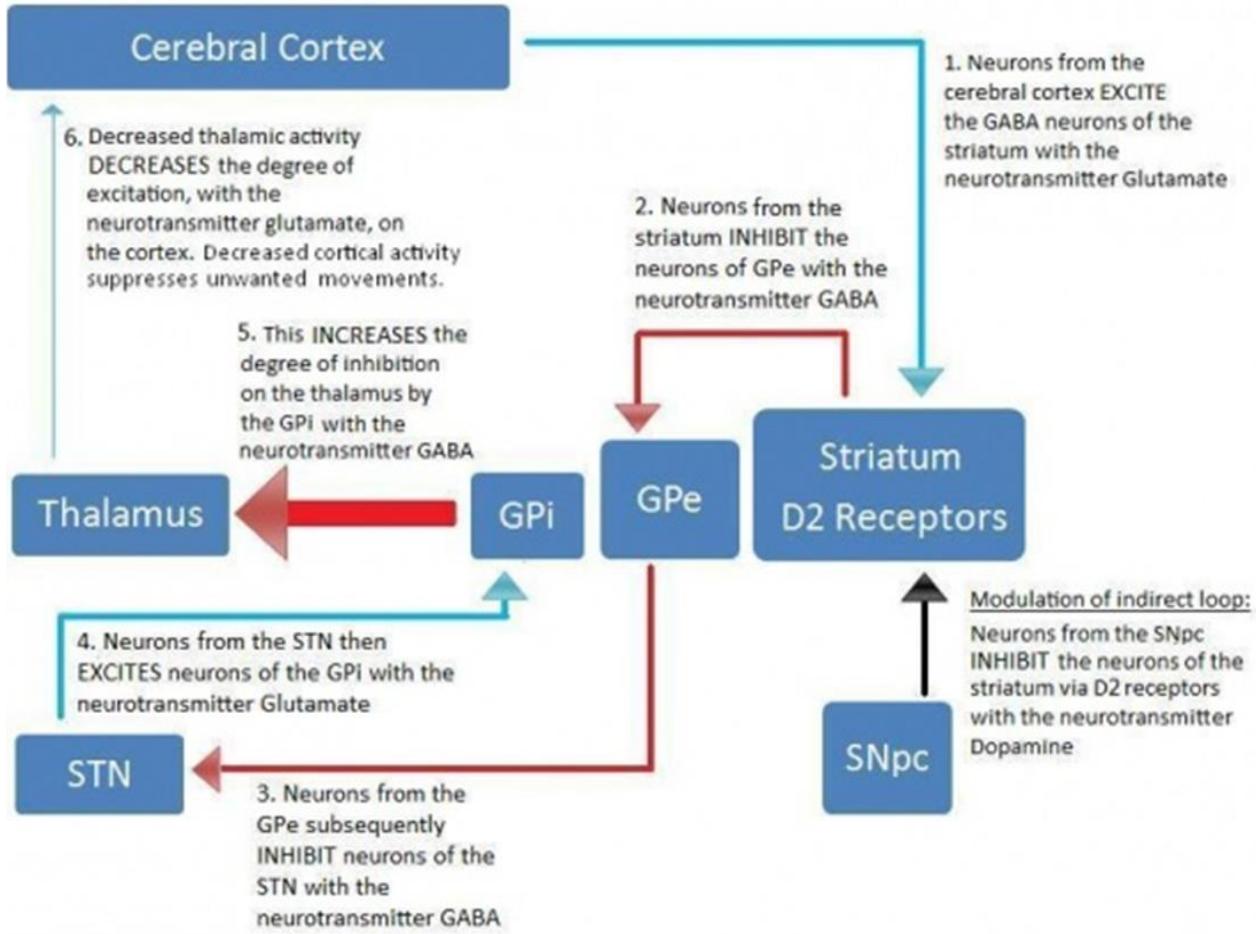


Modified with permission from Hendelman WJ: Student's atlas of neuroanatomy, *Philadelphia, 1994, WB Saunders, p 39.*

The Direct Loop



The Indirect Loop



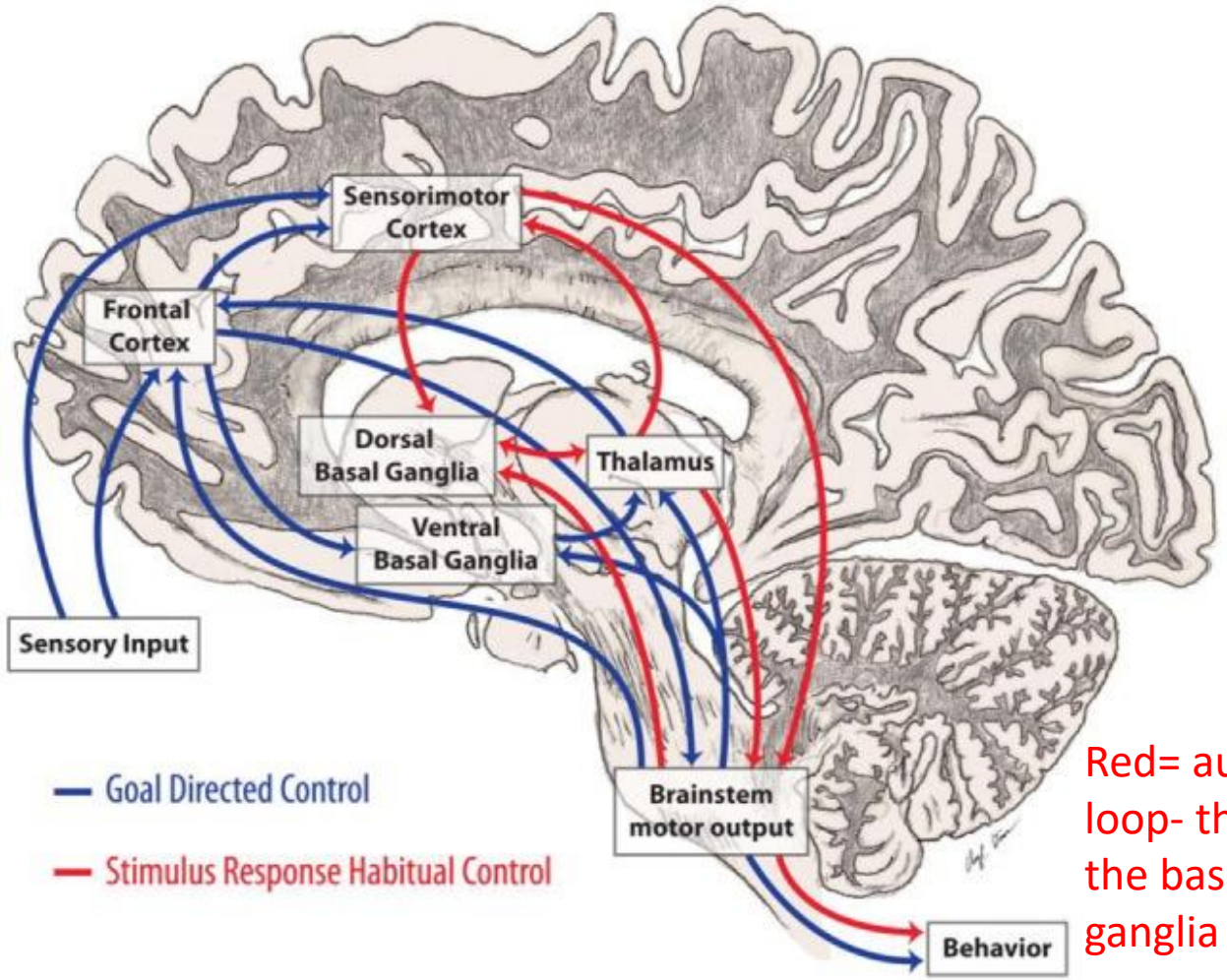
Degeneration of dopaminergic neurons in substantia nigra

Loss of Dopamine→ NET Decreased excitation of the motor cortex

LOSS OF MODULATION OF DIRECT AND INDIRECT LOOPS

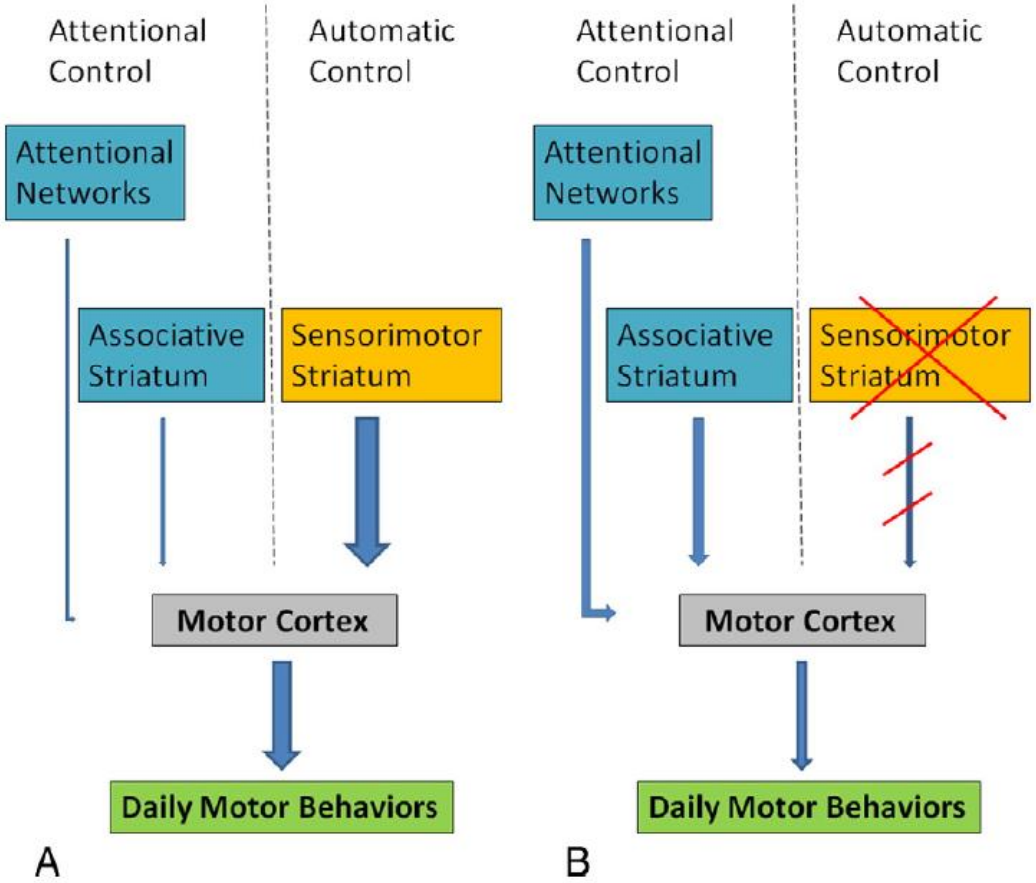
Diagram adapted from Kandel, Schwartz, & Jessell (2000)

Automaticity of Movement



Red= automatic loop- through the basal ganglia

Leisman G, Moustafa AA, Shafir T. Thinking, Walking, Talking: Integratory Motor and Cognitive Brain Function. *Frontiers in Public Health*. 2016;4:94. doi:10.3389/fpubh.2016.00094.

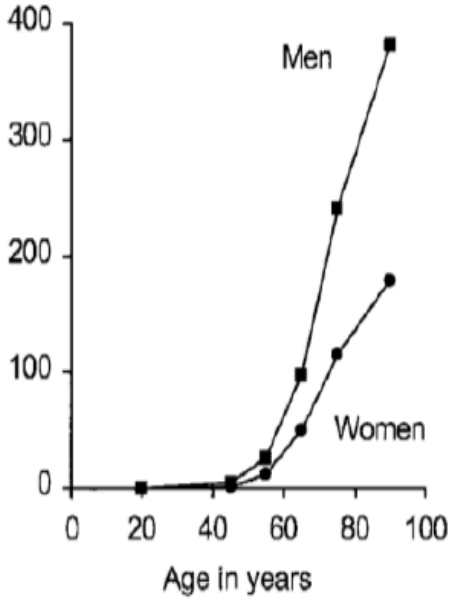


More attentional control for no longer automatic daily activities

Wu T, Hallett M, Chan P. Motor automaticity in Parkinson's disease. *Neurobiology of disease.* 2015;82:226-234.

PD- Who and why?

- WHO?



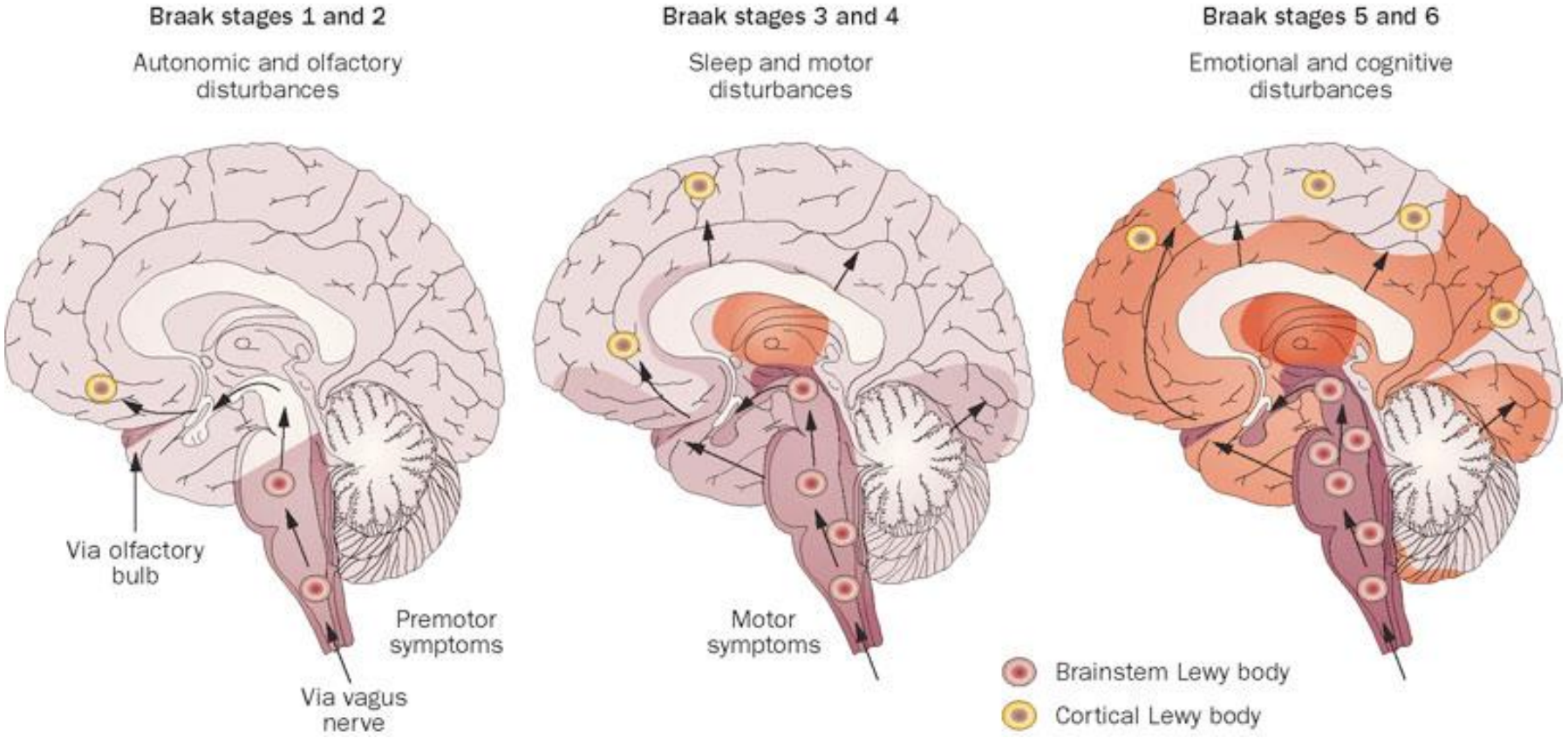
>65 yo = 1.6% have PD
>80 yo = 3 % will have PD

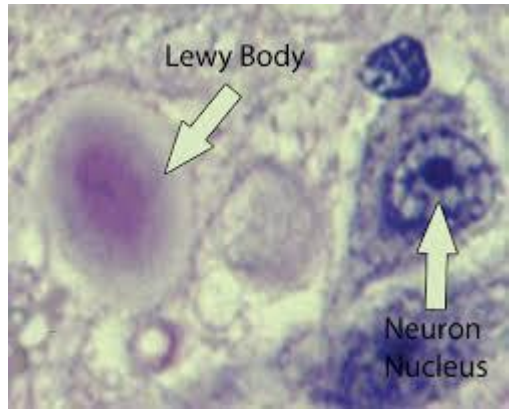
- 2nd most common neurodegenerative disease
- Men> Women
- Caucasian > African or Asian descent

PD- Who and why?

- WHY?
- < 5 % genetic
- AGE is most important risk factor
- Environmental Factors
  - Prolonged Pesticide
  - Repeated head injuries
  - Viral infection brain
  - Carbon monoxide and cyanide poisoning
- **MOST of PD is “Idiopathic” ish**

Braak Staging of PD- Lewy Bodies





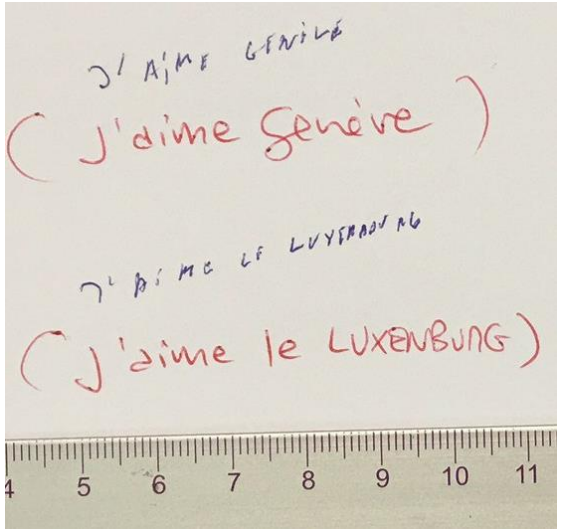
Intracellular accumulation of α –synuclein protein

Theory: may involve gut- lewy bodies found there as well

Braak H, Del Tredici K, Rub U, de Vos RAI, Steur E, Braak E: Staging of brain pathology related to sporadic Parkinson's disease. Neurobiol Aging 2003, 24:197–211.

Motor Symptoms- Hallmark Signs of PD

- Tremors- often first symptom reported
  - Resting Tremor
  - May progress to action (or intention) tremor with advanced disease
- Rigidity
  - Hypertonicity and Hyperreflexia
  - Lead pipe or cog-wheel
- Akinesia or Bradykinesia- slowness of movement
  - Most Common
  - Hypokinesia- decreased amplitude of movement “small” movement
  - Micrographia
- Postural instability- Changes in posture and balance
  - Festinating (aka shuffling) gait, ‘freezing,’ retropulsion, difficulty with turns
  - Difficulty with anticipatory (or feedforward postural control)



Freezing of Gait- *not everyone experiences this!*

https://www.youtube.com/watch?v=EQ0HG16EC3g

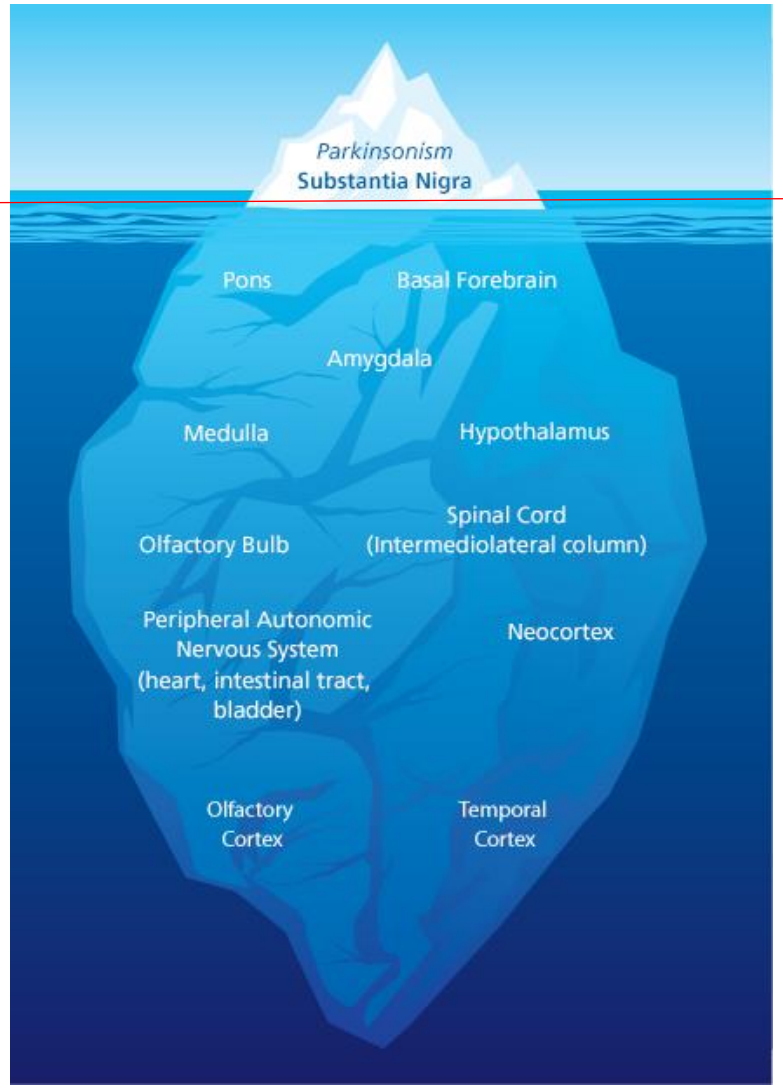
Commonly occurs with:

- Turns
- Thresholds
- Fear of Falling
- Cognitive tasks
- Dividing or switching attention (think distractions taking attention away from gait)

Gait no longer automatic→ requires conscious attention→ something is distracting→ takes necessary attention away from gait

Non-Motor Symptoms

Motor Symptoms



Non-motor Symptoms

- Mood disorders
  - Anxiety, depression apathy
- Cognitive Dysfunction
- Visual changes
  - Color discrimination
- Sleep Disorders
  - Insomnia
  - REM behavior disorder
- Autonomic Dysfunction
  - Orthostatic hypotension
  - Reduced HR variability
  - Constipation
  - Urinary dysfunction
  - Temperature regulation
- Pain/Sensory
- Respiratory difficulties
- Olfactory dysfunction

Langston JW. The Parkinson's complex: parkinsonism is just the tip of the iceberg. Ann Neurol. 2006;59:591-596.

Clinical Subtypes of PD

Tremor-dominant (TD)

- Resting tremor
- Normal gait
- Mild disease progression
- Less mood/cognitive deficits
- More responsive to Gpi DBS

<u>Postural instability/gait difficulty (PIGD)</u>

- Bradykinesia
- Rigidity of movement
- Greater subjective impairment
  - Cognition
  - Motor
  - Occupational
- Greater incidence of:
  - Depression, dementia, apathy
- More rapid disease progression
- Less overall benefit with DBS

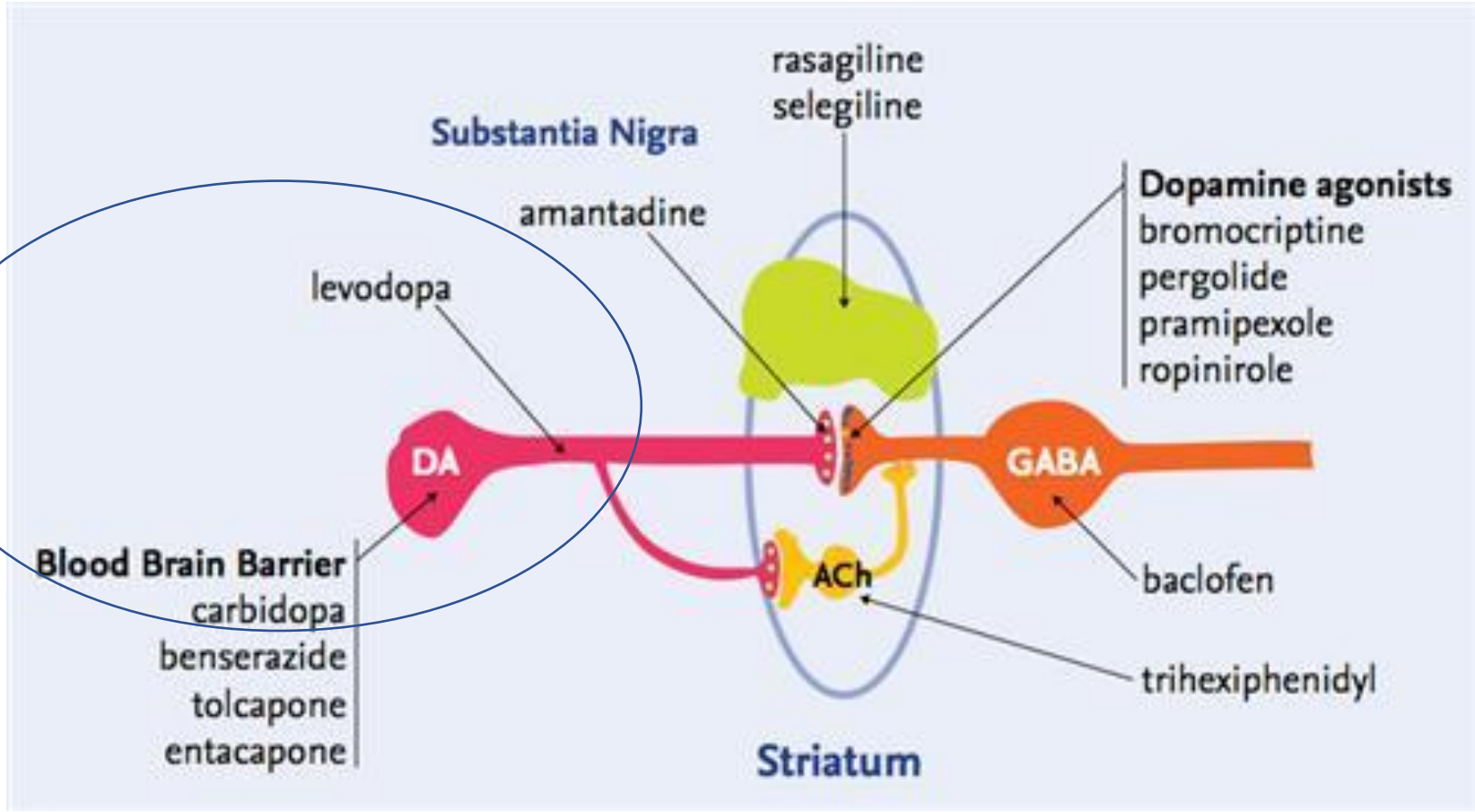
Prime M, McKay JL, Bay AA, et al. Differentiating Parkinson Disease Subtypes Using Clinical Balance Measures. *Journal of neurologic physical therapy : JNPT.* 2020;44(1):34-41.

Hoehn-Yahr Classification of PD adapted from table: O'Sullivan (6th ed) page 817

Table 18.1	Hoehn-Yahr Classification of Disability	
Stage	**Characteristics of Disability**	**Clinical Presentation**
I	Minimal or absent; Unilateral symptoms	Unilateral symptoms
II	Minimal bilateral or midline involvement; balance not impaired	Bilateral symptoms
III	Impaired righting reflexes, unsteadiness when turning or rising from chair, patient can live independently and maintain some forms of employment	Impaired balance
IV	All symptoms present and severe. Standing and walking possible only with assistance	Severe bradykinesia, rigidity, festinating gait
V	Confined to bed or wheelchair	

Pharmaceutical Management

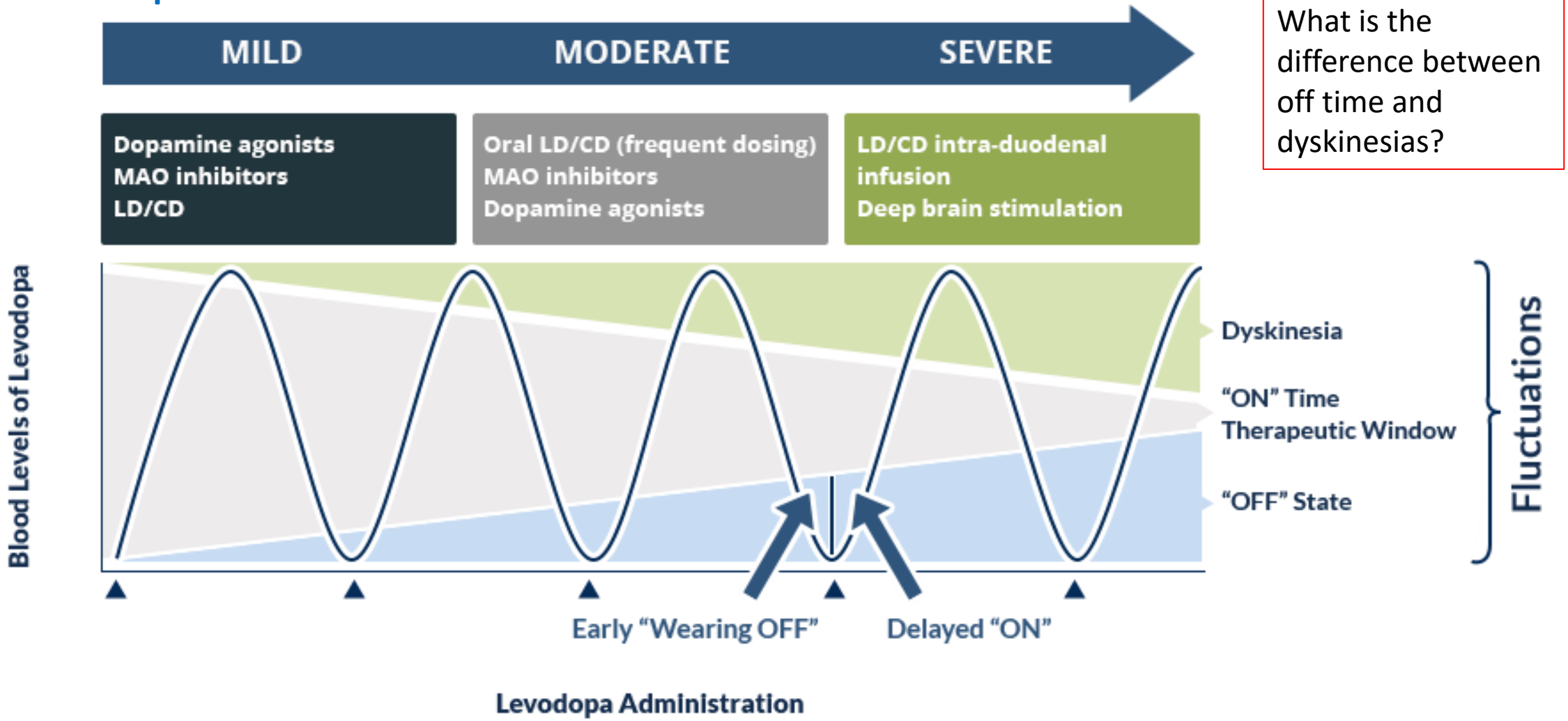
- Carbidopa-Levodopa (sinemet)
  - Crosses blood-brain barrier and converts to Dopamine (DA)



https://www.medscape.org/viewarticle/701955

Narrowing Therapeutic Window: Motor Complications

What is the difference between off time and dyskinesias?



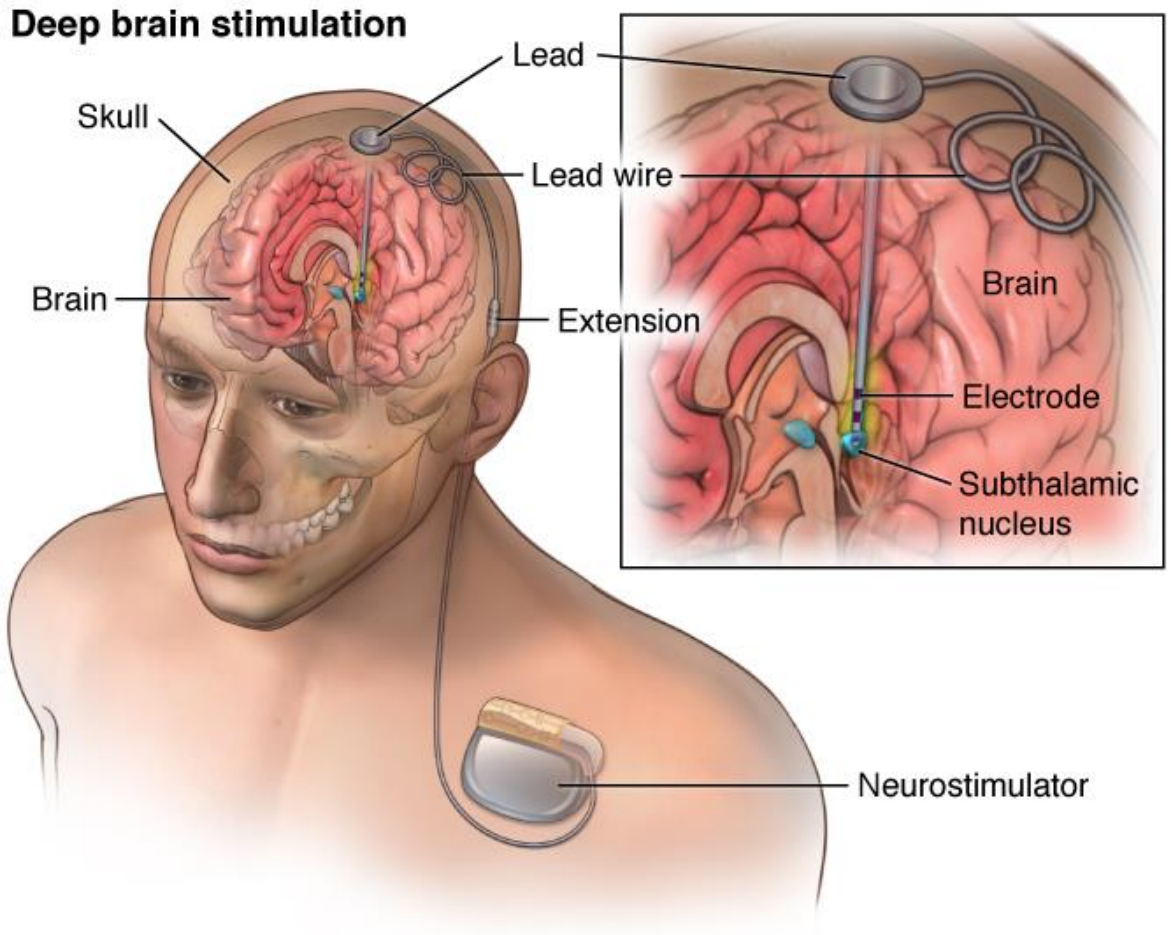
Video dyskinesias- “wiggly” “squirmy”

https://youtu.be/ECkPVTZlfP8?t=8

Surgical Management- DBS

- Two Targets
  - Gpi and STN (subthalamic nucleus)
- Goal- Reduce abnormal firing patterns of GPi and STN (more common)

- Benefits: reduce dykinesias, dystonia, tremor, hypo and bradykinesia
- Not expected to improve dementia, non-motor symptoms, or balance!



https://www.indicure.com/medical-tourism-india/deep-brain-stimulation/

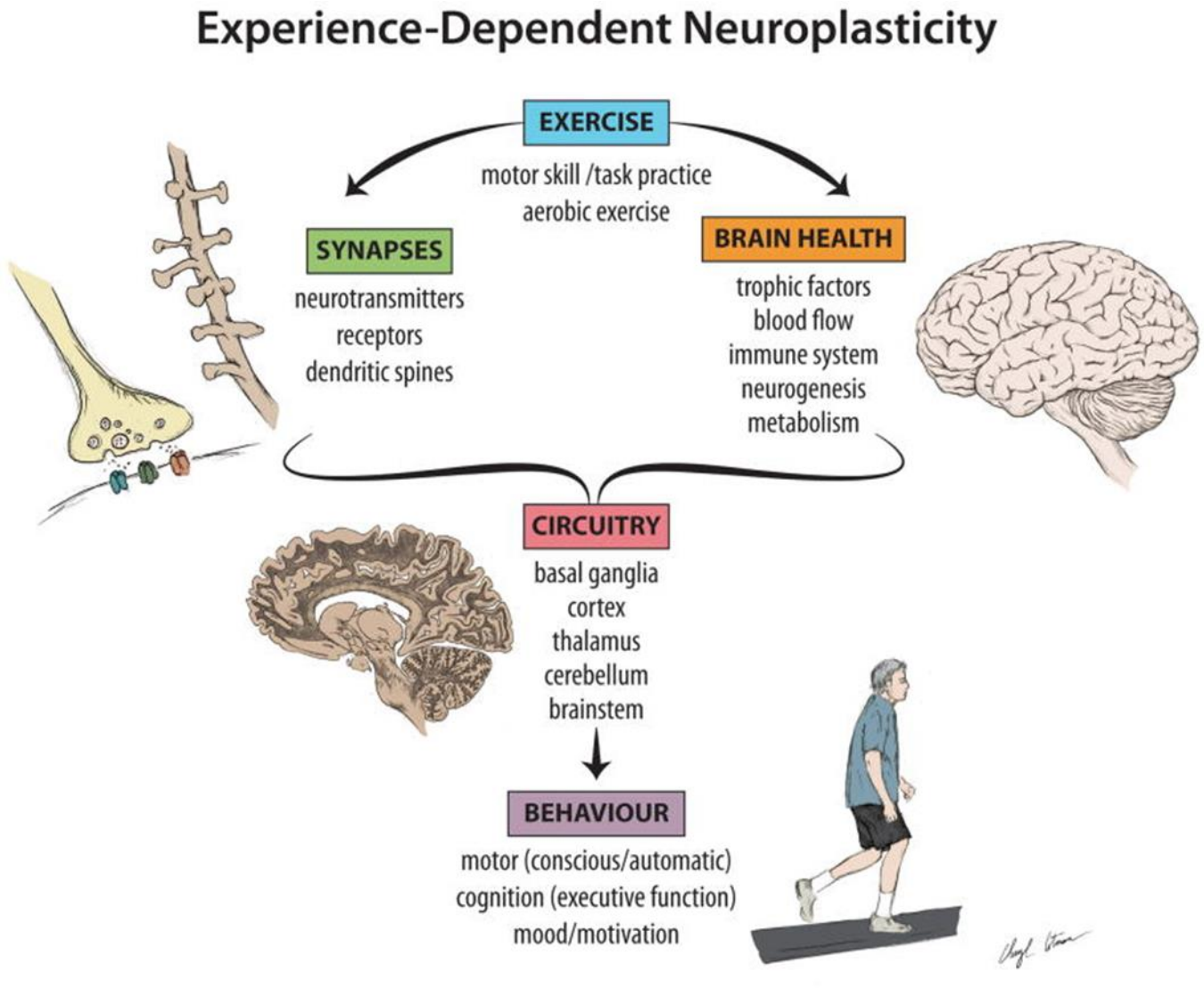
General Goals of Physical Therapy

Prevention of secondary impairments

- Fall Prevention
- Slow Disease Progression ?- *Cardiovascular exercise!*

Recovery/ Remediation- Improvement

- Body Structure and Function
  - Muscle strength, joint flexibility, cardiovascular fitness
  - Bradykinesia, Hypokinesia, rigidity
- Activity and Participation
  - Mobility, Balance, QOL



Petzinger GM, Fisher BE, McEwen S, Beeler JA, Walsh JP, Jakowec MW. Exercise-enhanced neuroplasticity targeting motor and cognitive circuitry in Parkinson's disease. *The Lancet Neurology.* 2013;12(7):716-726

General Goals of Physical Therapy

Compensation

- Management of later-stage Complications
- Assistive device use
- *External cues/strategies*

- Rhythmic Auditory Stimulation (RAS)- External AUDITORY cues
  - Metronome (apps)
  - Music with tempo
  - Counting
- Be intentional about your speed!
- Goal
  - Festinating gait→ slower beats to encourage slower bigger steps
  - Slow gait speed→faster beats to increase speed

General Goals of Physical Therapy

External Visual cues

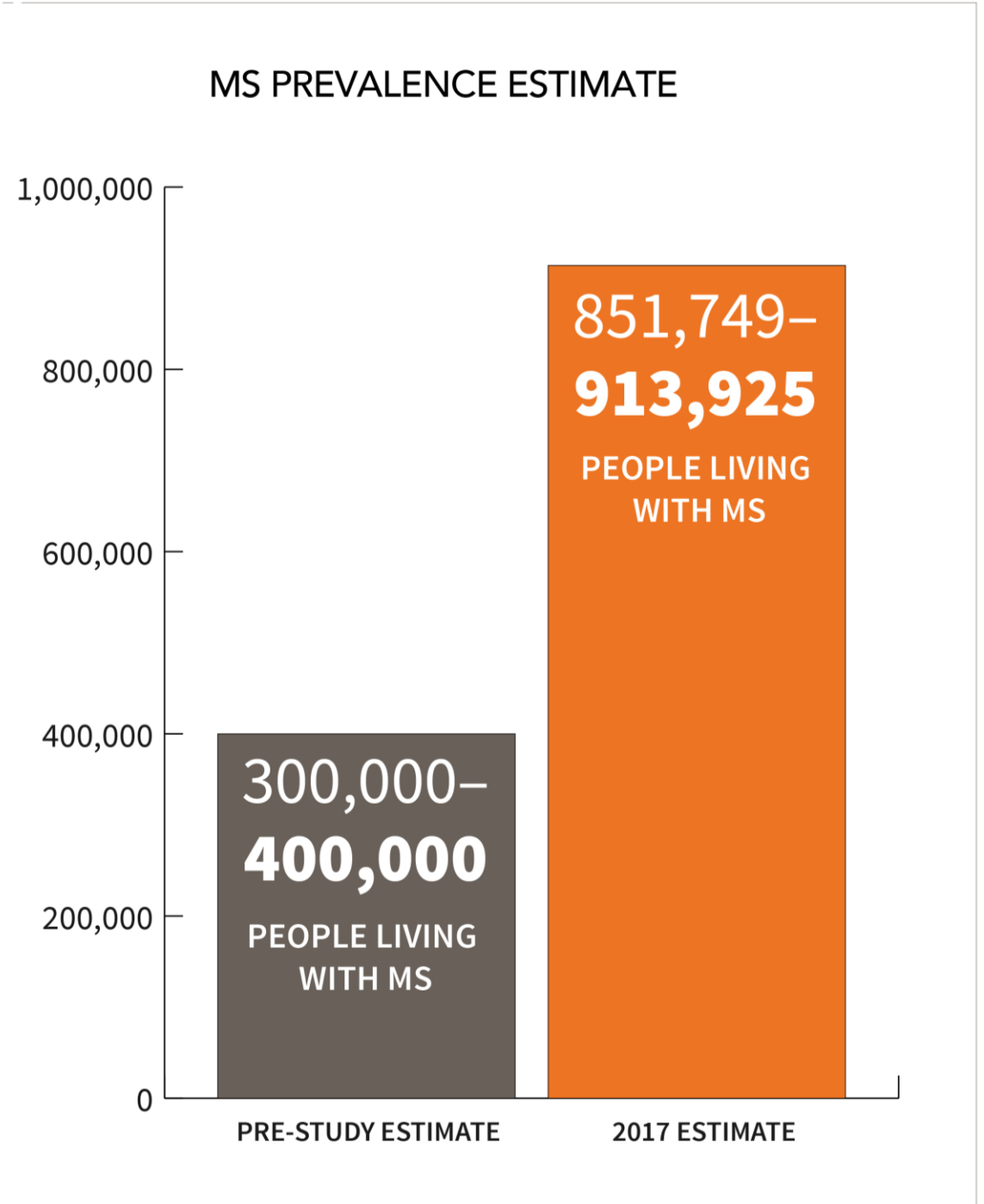
- Lasers (Ustep, Laser pointers)
- Tape
- Theraband

- Strategic use
  - Turns
  - Narrow spaces
  - Thresholds

Brief Review of Multiple Sclerosis (MS)

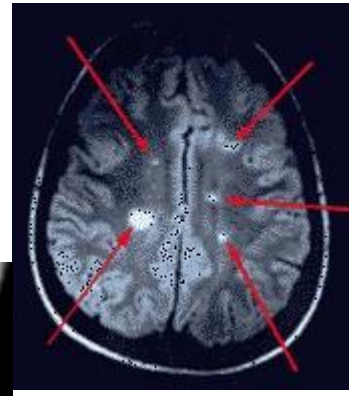
Multiple Sclerosis (MS)

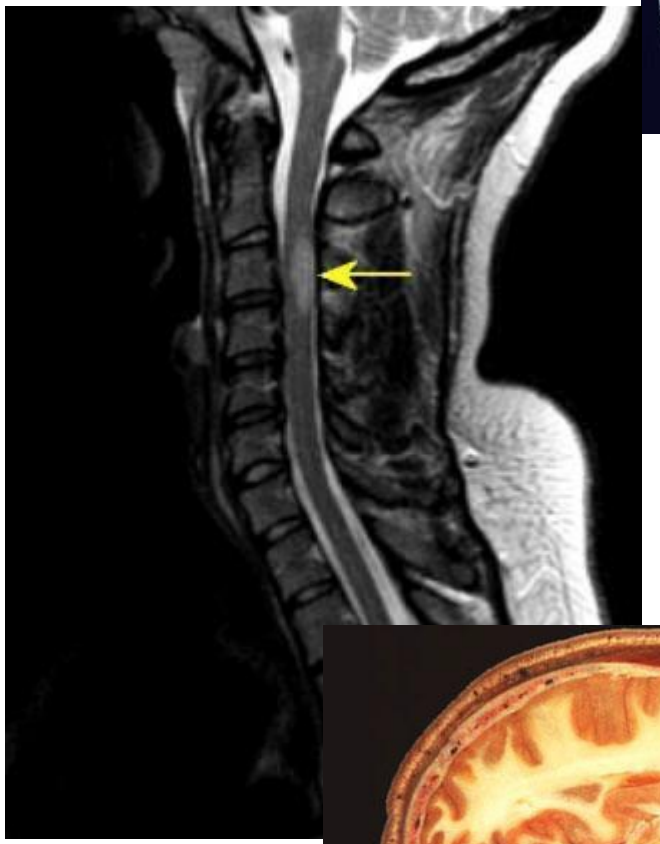
- Onset
  - Females > males (3-4:1)
  - 20-40 years
  - Predominately Caucasian
  - Farther away from equator→higher risk



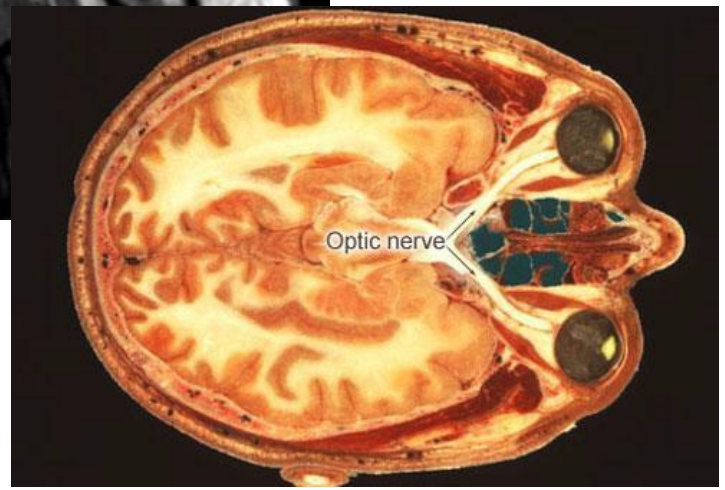
Multiple Sclerosis (MS) Pathophysiology

- Autoimmune process involving white matter of CNS (Cortex,Cerebellum, brainstem, SC)





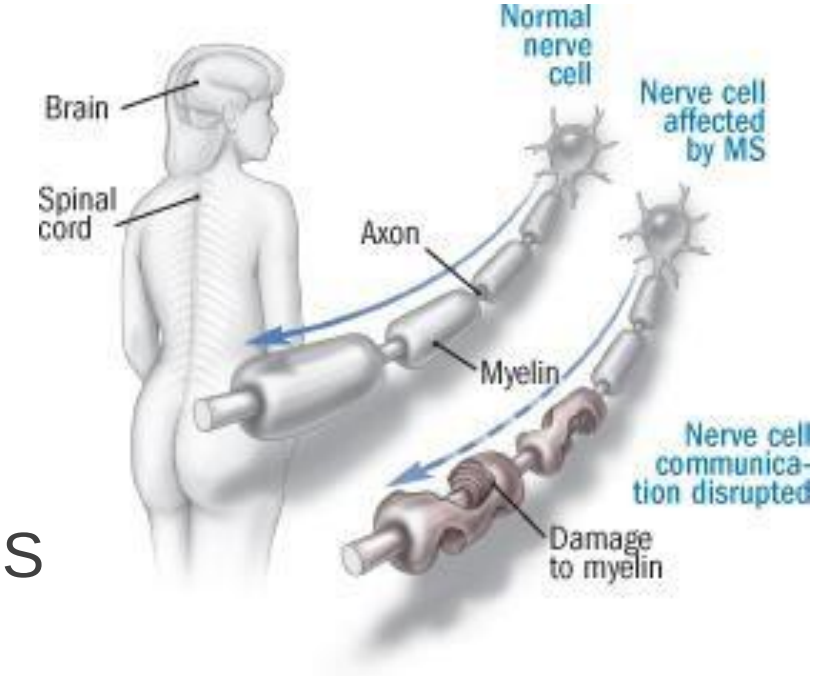
Disease course is HIGHLY variable within and between individuals



  - Inflammation
  - Scarring (**M**ultiple **S**cars)
  - Chronic→ gliosis (glial scar formation)
    - →axonal disruption/degeneration
    - →cause of neurologic disability
  - Common areas of impact
    - Optic nerves (oligodendrocytes)
    - Posterior columns
    - Corticospinal tracts
    - Cerebellar peduncles
    - MLF
    - *40-76% have difficulty with eye movements*
    - *Due to cerebellar or brainstem lesions*

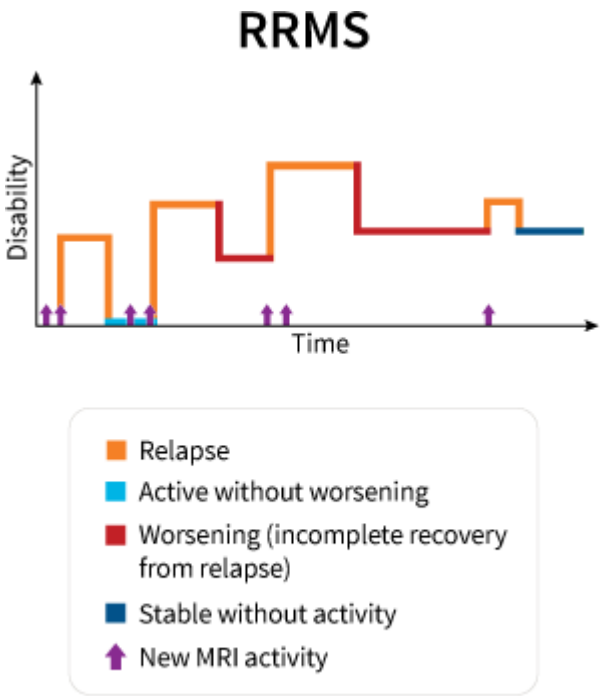
Multiple Sclerosis (MS) Pathophysiology

- Clinical Sub types (new terminology, 2013)
- 4 Clinical Sub types
- Subtype 1: Clinical Isolated Syndrome (CIS)
  - First episode lasts @ least 24 hours
    - Monofocal- single symptom (ie optic neuritis)
    - Multifocal- > 1 (ie optic neuritis + numbness/tingling)
  - Complete or partial recovery
- CIS with (+) MRI activity- 60-80% chance of developing MS within several years
- CIS with (-) MRI activity- 20% chance of developing MS within several years

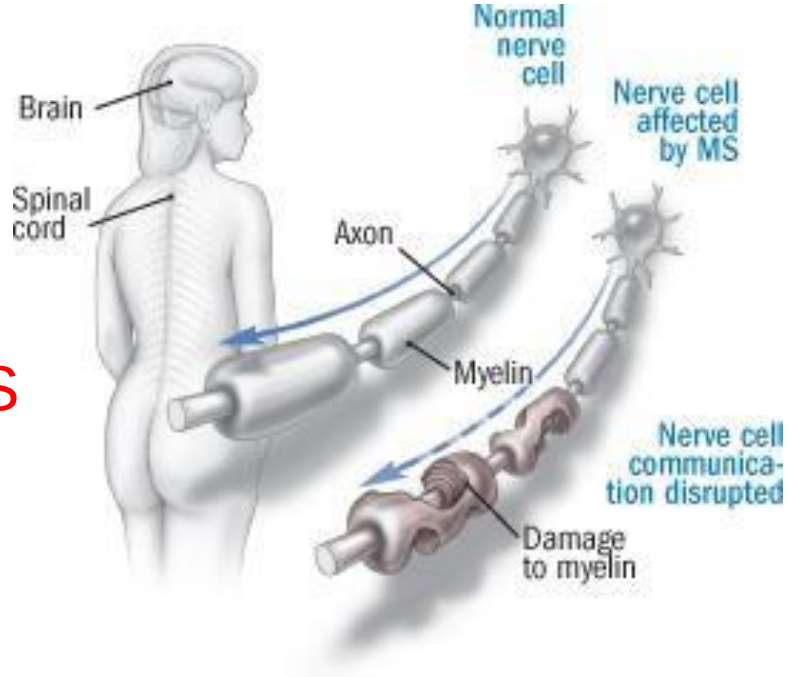


Multiple Sclerosis (MS) Pathophysiology

- 4 Clinical Sub types



Source: Lublin et al., 2014.



Subtype 2: Relapsing-Remitting MS

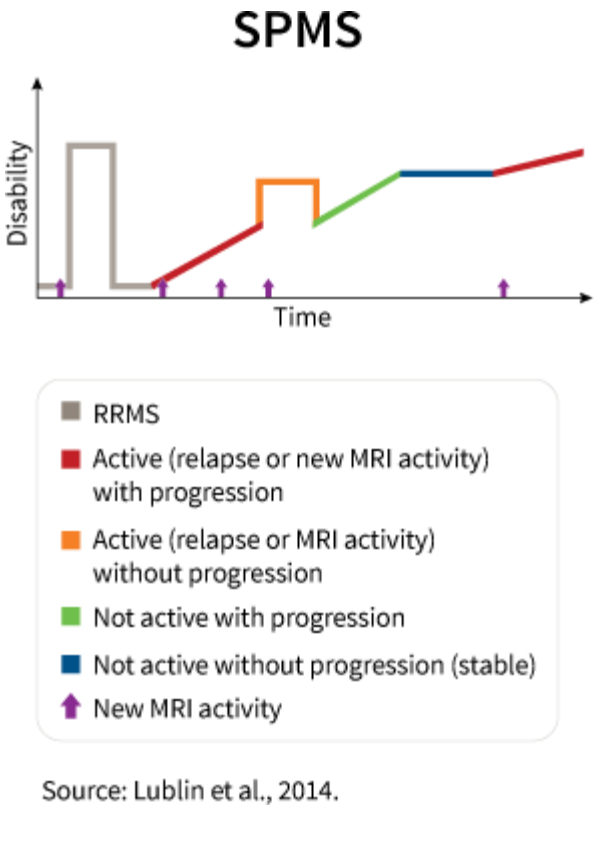
- 85% initially dx with RRMS
- Image- example disease course

Phenotype:

- Active
- Not Active

Multiple Sclerosis (MS) Pathophysiology

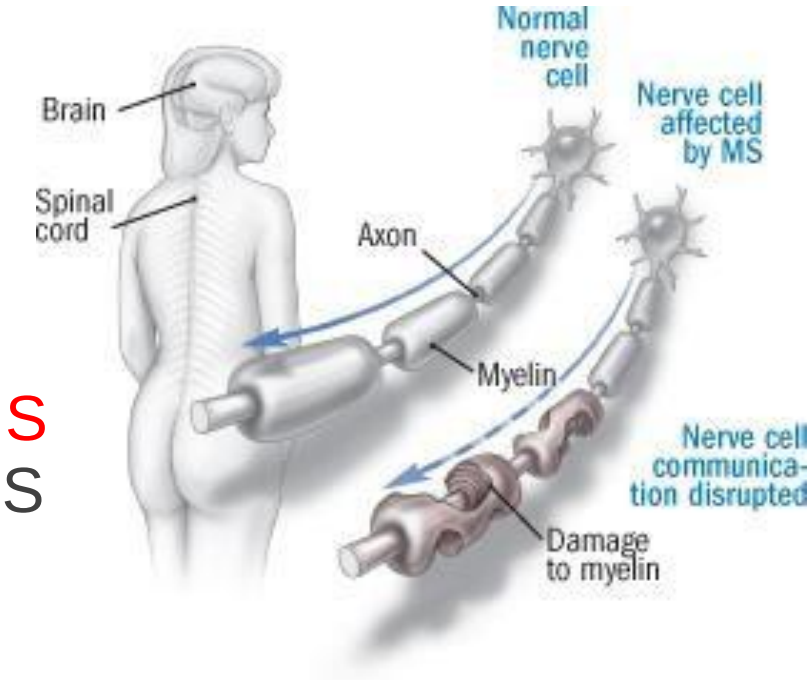
- 4 Clinical Sub types



Source: Lublin et al., 2014.

Subtype 3: Secondary Progressive MS

- Most with RRMS transition to SPMS

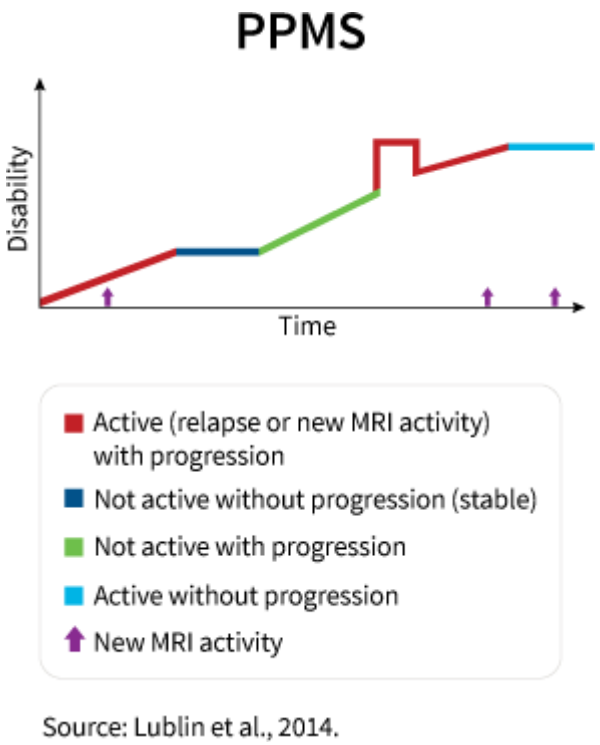


Phenotype:

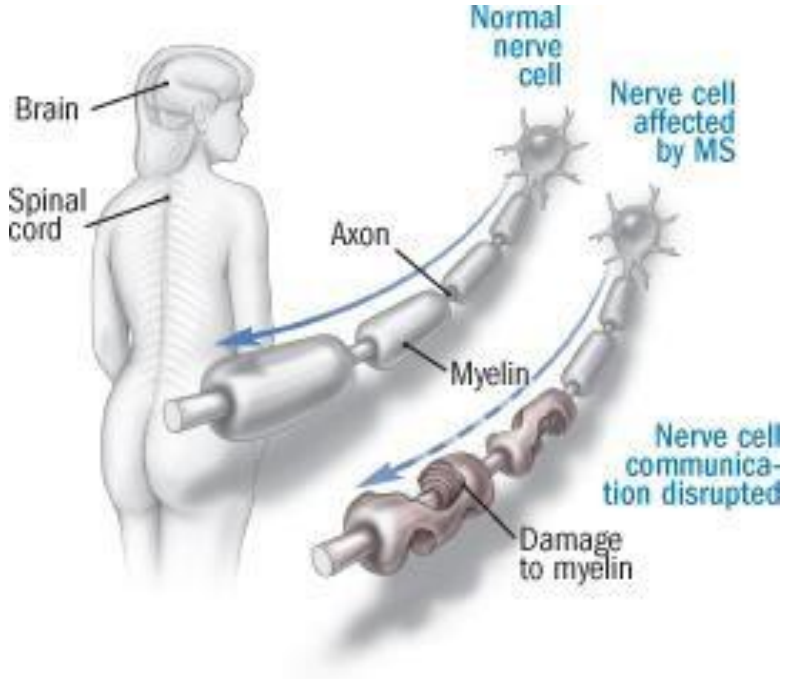
- Active + progression
- Active – progression
- Not active + progression
- Not active – progression (stable disease)

Multiple Sclerosis (MS) Pathophysiology

- 4 Clinical Sub types



Source: Lublin et al., 2014.



Subtype 4: Primary Progressive MS

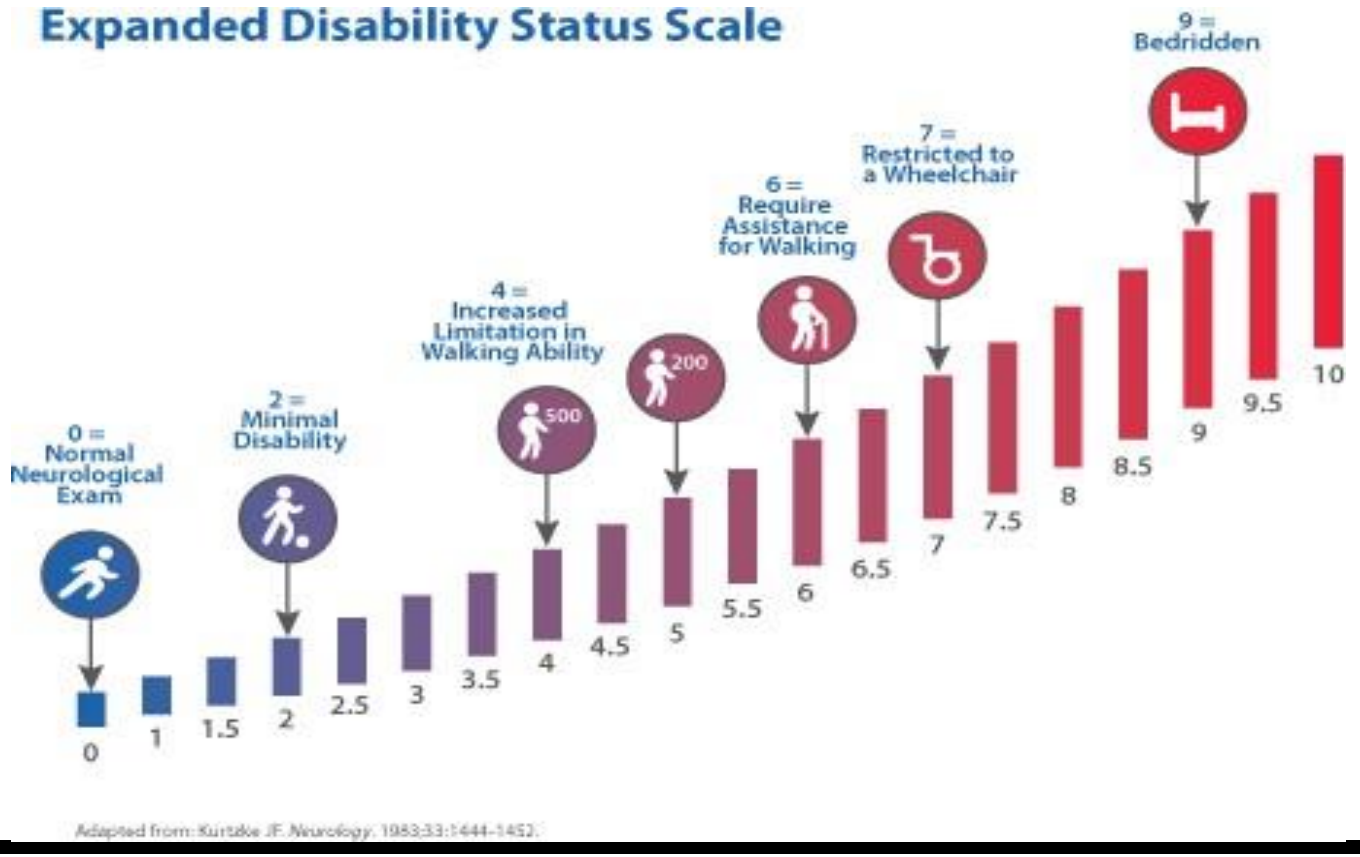
- 15% initially dx with PPMS
- Accumulation of symptoms/disability without early relapses or remissions
- ***More commonly impacts Spinal Cord > Cortical areas***

Phenotype:

- Active + progression
- Active – progression
- Not active + progression
- Not active – progression (stable disease)

Clinical Disability: Expanded Disability Status Scale (EDSS)

Higher number= increased disability



Diagnostic Criteria

2017 McDonald Criteria: Additions to the 2010 Criteria

Dissemination in space

≥1 T2 lesions in ≥2 locations

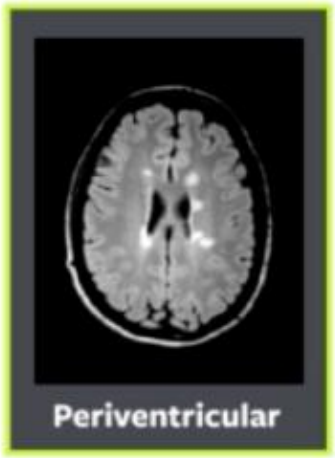
- periventricular lesion
- infratentorial lesion
- asymptomatic **or symptomatic** brainstem or spinalcord lesion
- **cortical** or juxtacortical lesion

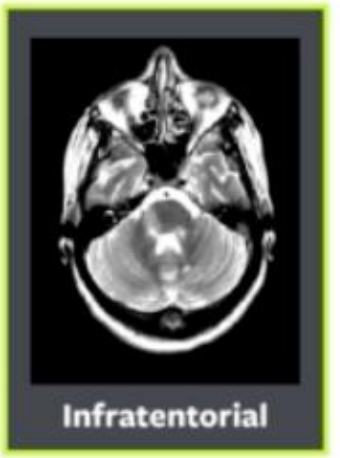
Dissemination in time

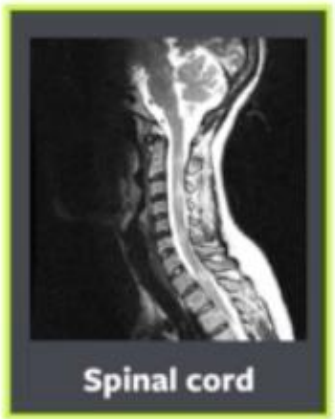
Simultaneous presence of asymptomatic **or symptomatic** gadolinium enhancing and nonenhancing lesions at any time

or

≥1 new T2 or gadolinium enhancing lesion


Periventricular


Infratentorial

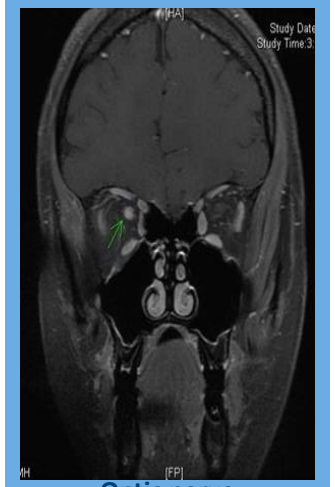

Spinal cord

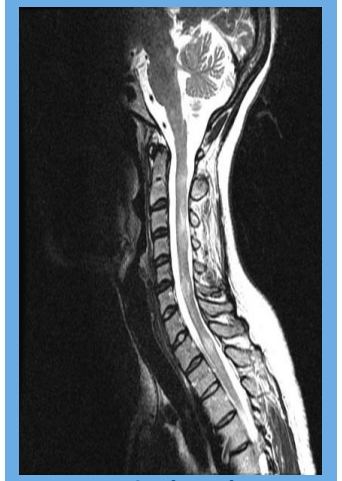

Cortical/Juxtacortical

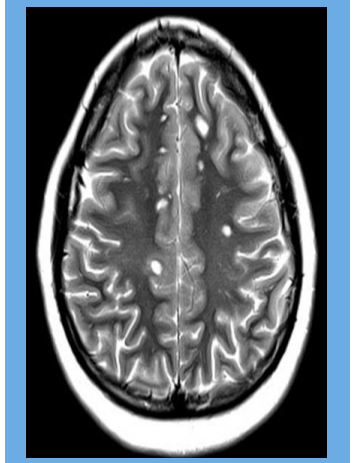
Images Courtesy of Dr. Stephen Krieger, Icahn School of Medicine at Mount Sinai, New York, NY

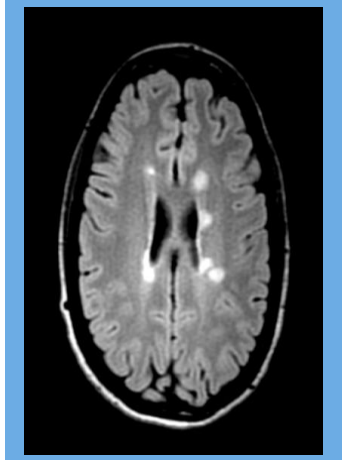
Bolded text indicates changes to the 2010 guidelines.

MRI lesion location corresponds to symptoms


Optic nerve


Spinal cord

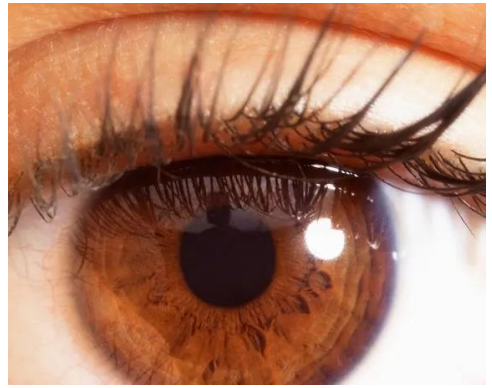

Juxtacortical


Periventricular

- **Where lesions are located in the CNS can be important[1,2]**
  - Lesion location may suggest what kind of symptoms you may experience and how MS may progress. For example:
    - A lesion on the spinal cord in the neck might cause numbness and tingling in the arms
    - Lesions of the optic nerve can cause visual disturbances

References: 1. Frohman TC, O'Donoghue DL, Northrop D (eds.) *Multiple Sclerosis for the Physician Assistant: A Practical Primer*. New York, NY: National MS Society; 2011. **2.** Stankeiwitz JM, Buckle GJ. In: Rizvi SA, Coyle PK, eds. *Clinical Neuroimmunology: Multiple Sclerosis and Related Disorders.* New York, NY: Humana Press; 2011.

Common Signs/Symptoms of MS
ICF Body Function/Structure



- Visual changes (blurred, poor color differentiation, pain in eye)
  - Optic Neuritis
- Eye Movement
  - Nystagmus (cerebellum or central vestibular pathways)
  - Difficulty with conjugate gaze (brainstem involvement- CN 3,4,6 or MLF)- double vision
- Motor
  - UMN signs (paresis, spasticity (75%), clonus, hyperreflexia)
  - Weakness (denervation vs. atrophy)

Common Signs/Symptoms of MS ICF Body Function/Structure

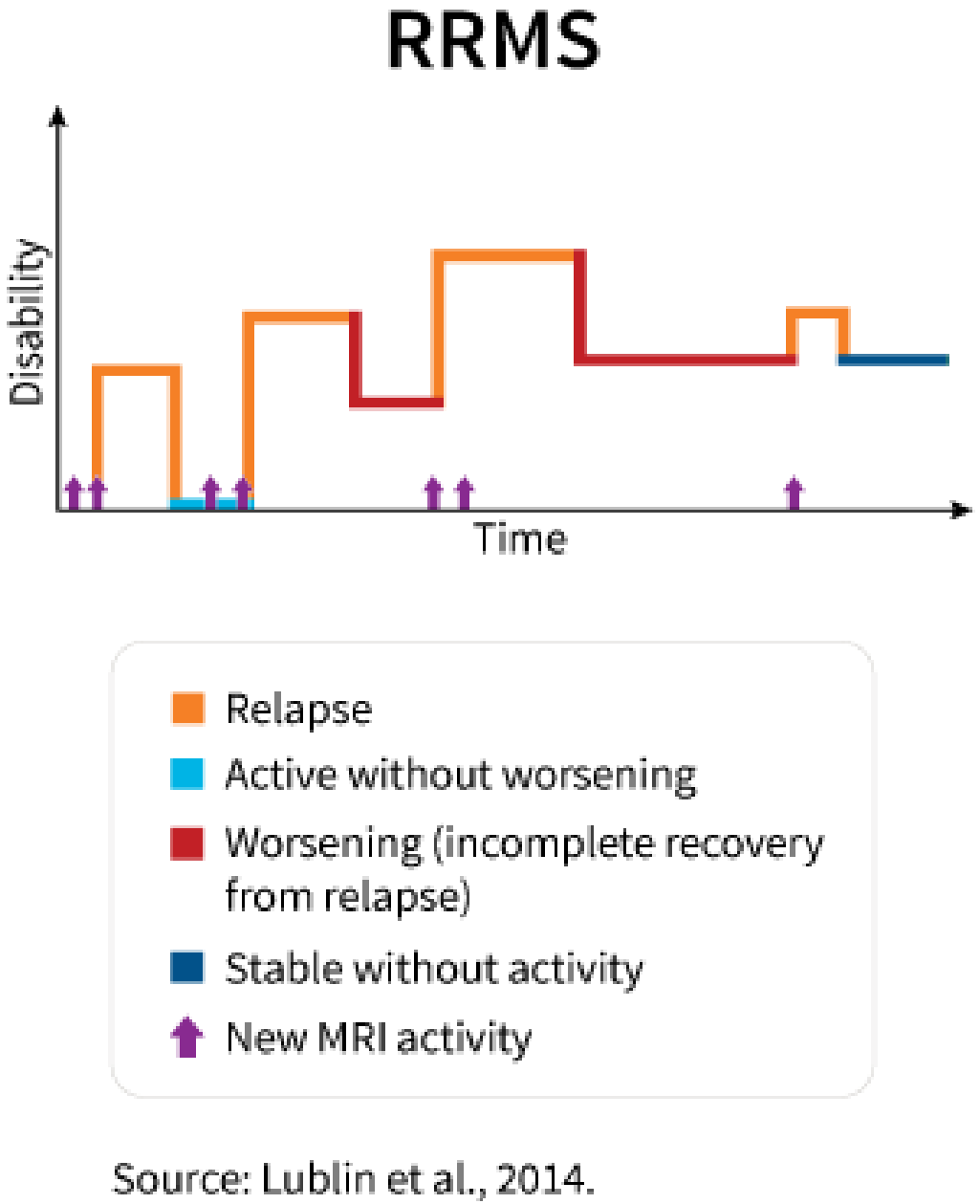
- **<u>Fatigue (80%)</u>**
  - "subjective lack of physical and/or mental energy that is perceived by the individual or caregiver to interfere with usual and desired activities"
    - CPG Panel on Fatigue of the MS Council
  - Abrupt, without warning, worse throughout day
  - Reports: overwhelming tiredness, exhaustion, weakness, difficulty concentrating
  - Exacerbated by- physical exertion, heat, reduced/disturbed sleep, depression, medical conditions (ie respiratory infection)

ICF Body Function/Structure- Common Signs/Symptoms of MS

- Dizziness/Vertigo/ Disequilibrium
  - CN 8 Nuclei in brainstem
- Cerebellar signs
  - Ataxia, dysmetria, dysdiadochokinesia, dyssynergia
  - Intention tremor
  - Decreased coordination and balance
- Gait difficulties (weakness, spasticity, decreased balance, sensory deficits, fatigue)

Pharmaceutical management

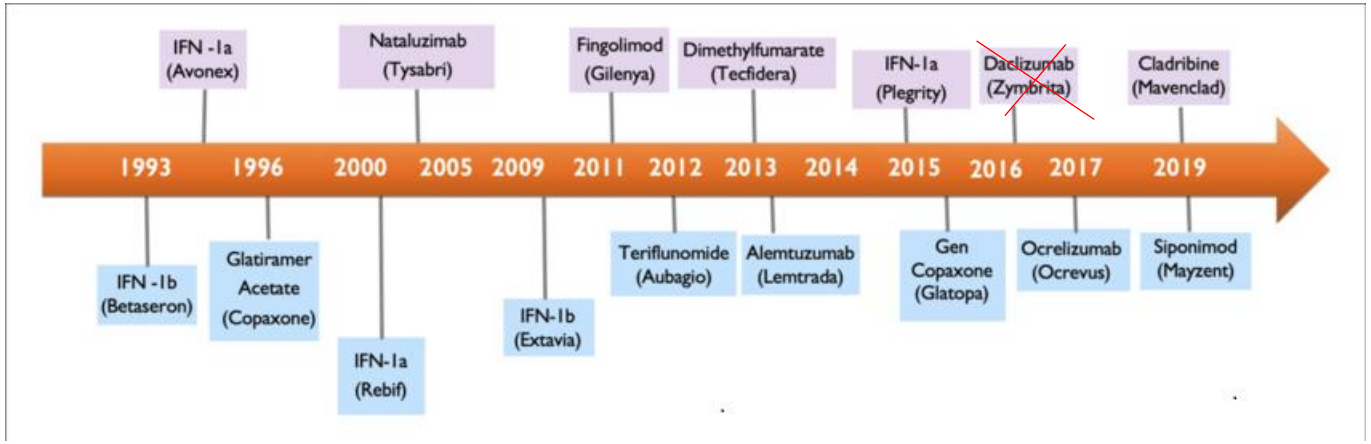
- Relapse/Acute Exacerbation- new or increased symptoms lasting > 24 hours
  - Pseudorelapse (< 24 hours- exercise, heat, UTI, fatigue)
- Medications (3-5 day course, IV)
  - Methylprednisolone
  - Prenisone



Source: Lublin et al., 2014.

Pharmaceutical management- Disease Modifying Medications- Immunomodulators

- Injections (varied schedules)
  - Avonex
  - Betaseron
  - Copaxone
  - Extavia
  - Rebif
  - Biogen
- Oral Medications
  - Aubagio
  - Gilenya
  - Tecfidera
- Infusions
  - Lemtrada
  - Novantrone
  - Ocrevus (only FDA approved med for PPMS- within last year)
  - Tysabri



https://www.nationalmssociety.org/Treating-MS/Medications

Pharmaceutical management- Disease Modifying Medications- Immunomodulators

- When are DMD (disease modifying drugs) recommended?
  - At diagnosis
  - Continued indefinitely UNLESS:
    - Failure to control disease
    - Side effects are intolerable
    - Adverse event (ie progressive leukoencephalopathy (PML)- fatal brain infection)
    - Inability to follow treatment regimen
    - More appropriate treatment becomes available
- Step Therapy issue

https://www.nationalmssociety.org/Treating-MS/Medications

Pharmaceutical management- Symptom Management

- Medications for individual symptoms- many people are on multiple medications
- Ampyra- specifically FDA approved to improve gait in MS
- – Improved speed and endurance

Non-Pharmaceutical - Symptom Management

- Psychosocial Interventions
  - Case management
  - Support groups
  - Vocational rehabilitation
  - Centers of Independent Living (AbleSC)
- Education
  - Lifestyle modification (exercise, energy management)
  - https://www.nationalmssociety.org/Resources-Support/Library-Education-Programs
- Rehabilitation (prevention, recovery, compensatory)

General Goals of Physical Therapy

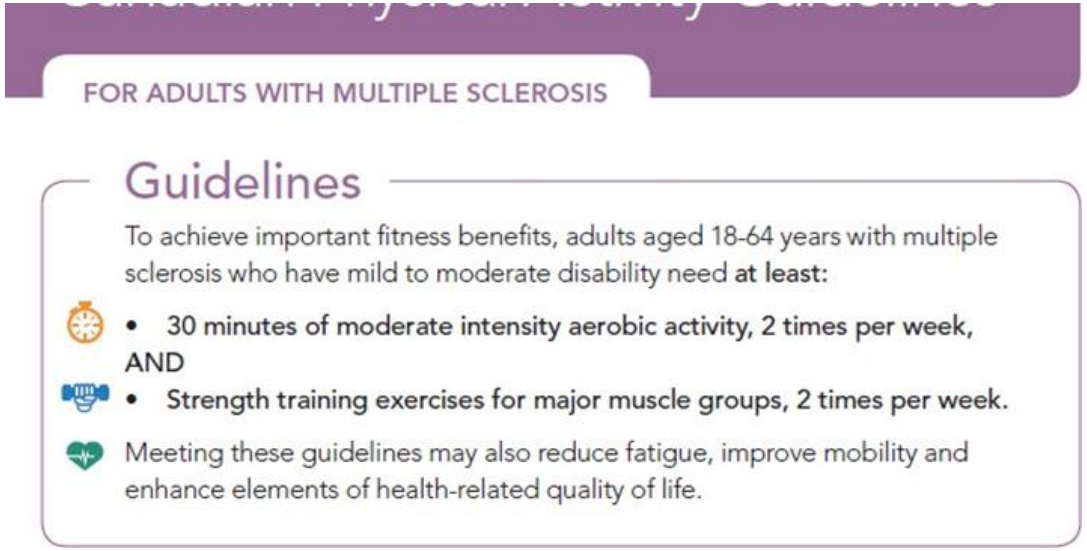
Prevention of secondary impairments

- Fall Prevention
- Slow Disease Progression ?- *Cardiovascular exercise!*

Behavioral Recovery/Remediation- Improvement

Preserve/improve strength and function

- Body Structure and Function
  - Strength, flexibility, spasticity
- Activity and Participation
  - Mobility, Balance, QOL



https://csepguidelines.ca/wp-content/uploads/2018/10/CSEP_MS_PAGuidelines_adults_en.pdf

General Goals of Physical Therapy

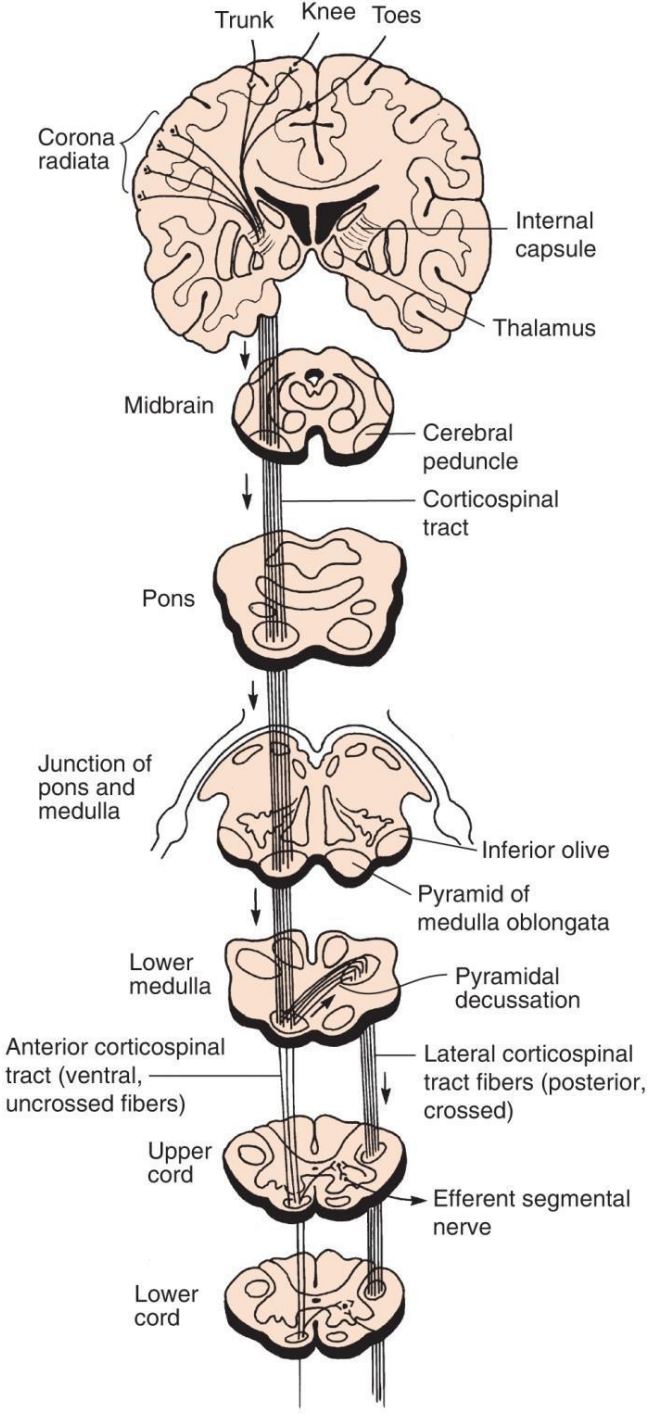
Compensation

- Can fluctuate throughout a day!
- Assistive device use
- Fatigue management, energy conservation
  - Log symptoms, fatigue, activity
- Heat Sensitivity

Education

- Safety Education
- Promote self-efficacy
  - Peer support
  - Self-paced/guided learning
    - https://www.nationalmssociety.org

Brief Review of Amyotrophic Lateral Sclerosis (ALS)

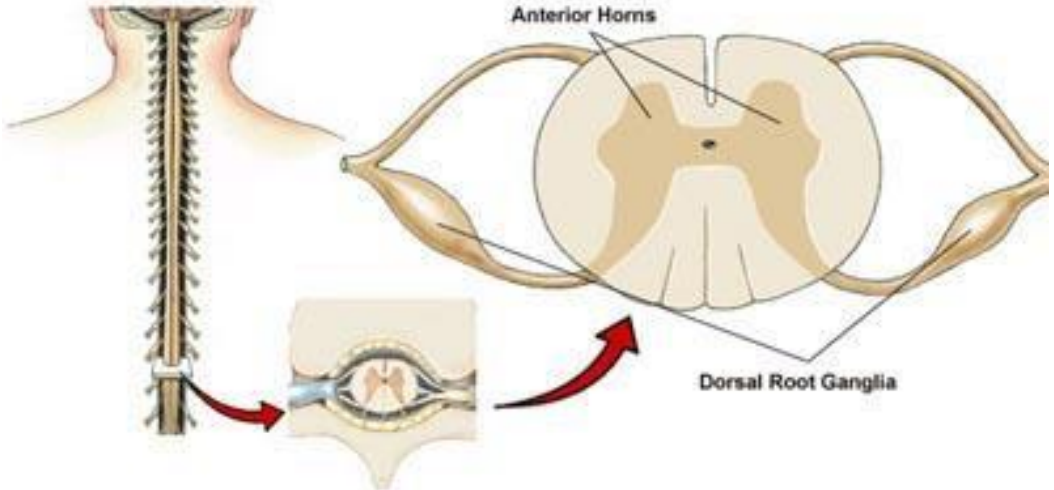


ALS- Pathophysiology
Motor Cortex and Spinal Cord

Involved:

- Corticospinal Tracts
- Anterior Horn Cells (motor neurons)
  - S2 level anterior horn spared (bowel and bladder)
- Brainstem- pyramidal decussation
- Motor Cortex
- Spared: sensory system (may just be involved but to lesser extent)

Figure F-6: Dorsal Root Ganglion & Anterior Horn

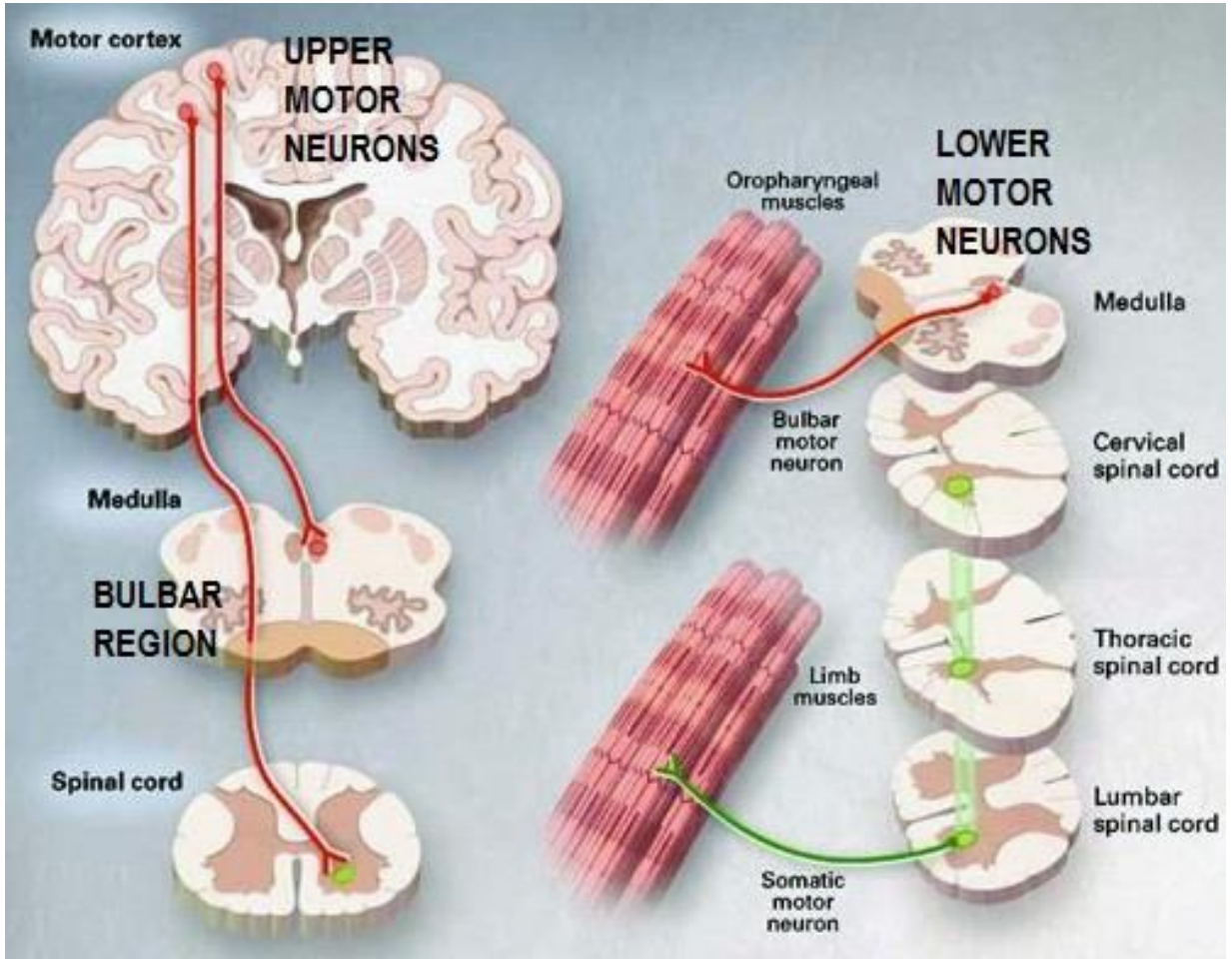


The dorsal root ganglion transmits *sensory* information while the anterior horn directs *motor* neurons.

ALS- Diagnosis

- Presence of:
  1. LMN signs
  2. UMN signs
  3. Progression of disease within a region or to other regions
- Absence of:
  1. Evidence of other disease that would explain UMN/LMN signs
  2. Neuroimaging of other disease processes

https://med.emory.edu/departments/neurology/programs_centers/emory_als_center/what_is_als/index.html



- Most Common motor neuron disease in adults
- 4-10: 100,000
- Average onset mid-50's
- 1.7:1 (men:women)

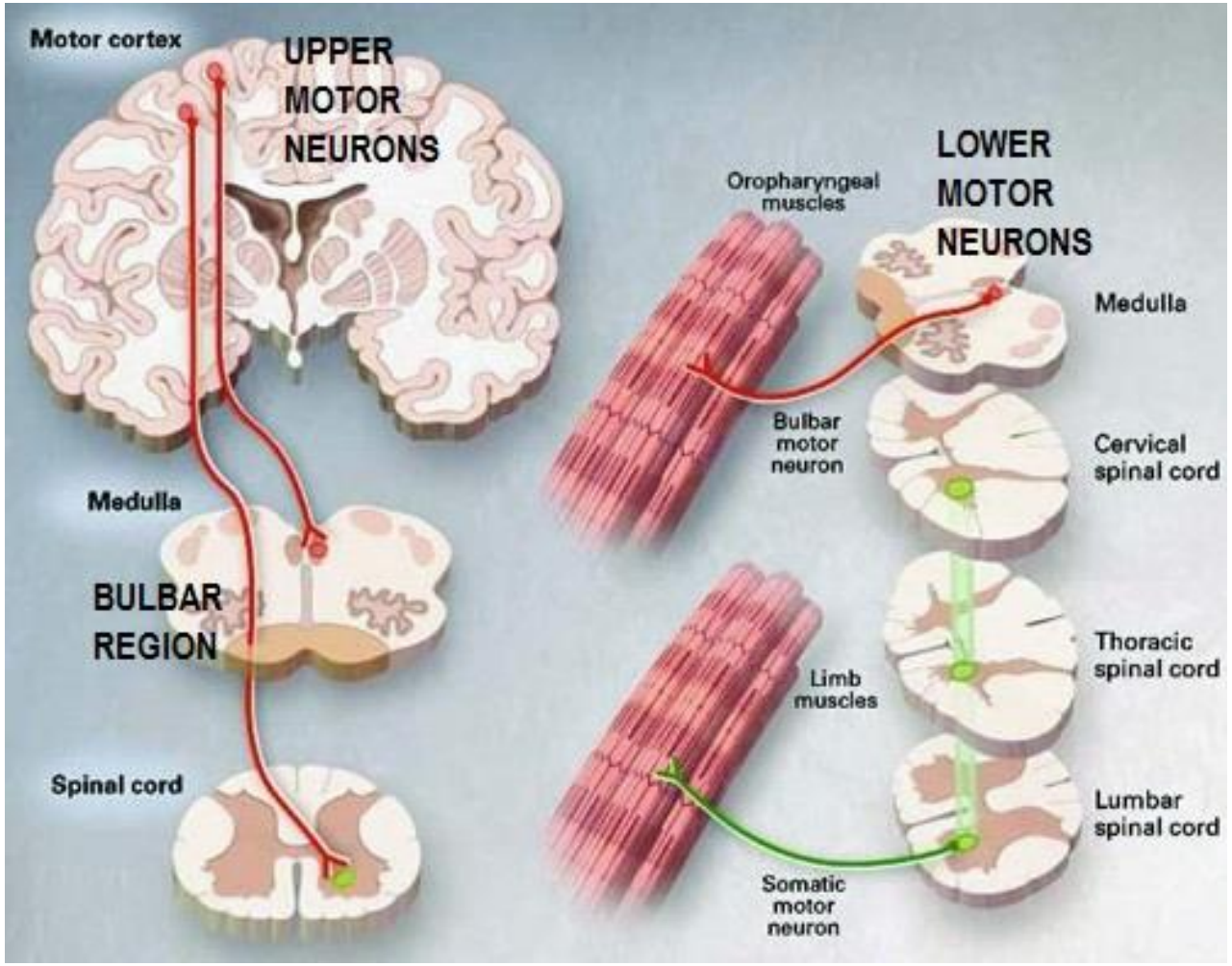
ALS- Patterns of Weakness

Limb Onset (70-80%)

- Asymmetric and Focal

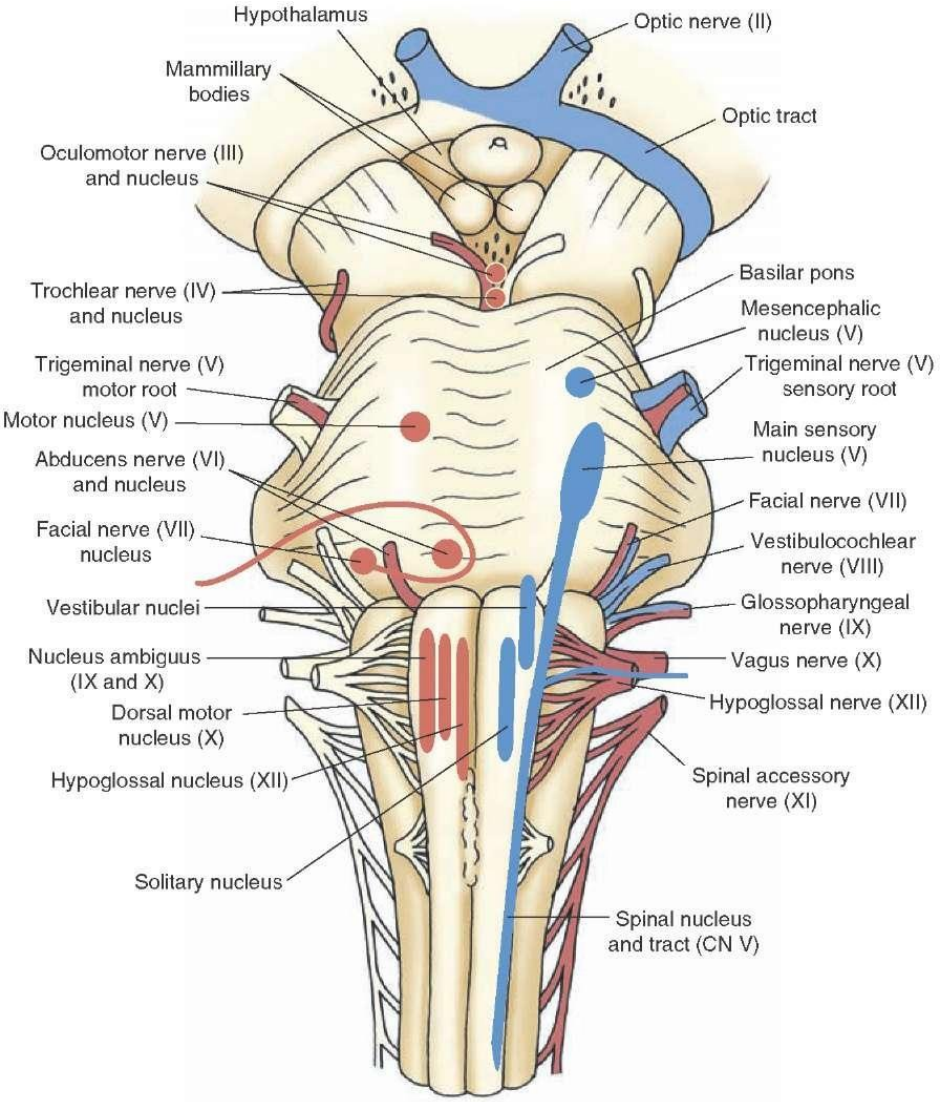
- Progression Patterns

1. UE > LE
    - associated with longer survival
2. Distal LE first



https://med.emory.edu/departments/neurology/programs_centers/emory_als_center/what_is_als/index.html

ALS- Patterns of Weakness



Bulbar Onset (brainstem)- 20-30%

- Dysarthria
- Dysphagia
- Pseudobulbar Affect- emotional lability

UMN signs>LMN

<u>Brainstem CN Nuclei Involved:</u>

CN V, VII, IX, X, and XII

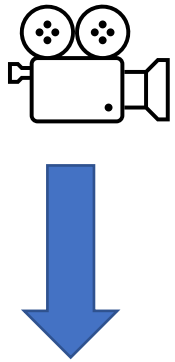
<u>Brainstem CN Nuclei Spared:</u>

CN III, CN IV, CN VI

ALS Prognosis

Survival (fast progression)

- Ranges months to >20 years
- Average 27 and 43 months
- Typically, death within 3-5 years of diagnosis
  - Respiratory failure



https://www.cnn.com/2018/03/14/health/stephen-hawking-dead/index.html

ALS- Primary Impairments

UMN

- Spasticity, Hyperreflexia, muscle weakness

LMN

- Hyporeflexia, hypotonicity, atrophy, muscle cramping and fasciculation, muscle weakness

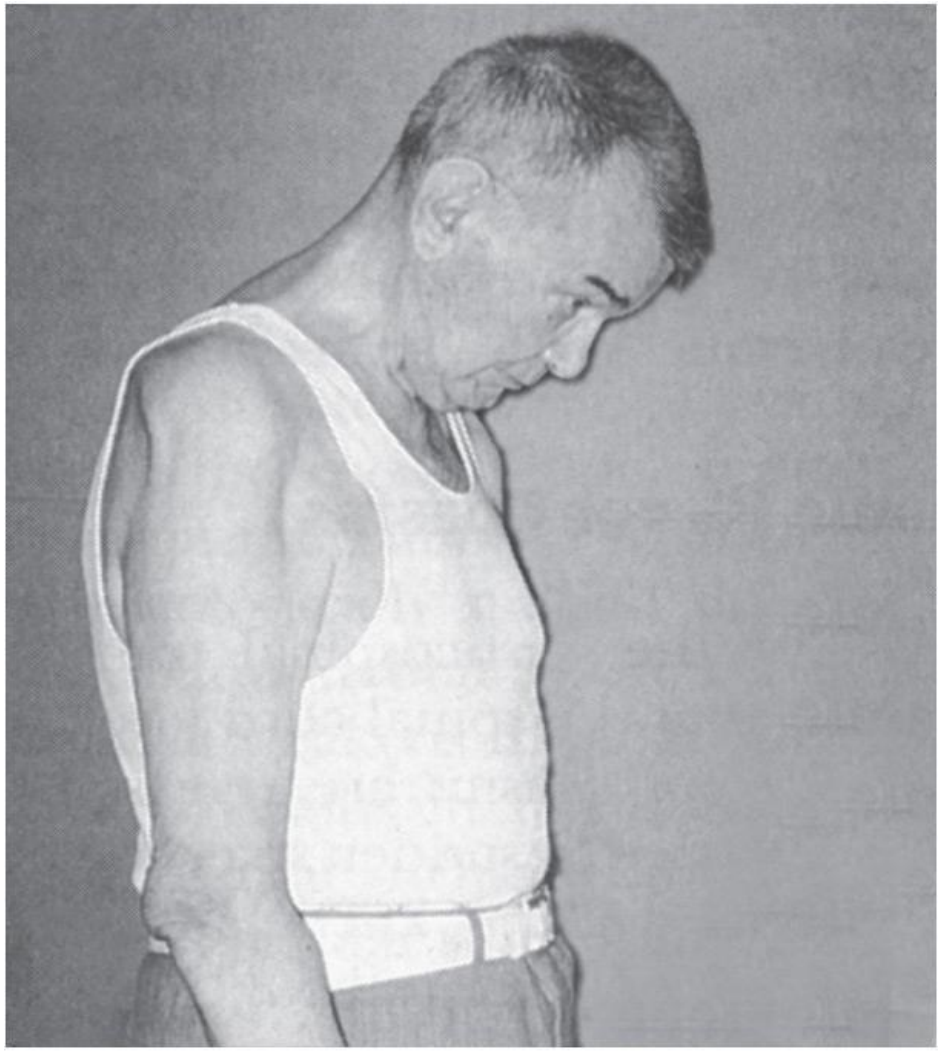
Respiratory

- Inspiratory and Expiratory muscle weakness, dyspnea, orthopnea, hypoventilation, decreased cough production

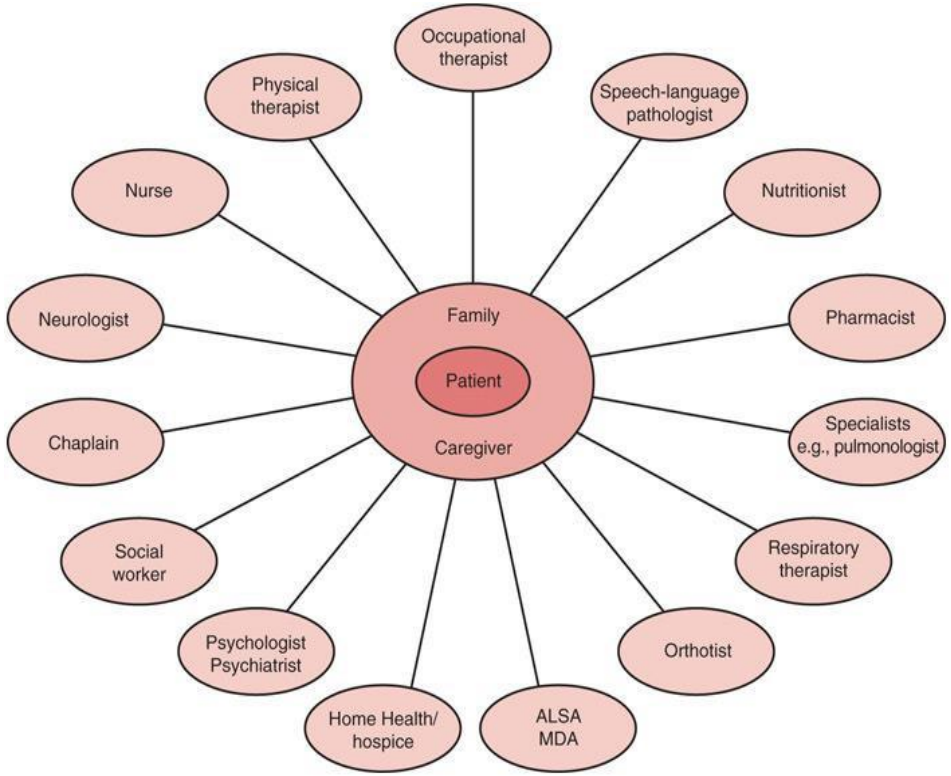
Video Example of Muscle Fasciculation with ALS https://www.youtube.com/watch?v=P-QeuP_Z2z0

ALS- Secondary Impairments

- Fatigue
- Weight loss
- Joint Contracture
- Joint subluxation
- Adhesive capsulitis
- Pain
- Balance and Gait disturbances
- Postural Changes
- Deconditioning
- Depression
- Anxiety



ALS-Management

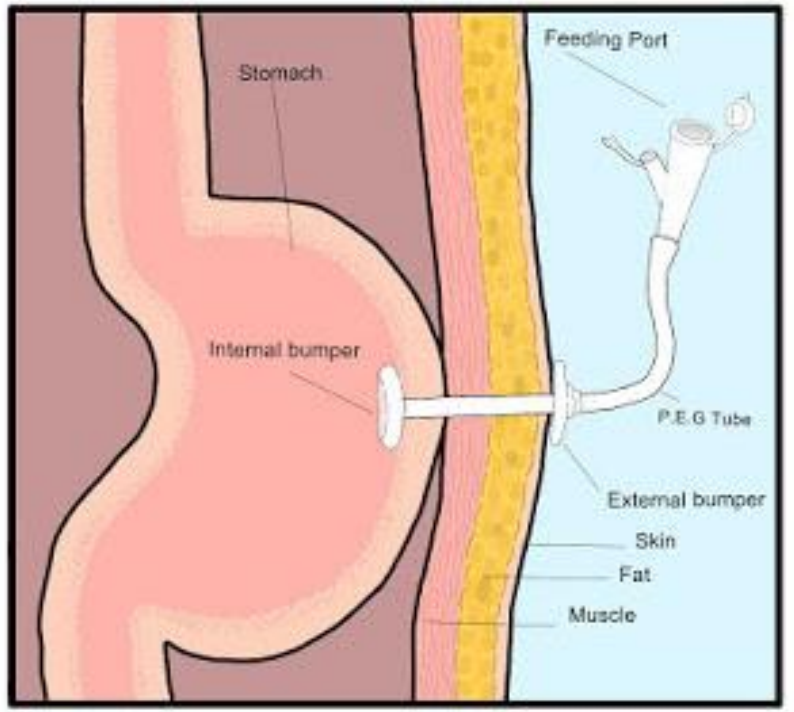


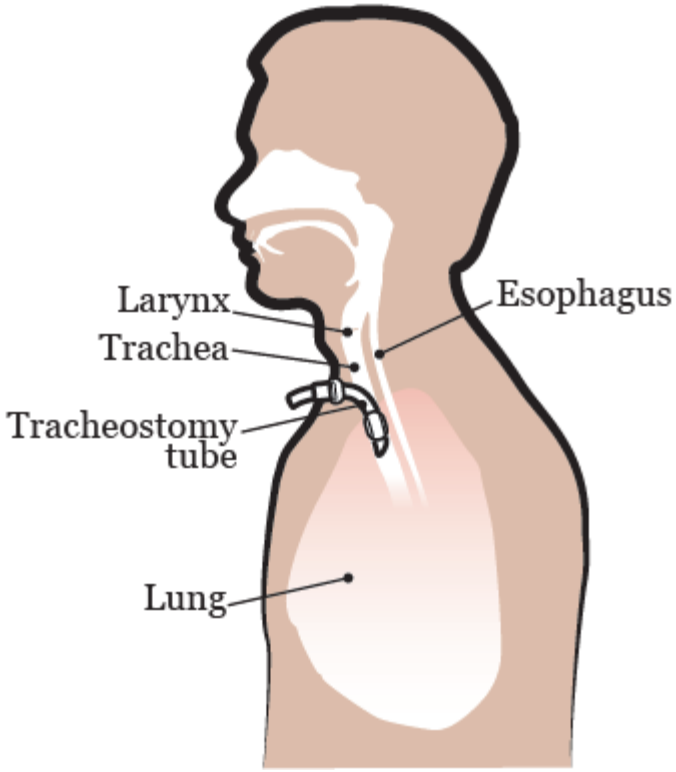
- Disease Modifying Agents
  - FDA approval of Riluzole- *may extend survival 2-3 months*
- Interdisciplinary Management and coordinated care
  - Relative risk of mortality ***45% less than non-coordinated care*** (Cordesse et al 2015)
- Amyotrophic Lateral Sclerosis Functional Rating Scale

ALS- Procedure Consideration

Life extending procedures:

- PEG tube placements
- Mechanical Ventilation
  - Tracheostomy

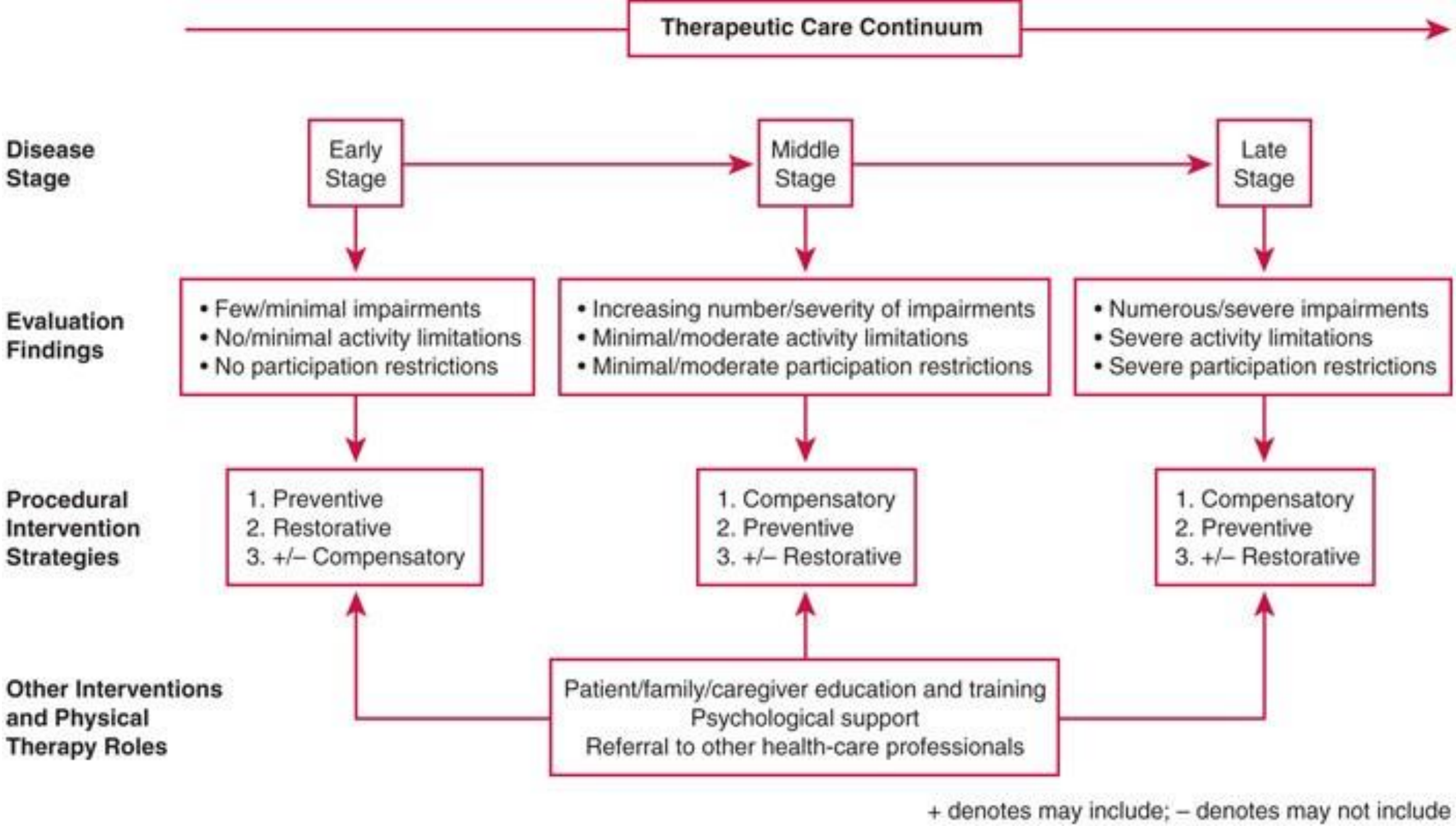




Lechtzin N, Wiener CM, Clawson L, Chaudhry V, Diette GB. Hospitalization in amyotrophic lateral sclerosis: causes, costs, and outcomes. *Neurology.* 2001;56(6):753-757.

Steve Gleason's story

https://www.youtube.com/watch?v=B4wVm6YuhqE&t=8s



General Goals of Physical Therapy

EARLY STAGES

- Behavioral Remediation- Improvement
  - Body Structure and Function
    - Muscle strength, joint flexibility, cardiovascular fitness
  - Activity and Participation
    - Mobility, Balance, QOL

Middle to LATE stages

- Behavioral *Compensation-* Management of later-stage Complications
  - Assistive device use

ALL STAGES:

- *Education*
  - Safety Education
- *Prevention* of secondary impairments
  - Fall Prevention, skin integrity

Early-Stage ALS-Intervention Strategies

- Recovery/Preventative
  - Strengthening
  - Endurance
  - AROM, AAROM, stretching
- Compensatory
  - Energy Conservation
  - AD or adaptive equipment
  - Home or Office Modifications

Middle-Stage ALS- Intervention Strategies

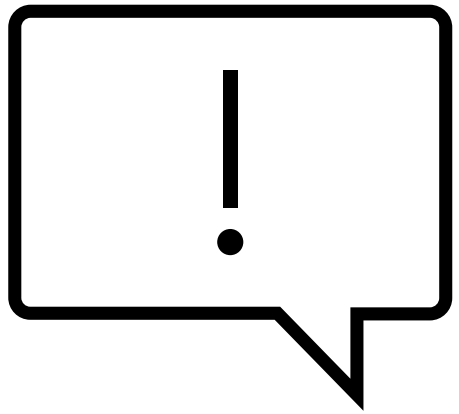
- Preventative
  - Strengthening
  - Endurance
  - AROM, AAROM, stretching
  - Pressure relief strategies
- Compensatory
  - Energy Conservation
  - AD or adaptive equipment
  - Home or Office Modifications
  - Wheelchair prescription
  - Brace prescription (orthoses, slings, etc)

Late-Stage ALS-Intervention Strategies

- Preventative
  - PROM
  - Hospital Bed and Pressure relief devices
  - Skin care and hygiene
- Compensatory
  - Caregiver education regarding mobility
  - Mechanical Hoyer Lift

ALS- General Exercise Recommendations

- Avoid Maximal Strengthening
- Avoid Heavy Eccentric Training
- Avoid excessive fatigue
- Moderate intensity strengthening can increase strength (indicated for individuals with MMT 3 or >)



"The current state of the evidence indicates that current practice guidelines for physical therapy management heavily relies on expert opinion and consensus, although physical therapy research is being to emerge."

Bello-Haas VD. Physical therapy for individuals with amyotrophic lateral sclerosis: current insights. Degenerative neurological and neuromuscular disease. 2018;8:45-54.

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