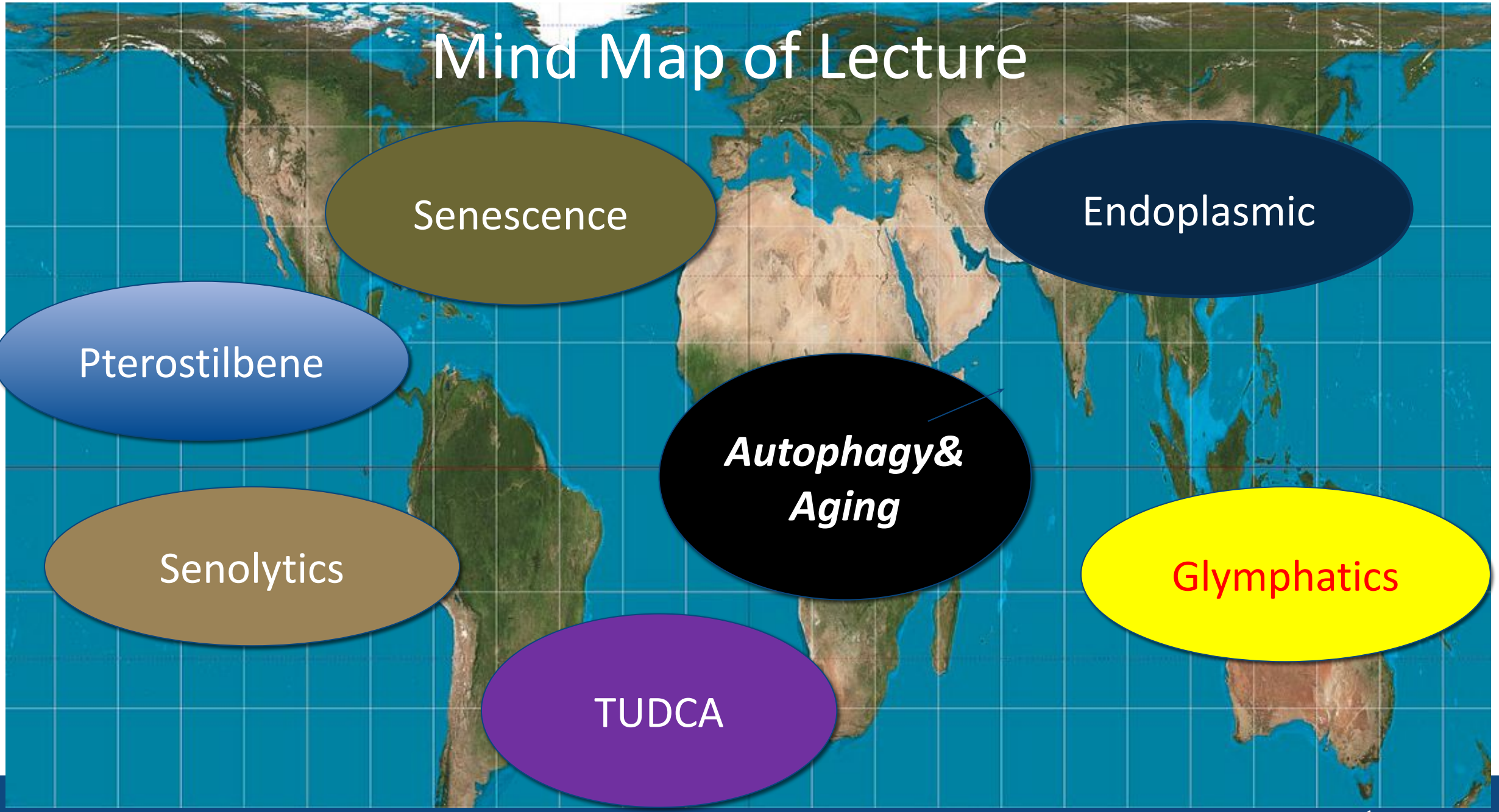
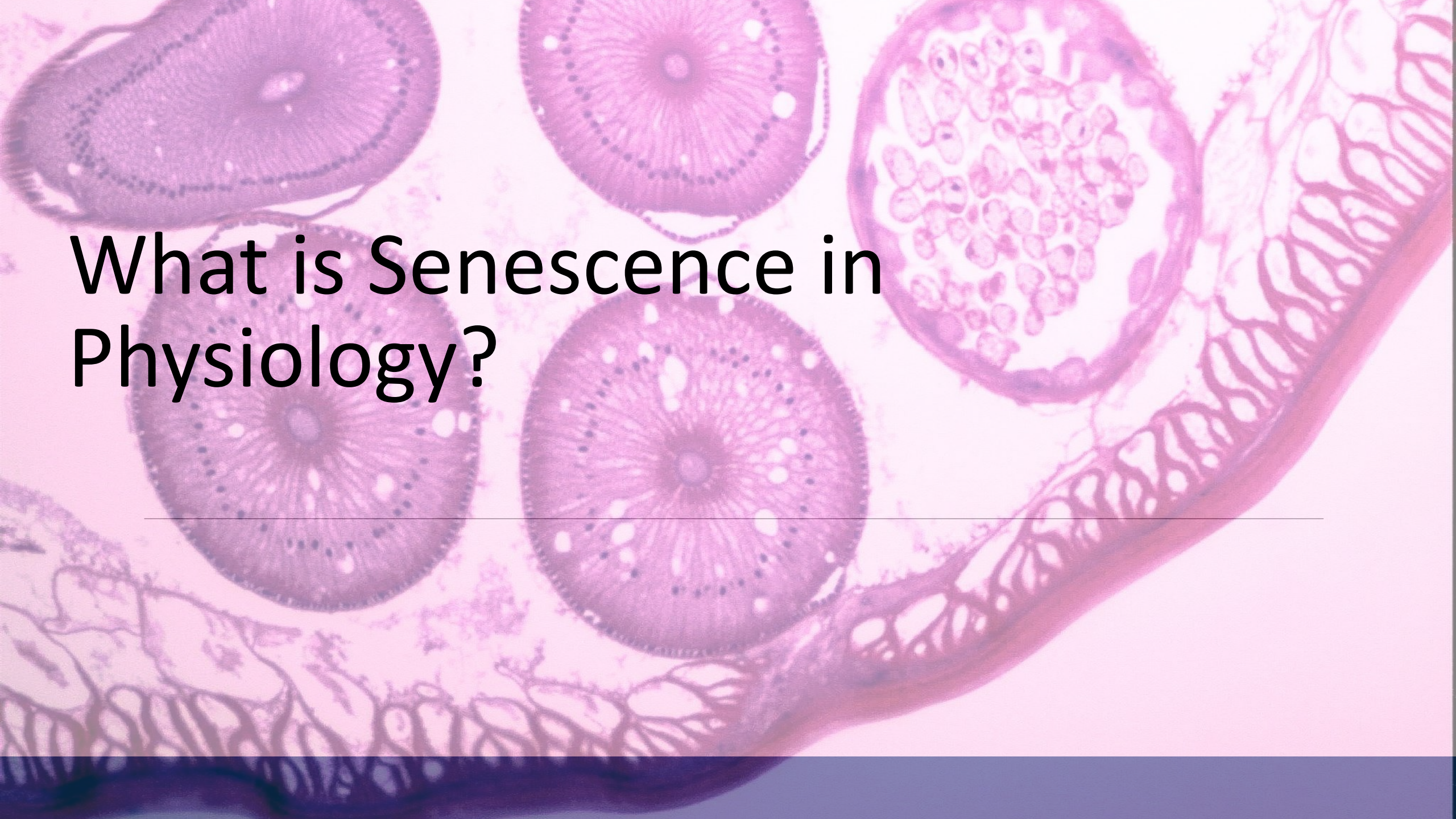
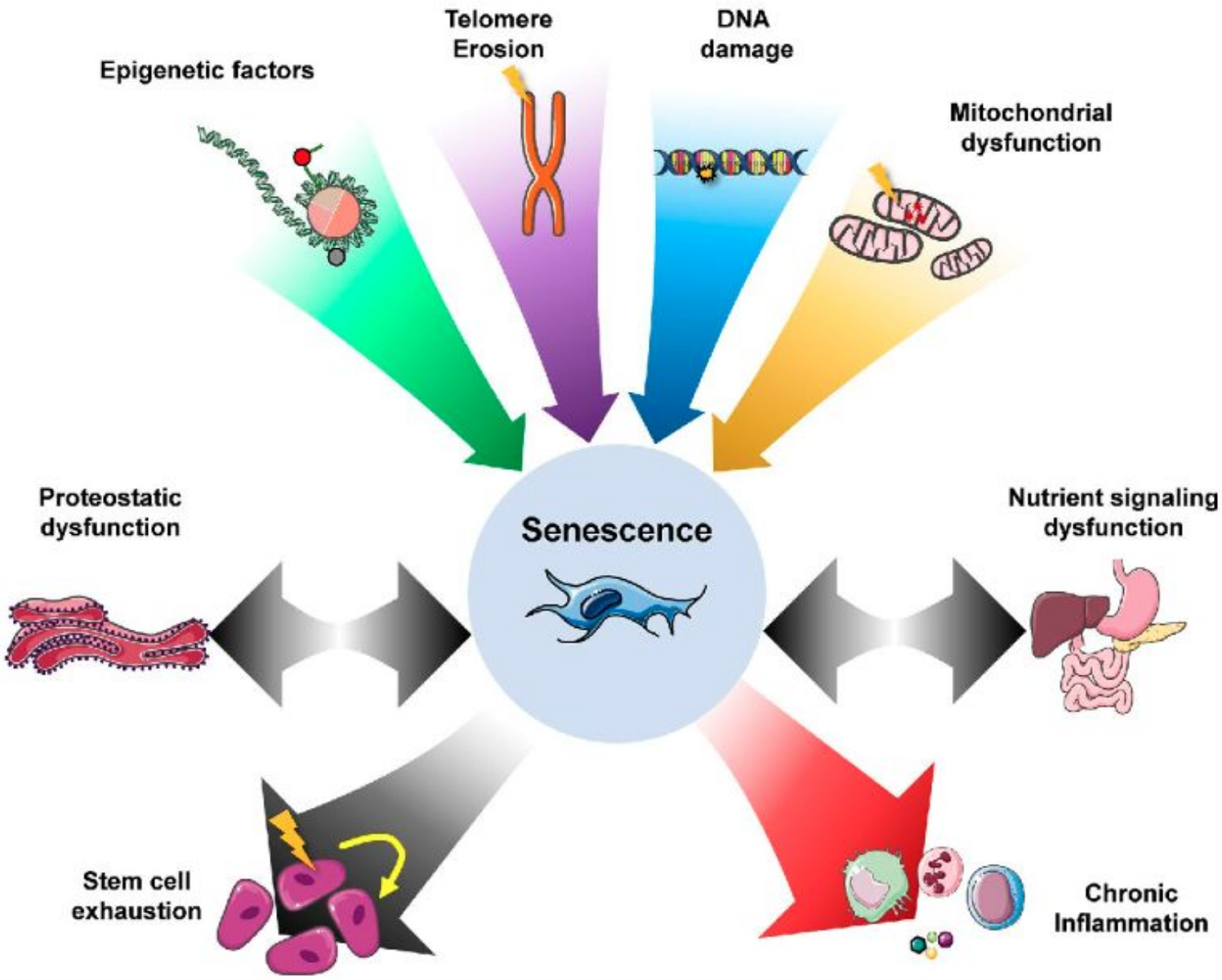
Mind Map of Lecture





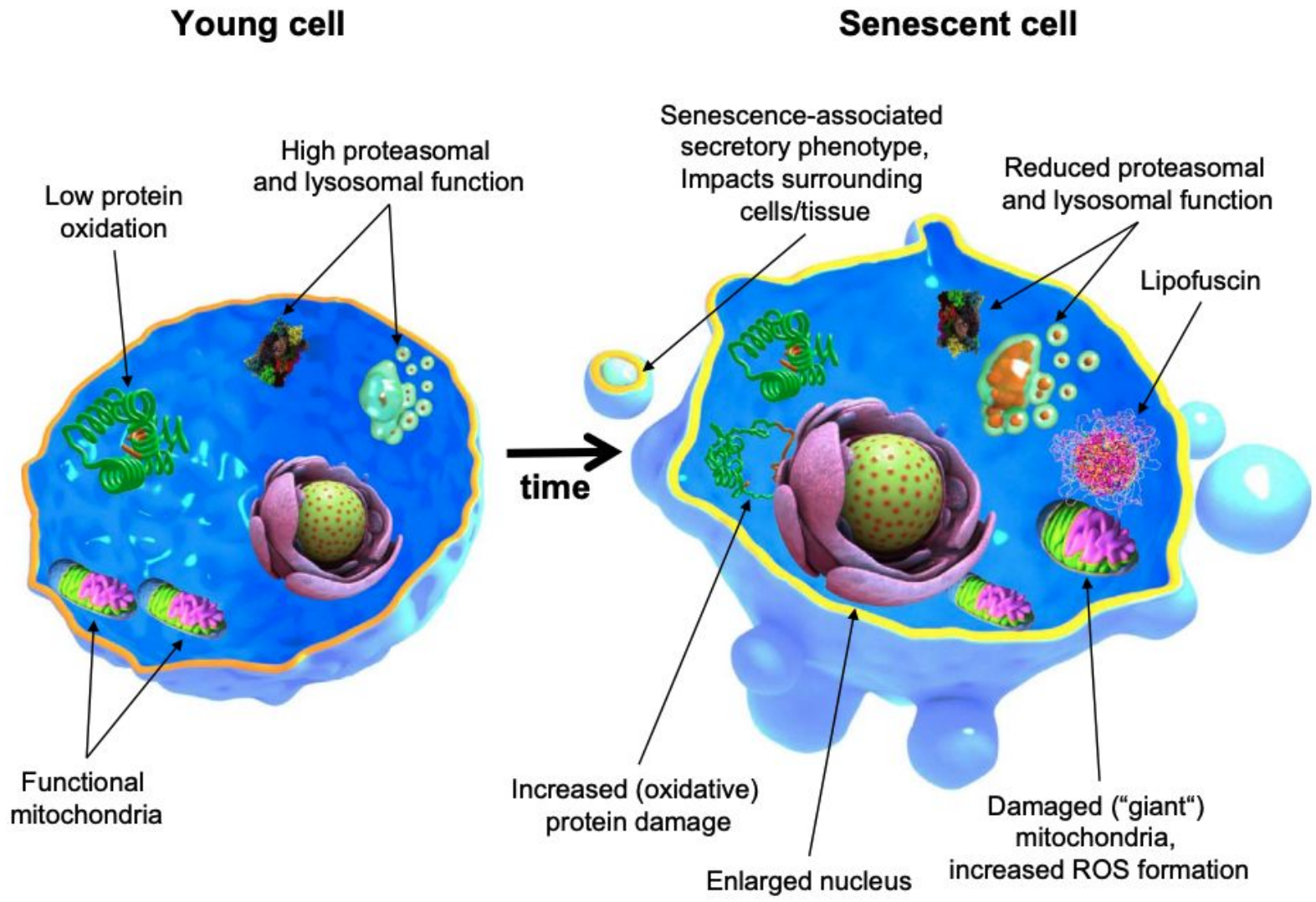
What is Senescence in Physiology?

Senescence as a Central Hallmark of Aging



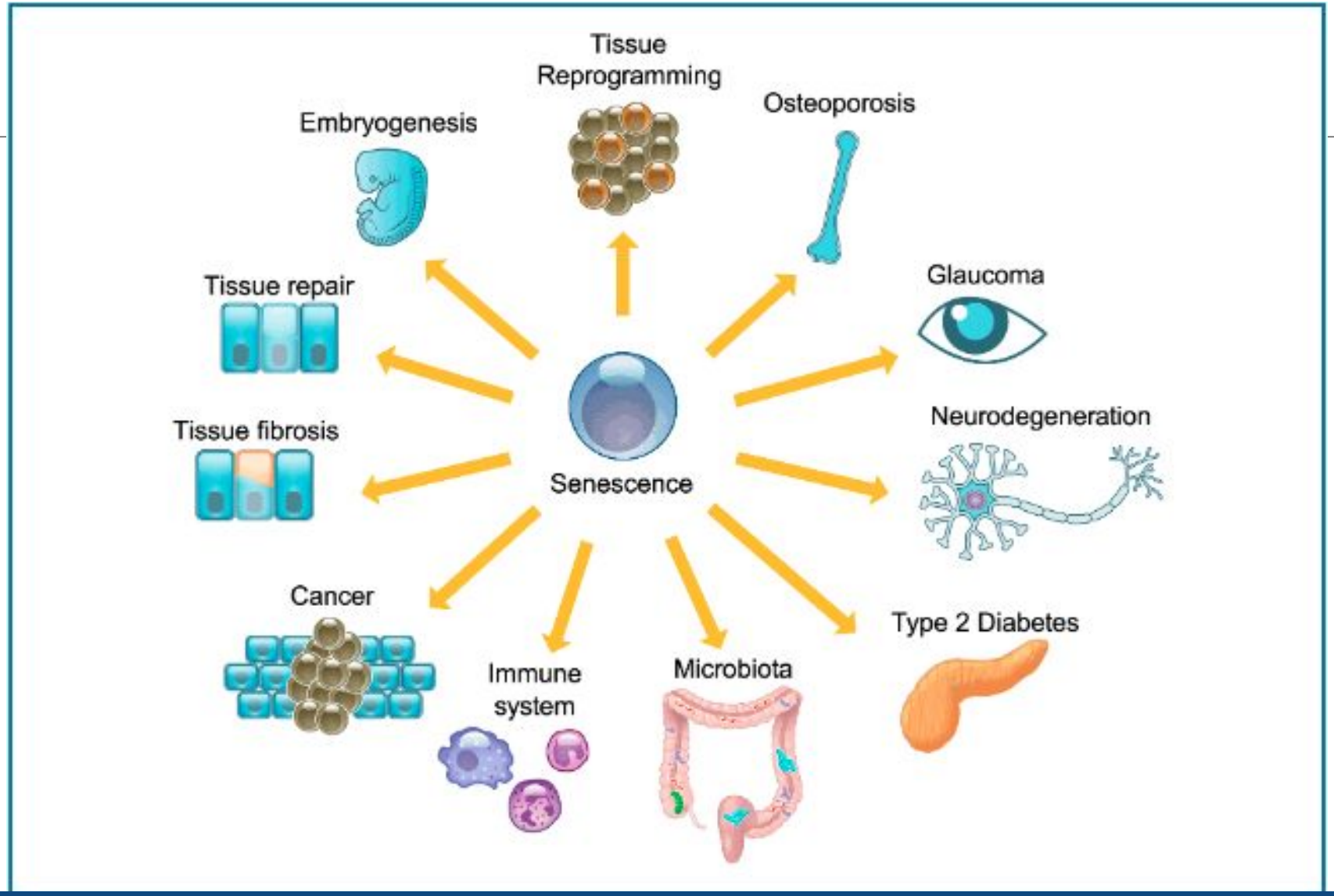
McHugh D, Gil J. Senescence and aging: Causes, consequences, and therapeutic avenues. *J Cell Biol*. Jan 2 2018;217(1):65-77.

Cellular & Molecular Features of Young & Aged Cells



Höhn A, *et al*. Happily (n)ever after: Aging in the context of oxidative stress, proteostasis loss and cellular senescence. *Redox Biol*. Apr 2017;11:482-501.

Consequences of Cellular Senescence



Calcinotto A, *et al*. Cellular Senescence: Aging, Cancer, and Injury. *Physiol Rev*. 2019;99(2):1047-1078.

Autophagy

Autophagy is the body's way of cleaning out damaged cells, in order to regenerate newer, healthier cells within the cell itself

Impaired Autophagy leads to Aging and Senescecne



Glymphatic System

The glymphatic system's role in clearing metabolic waste and proteins from the brain is linked to autophagy, a process that removes damaged mitochondria from cells

- **Glymphatic system function**
- The glymphatic system is a network that clears metabolic waste and proteins from the brain. When the glymphatic system is impaired, waste and proteins build up in the brain, which can lead to neurodegenerative diseases and cognitive decline.

Triggers of cellular senescence and Impaired autophagy

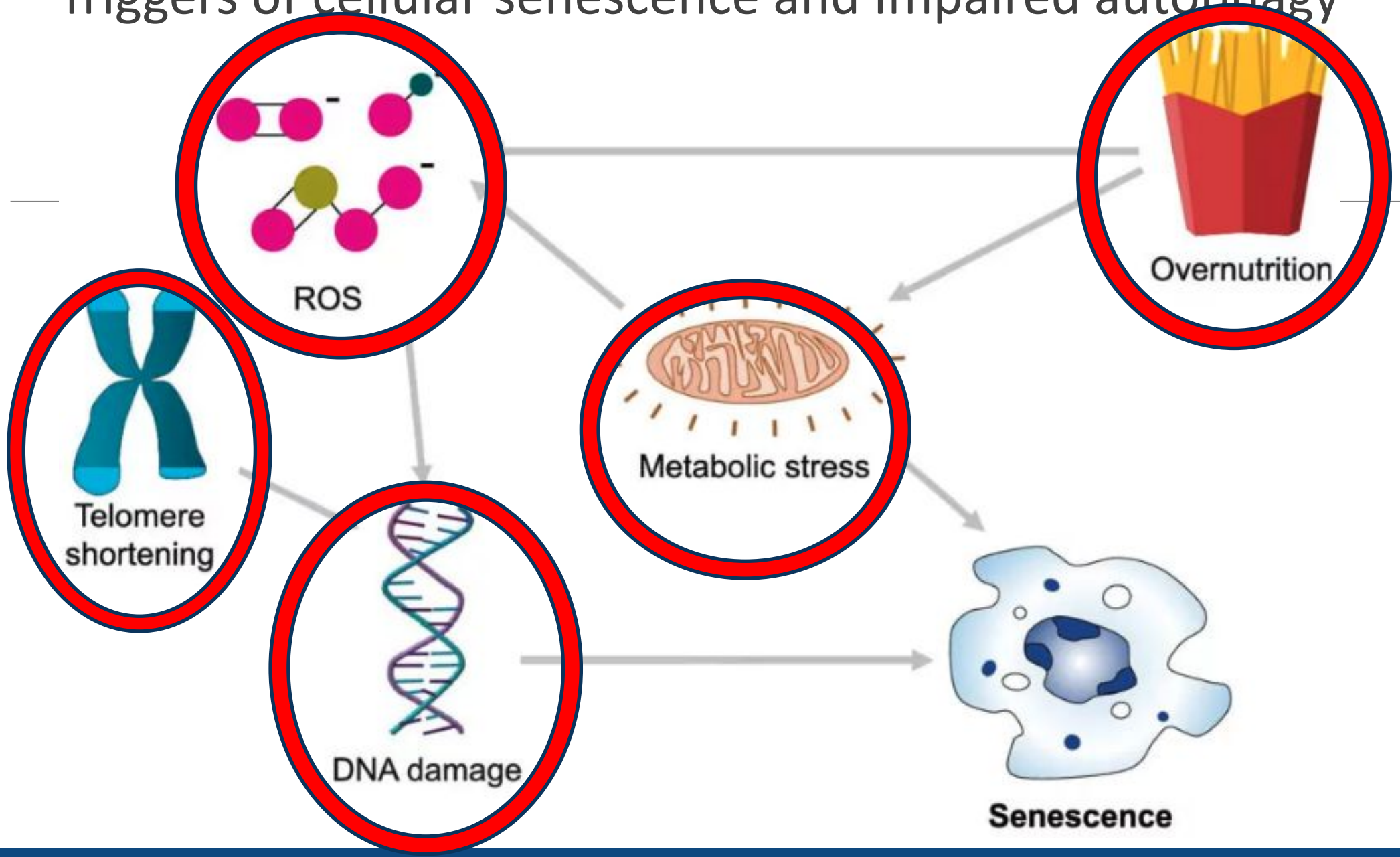


Image Modified from Amaya-Montoya M, *et al*. Cellular Senescence as a Therapeutic Target for Age-Related Diseases: A Review. *Adv Ther* Apr 2020;37(4):1407-1424.

Fecal microbiota transplantation (FMT) is a procedure that involves transferring stool from a healthy donor to a patient's gut to treat neurological disorders. FMT has shown promising results in research on neurodegenerative diseases, including:

- **Alzheimer's disease (AD)**: FMT can improve cognitive function, reduce Aβ plaque burden, and reduce neuroinflammation. FMT can also reverse the disturbance of gut microbiota in AD mice and enhance learning and memory ability.
- **Parkinson's disease (PD)**: FMT can improve motor function, reduce dopaminergic neuron loss, and reduce tremor. FMT can also alleviate physical impairment in PD mice.
- **Amyotrophic lateral sclerosis (ALS)**: FMT can improve bowel function and ALS symptoms.

Interventions in Senescence and Autophagy

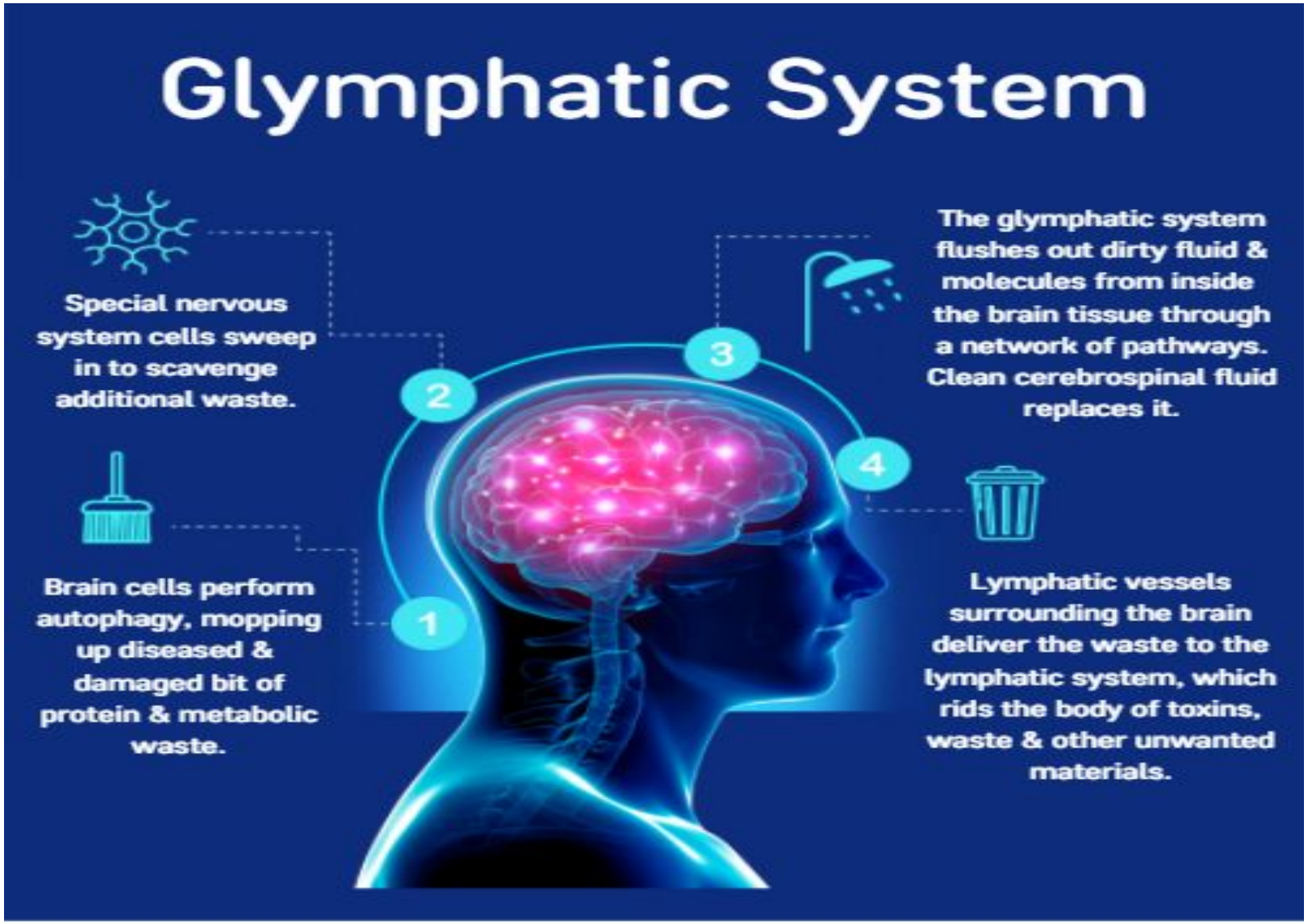
Support the glymphatic system

Support autophagy

Glymphatic

5 Choices to help Glymphatic System In the Brain

- Sleep
- Exercise
- Hydrate
- Healthy Microbiome
- Adaptogens



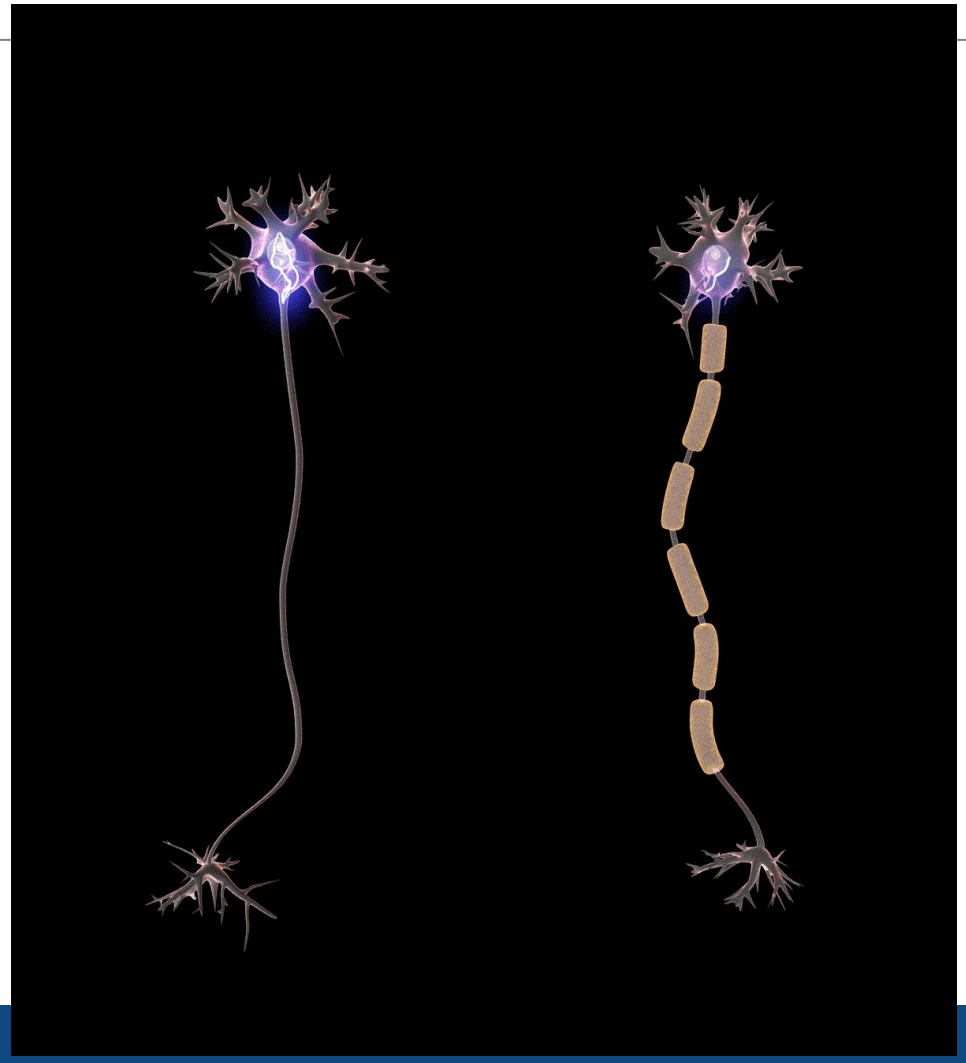
Stimulate Autophagy

- **Berberine**: This plant alkaloid triggers autophagy in a wide range of cell types, including liver, kidney, breast, myocardium, macrophages, lung, and neuron cells.
- **Curcumin**: Can enhance autophagy to protect cells from oxidative stress.
- Pterostilbene: Can boost autophagy by regulating the levels of key proteins.
- **Green tea**: Polyphenols in green tea can induce autophagy.
- **Coffee**: Caffeine promotes autophagy in skeletal muscle
- **Extra virgin olive oil**: Increases autophagy of brain cells.
- **Oily fish**: Polyunsaturated fats in fish oils may promote autophagy.
- **Spermidine**: found in wheat grass to stimulate autophagy.

Autophagy

Diet and Exercise4

- **Fasting**: Prolonged fasting for two to three days can increase autophagy by depriving the body of nutrients and stressing cells.
- **Exercise**: Physical exercise can damage cells, which triggers autophagy.
- **Ketogenic diet**: This diet deprives the body of carbohydrates, which can increase autophagy.



Impaired Autophagy and Glymphatics causes neurodegeneration

Podbielska, Maria et al. “Myelin Recovery in Multiple Sclerosis: The Challenge of Remyelination.” *Brain Sciences* 3.3 (2013): 1282–1324. *PMC*. Web. 4 Sept.2017.

Interventions in Senescence and Autophagy

Tauroursodeoxycholic acid 500 mg
Organic Ashwagandha Root 350 mg
Nicotinamide Riboside 250 mg
Pterostilbene 100 mg

Asian Black Bear



TUDCA – Tauroursodeoxycholic

It is a bile acid that is found in trace amounts in the human body.

Bile acids are compounds released from the gallbladder that help digest fats.

TUDCA

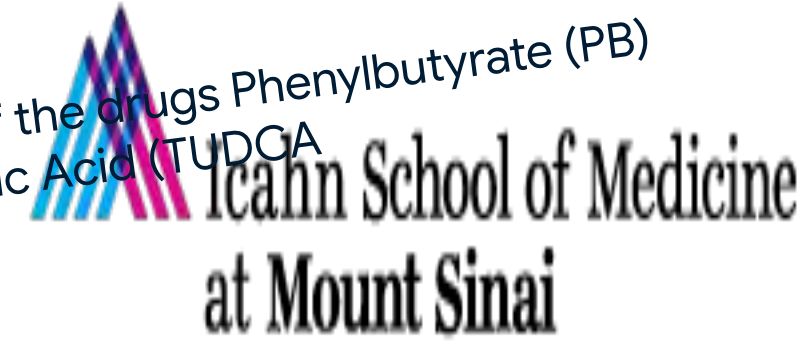
Promote healthy nerve cells

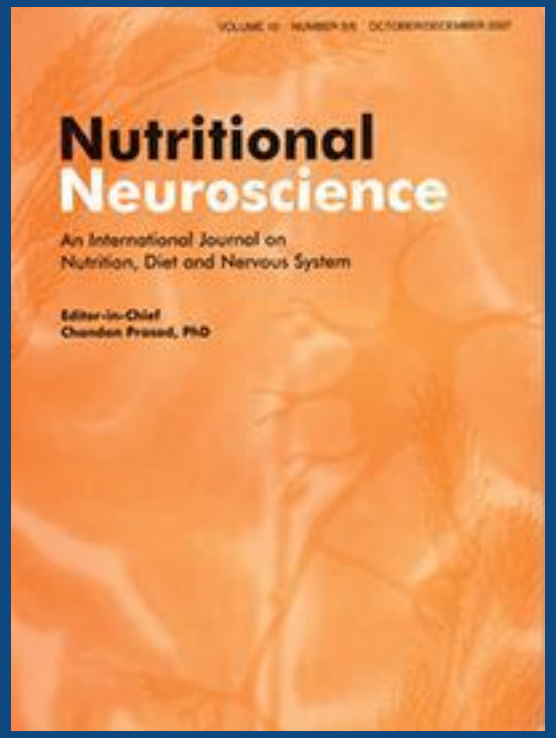
TUDCA – Tauroursodeoxycholic is a bile acid that is found in trace amounts in the human body. Crosses the blood-brain barrier accessing neuronal tissues.

Animal bile has been used in traditional Chinese medicine for thousands of years because of its potential pharmacological action to help with longevity

Current clinical trial for Alzheimer's disease

involves a combination of the drugs Phenylbutyrate (PB) and Tauroursodeoxycholic Acid (TUDCA





Parkinsons

A study in Nutritional Neuroscience found that pretreatment with TUDCA protected against dopaminergic neuronal damage in a model of Parkinson's disease. The study also found that TUDCA may attenuate the effects of autophagy, which may be involved in the progression of Parkinson's disease

Progressive MS

ongoing clinical trials investigating the use of TUDCA (tauroursodeoxycholic acid) in patients with progressive multiple sclerosis (MS),

TUDCA supplementation in individuals with low bile acid levels and progressive MS; this trial is registered as NCT03423121 on ClinicalTrials.gov.



JOHNS HOPKINS
MEDICINE

TUDCA Clinical Trials

- Amyotrophic lateral sclerosis (ALS)
- Alzheimer's disease
- Parkinson's disease
- Huntington's disease
- Multiple Sclerosis
- John Hopkins University
- European Commission

NAD/ Nicotinamide riboside

Efficient precursor to NAD+

A coenzyme vital to cellular health and to many biological functions.

Essential to the production of energy in the body and brain.

NAD+ levels decline with age and can impact healthy neurological and cellular aging processes.

.

Most clinical trials investigating NR currently focus on its effects on metabolic health, neurodegenerative diseases, and aging, where autophagy is considered a relevant pathway

CLINICAL AND TRANSLATIONAL REPORT Volume 34, Issue 3P396-407.E6March 01, 2022***Open access***Download Full Issue

The NADPARK study: A randomized phase I trial of nicotinamide riboside supplementation in Parkinson's disease

Brage Brakedal[1,2,9] · Christian Dölle[1,2,9] · Frank Riemer[1,3,10]. … · Renate Grüner[3] · David Eidelberg[4] · Charalampos Tzoulis[1,2,11] charalampos.tzoulis@uib.no… Show more

Pterostilbene induces autophagy

Stilbenes are Phenolic Compound found in many fruits such as grapes and blueberries.

Pterostilbene and resveratrol are structurally very similar and Pterostilbene has better bioavailability.

Pterostilbene reduces oxidative stress contributing to neuroprotective effects.

Pterostilbene supports cognition and working memory.



PTEROSTILBENE MAY PROTECT NEURONS IN VARIOUS NEURODEGENERATIVE DISORDERS

ALS

Multiple Sclerosis

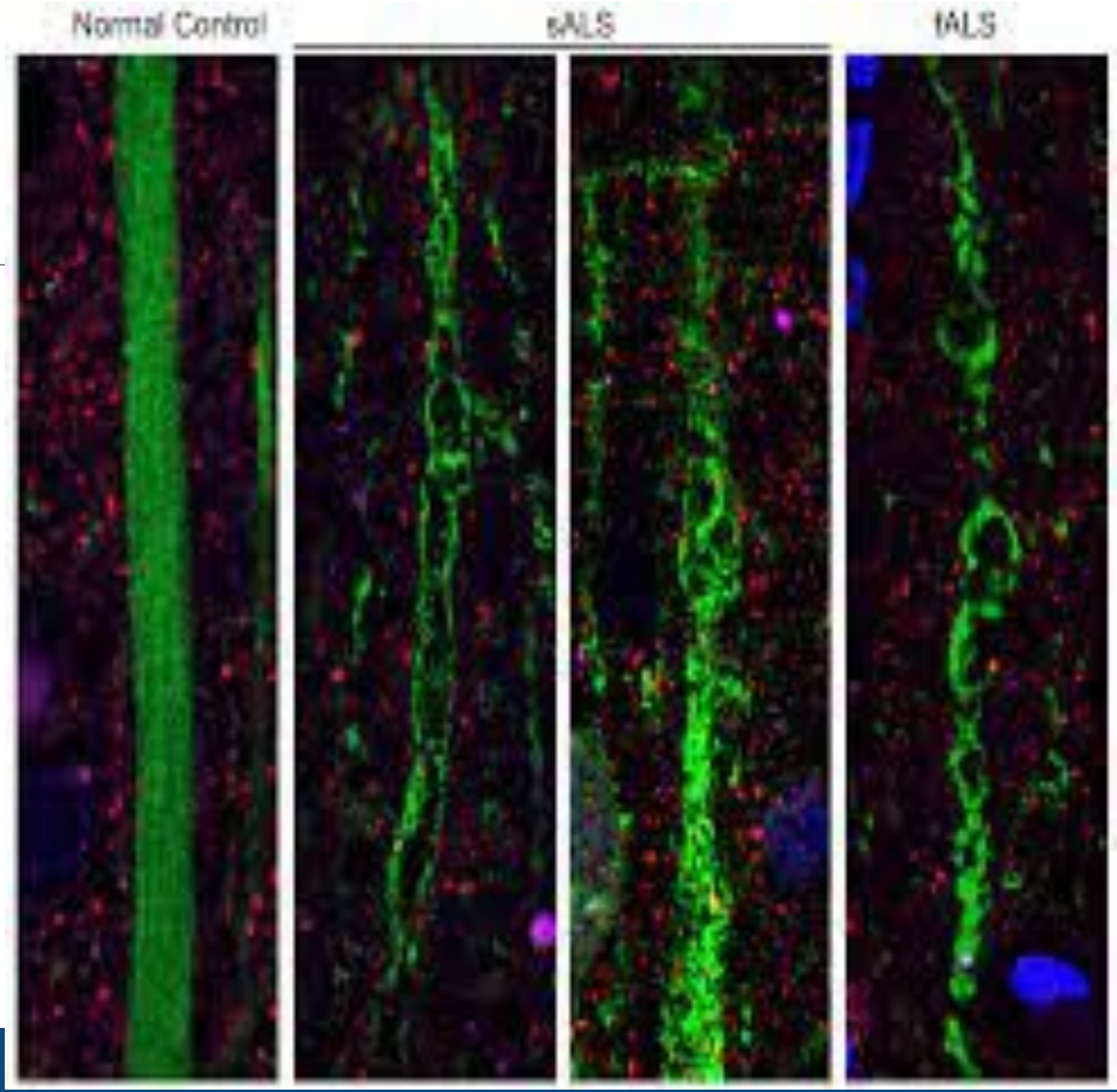
Mol Neurobiol 2021 Apr

Nicotinamide Riboside and Pterostilbene Cooperatively Delay Motor Neuron Failure in ALS SOD1G93A Mice

One human clinical trial showed that the combination of nicotinamide riboside (NR) and pterostilbene to increase the survival motor neurons in and ALS patients.

Neuroscience 2022 Apr 1

Pterostilbene Protects the Optic Nerves and Retina in a Murine Model of Experimental Autoimmune Encephalomyelitis via Activation of SIRT1 Signaling



Autophagy within the Lungs

Autophagy is the body's way of cleaning out damaged cells, in order to regenerate newer, healthier cells within the cell itself



RESTORATIVE FORMULATIONS

Impaired Autophagy Due to Smoking in COPD

It has been proposed that the pathology of **COPD** is associated with accelerated lung **aging**. In adults, lungs undergo a progressive decline in its ...

The dysregulation of autophagy in COPD

Dysregulated autophagy in COPD: A pathogenic process to ...

Bose A, Beal MF. Mitochondrial dysfunction in Parkinson's disease. J Neurochem. 2016

Lung Senescence

It has been proposed that the pathology of **COPD** is associated with accelerated lung **aging**. In adults, lungs undergo a progressive decline in its ...

COPD

Senolytic compounds containing Fisetin and Tudca

Turmeric Curcumin Products 2 caps 5 times a day

70 year old male

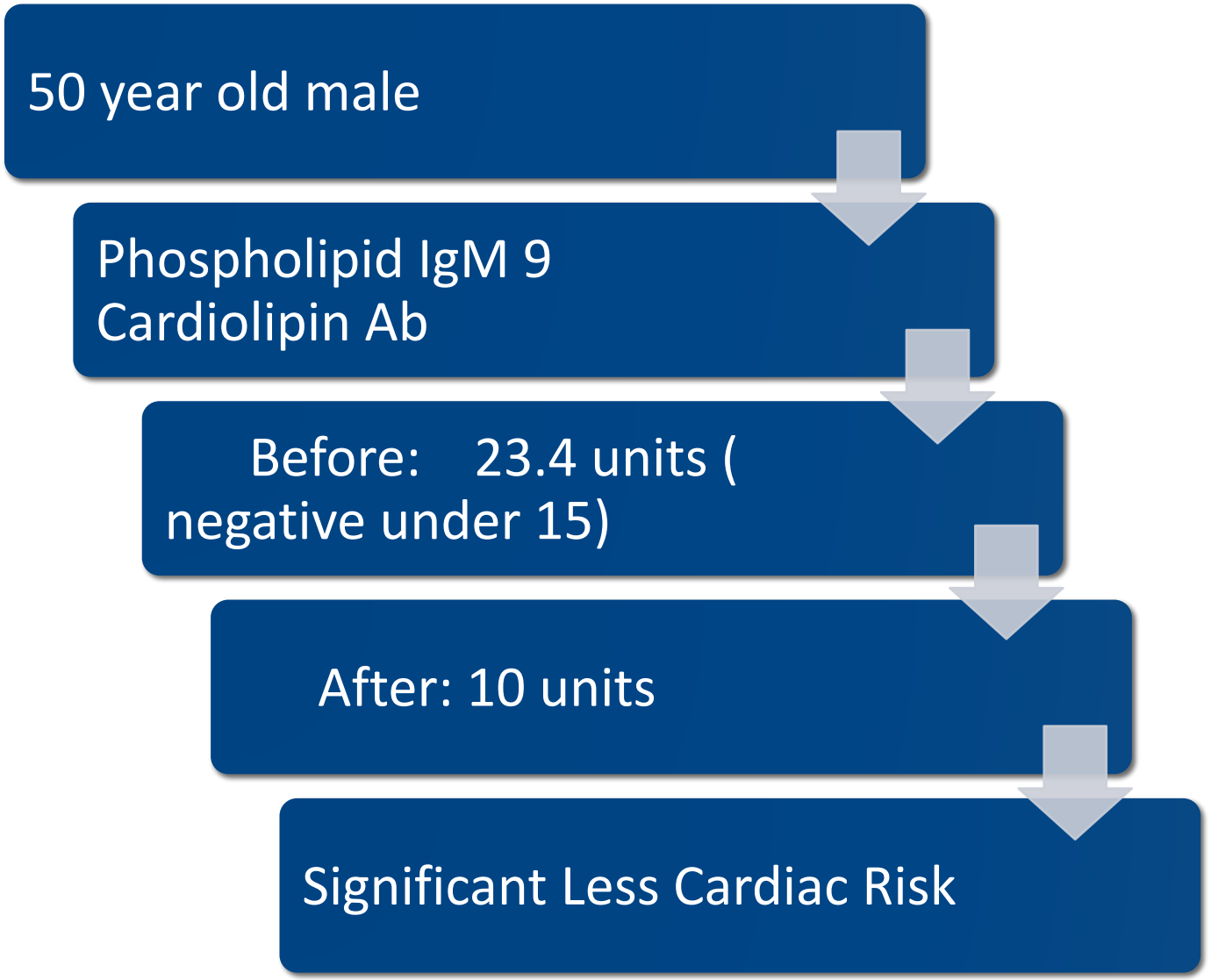
Before: Spirometry
Function 45%

After : Spirometry
Function 54%

Now can walk 45 minutes versus 10 minutes

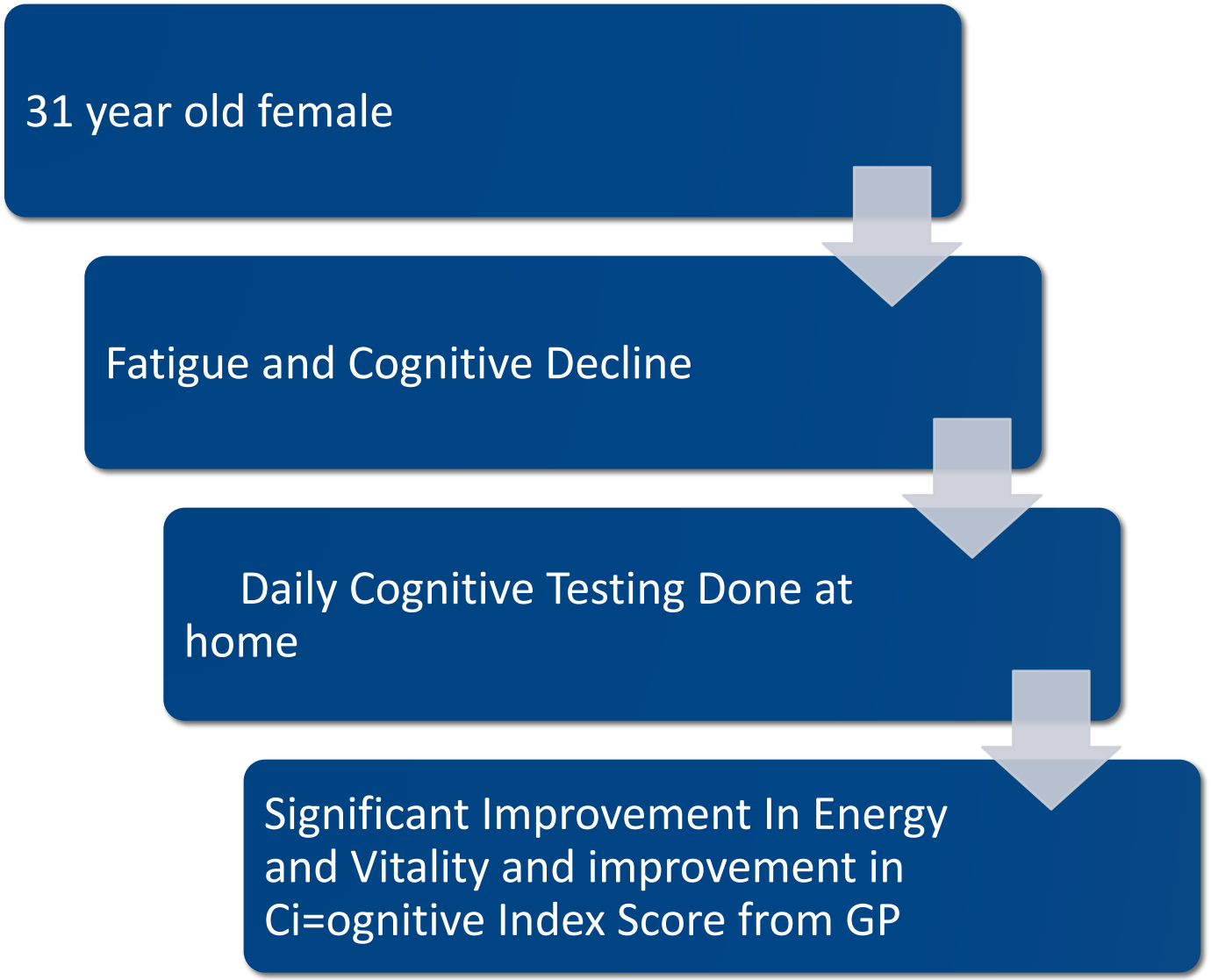
Lupus Coagulation Disorder Anti –Phospo-Lipids

TUDCA PX 2 caps BID for three months



Biliary dyskinesia

TUDCA PX 2 caps BID for two weeks

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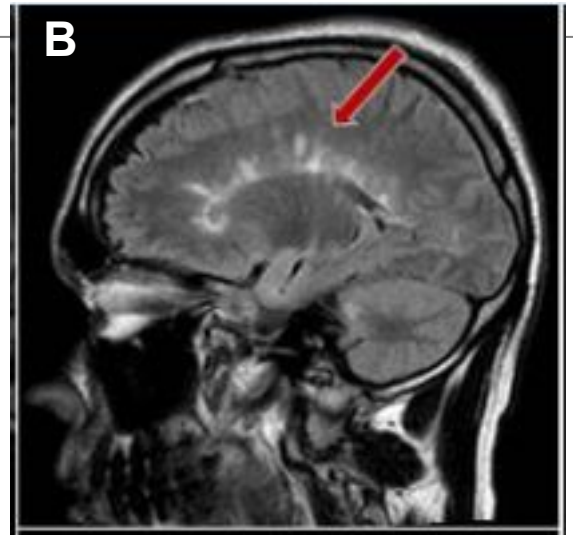
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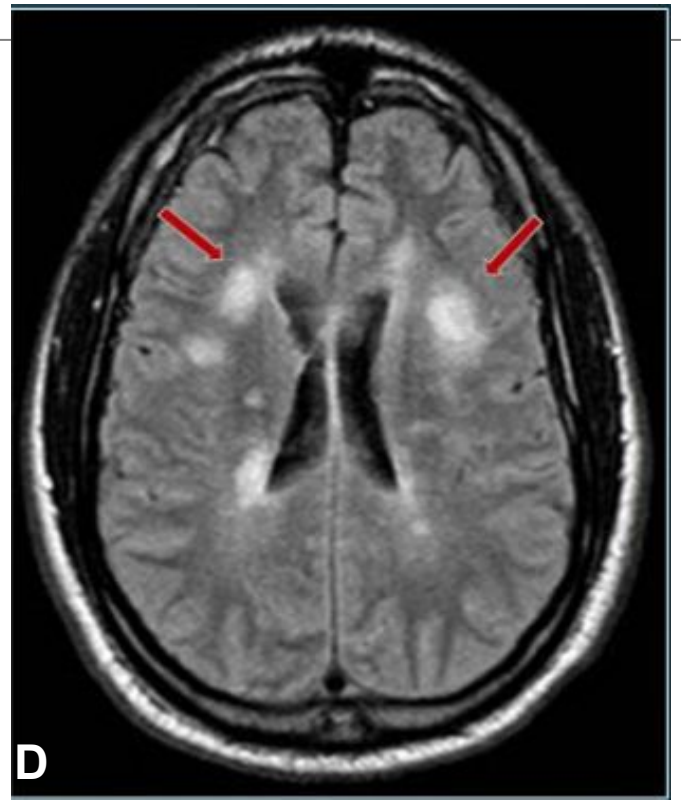
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SOCIAL SECURITY
DISABILITY CLAIM
APPROVED
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NA
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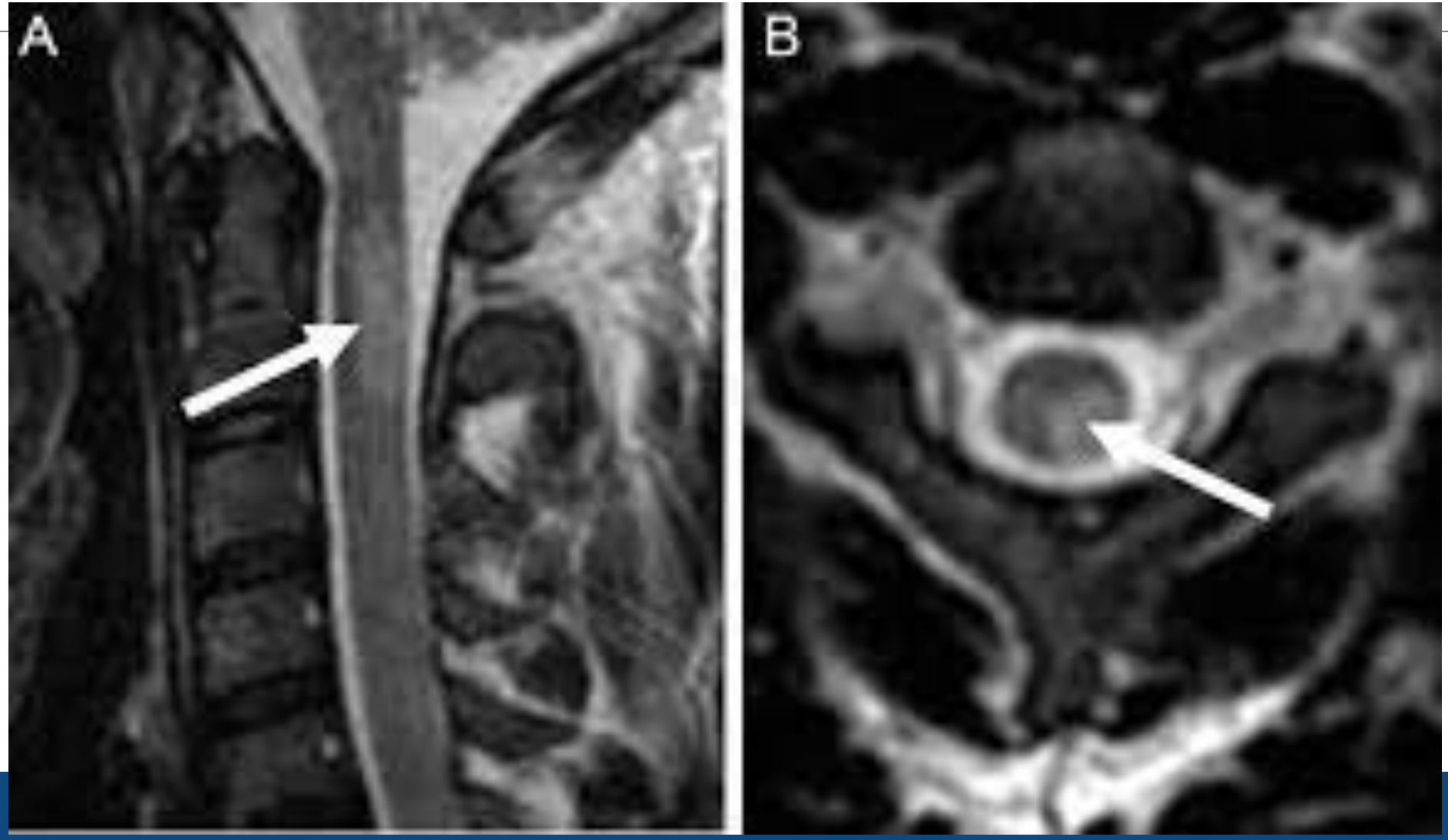
POLICYHOLDER'S INFORMATION
123 456-7890



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B






STEINWAY & SONS


WHO AM I?
TEDEd

I have Aphasia

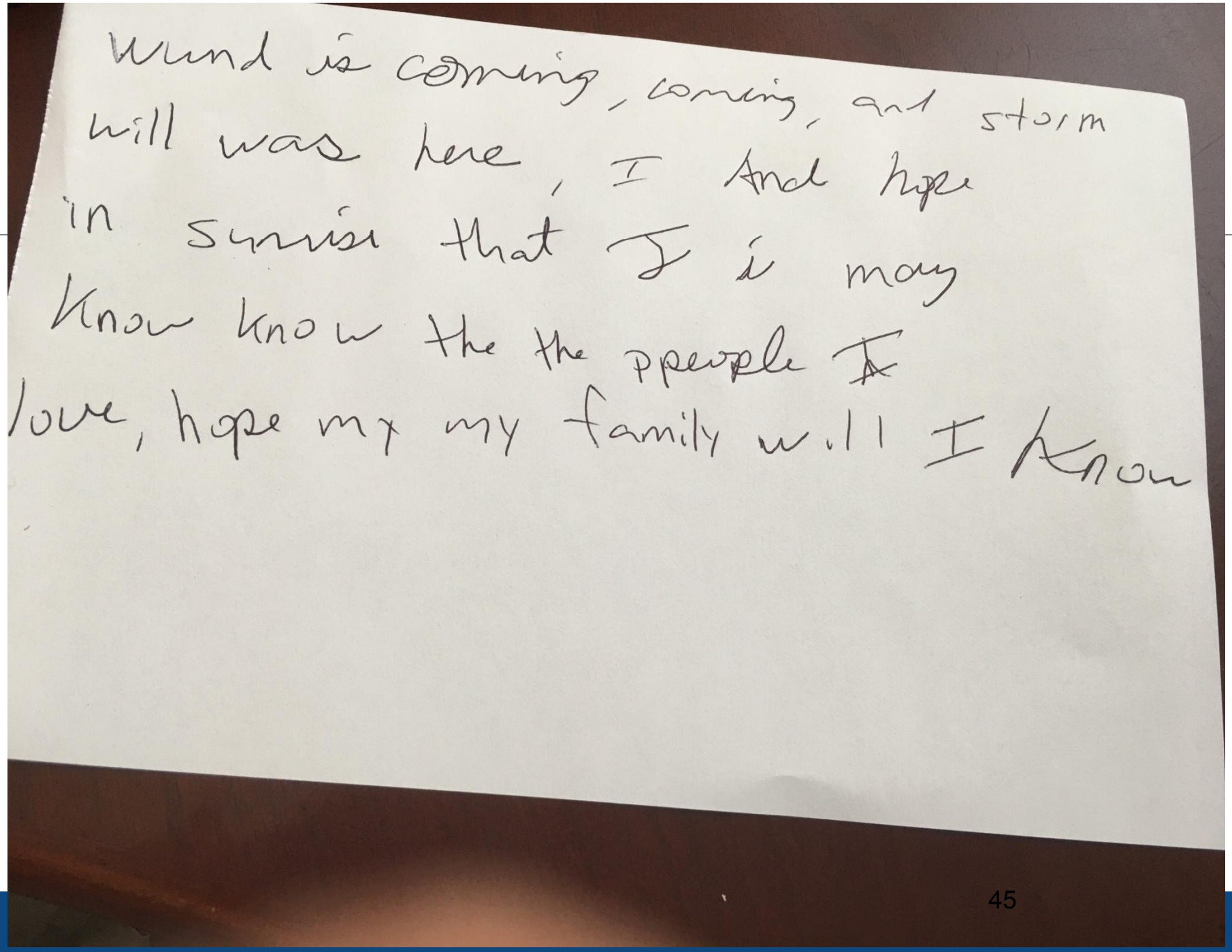
Aphasia affects my ability to SPEAK and can also affect reading, writing and understanding. My *intellect is not affected* -- only language!

Please take time to communicate with me:

- **Speak SLOWLY & Clearly**
- **Use SHORT sentences**
- **Give me TIME to respond**
- **Ask YES/NO questions**
- **Shouting doesn't help**
- **Keep it SIMPLE**

Thank you for your patience & understanding!




Wind is coming, coming, and storm
will was here, I And hope
in sunrise that I i may
know know the the people I
love, hope my my family will I know





Fasting

TUDCA

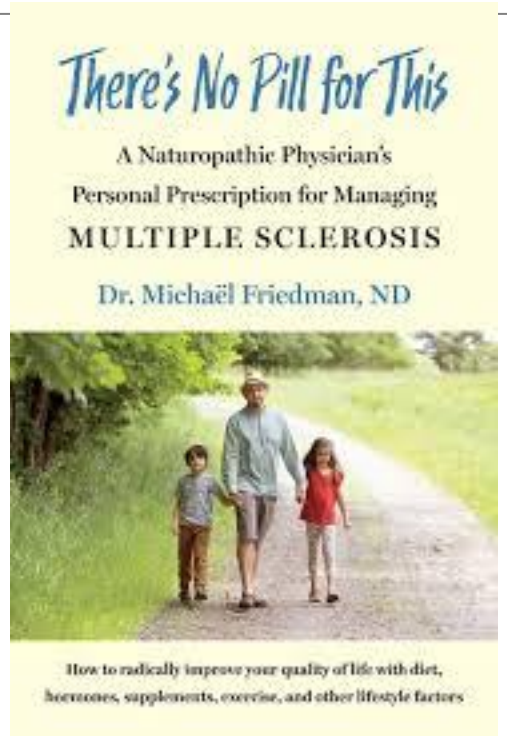
Nicotinamide Riboside

Pterostilbense

Ashwaganda

Goldenseal Berberine Combination

Bill Mitchel’s Fruit Anthocyanin Blend


There's No Pill for This
A Naturopathic Physician's
Personal Prescription for Managing
MULTIPLE SCLEROSIS
Dr. Michaël Friedman, ND
How to radically improve your quality of life with diet, hormones, supplements, exercise, and other lifestyle factors