

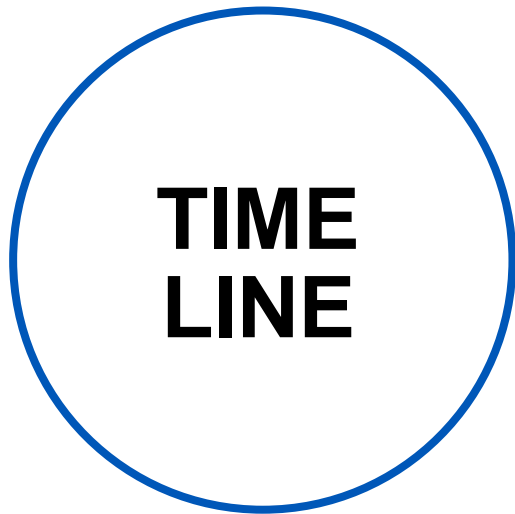


EXERCISE & PARKINSON'S DISEASE

MEDICAL EVIDENCE FOR A STRONG RELATIONSHIP

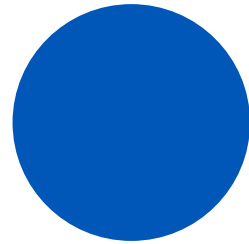
Philip W. Tipton, M.D. | Parkinson's Exercise Abilities Conference

November 14, 2020



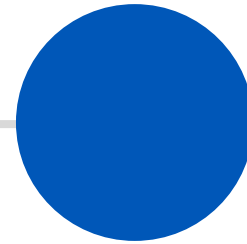
TIME LINE

NOVEMBER 14, 2020



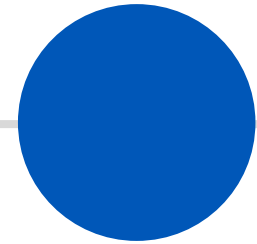
1. Introduction to the nervous system
2. Concept of neurodegeneration
3. Studying exercise & neurodegeneration
4. Animal studies

MARCH 20, 2021



1. Rapid review
2. Human studies of Alzheimer's disease
3. Human studies of Parkinson's disease

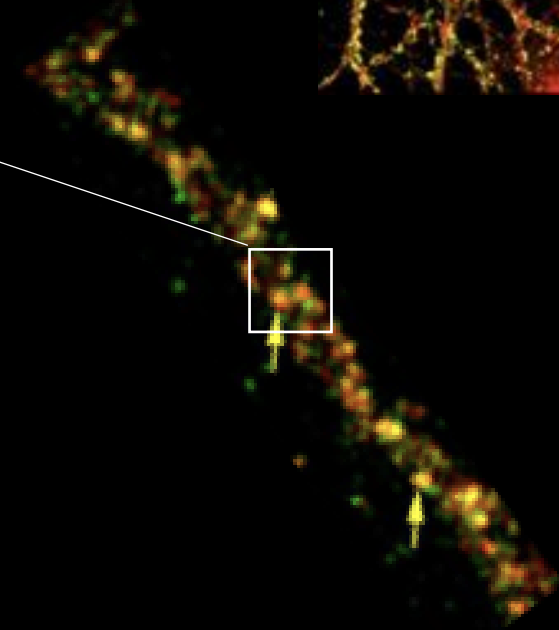
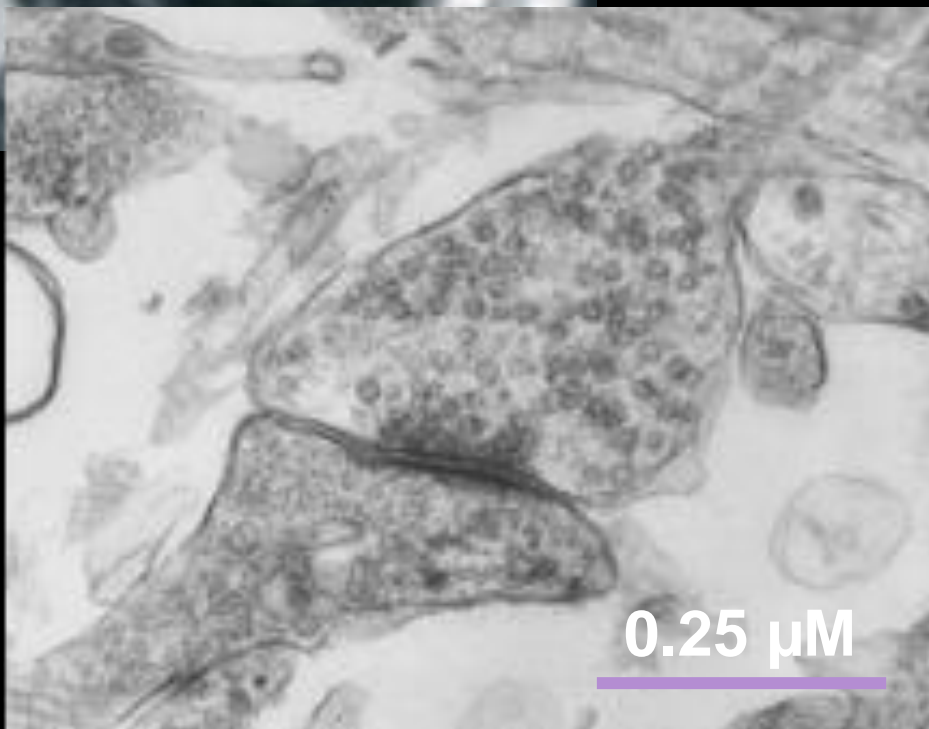
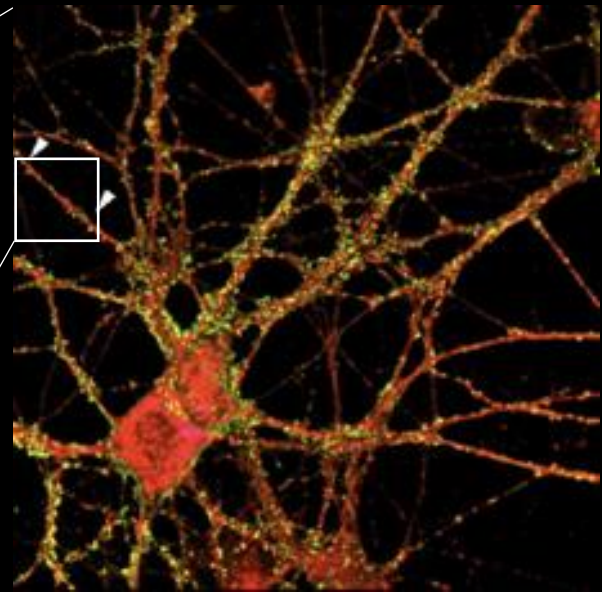
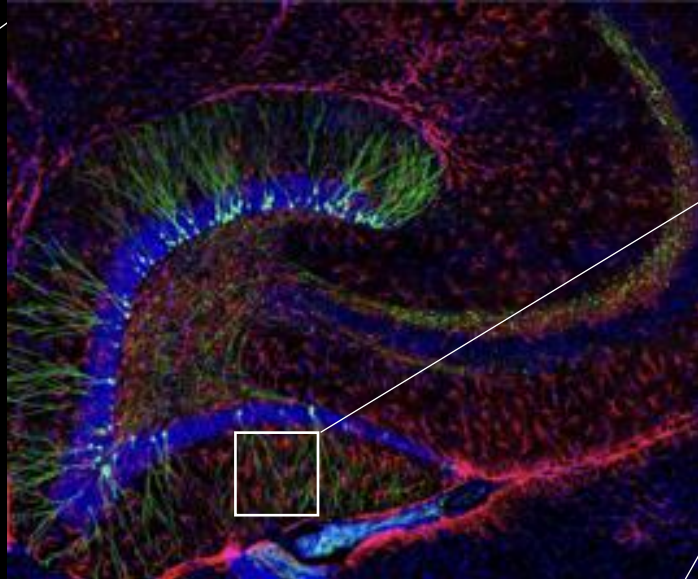
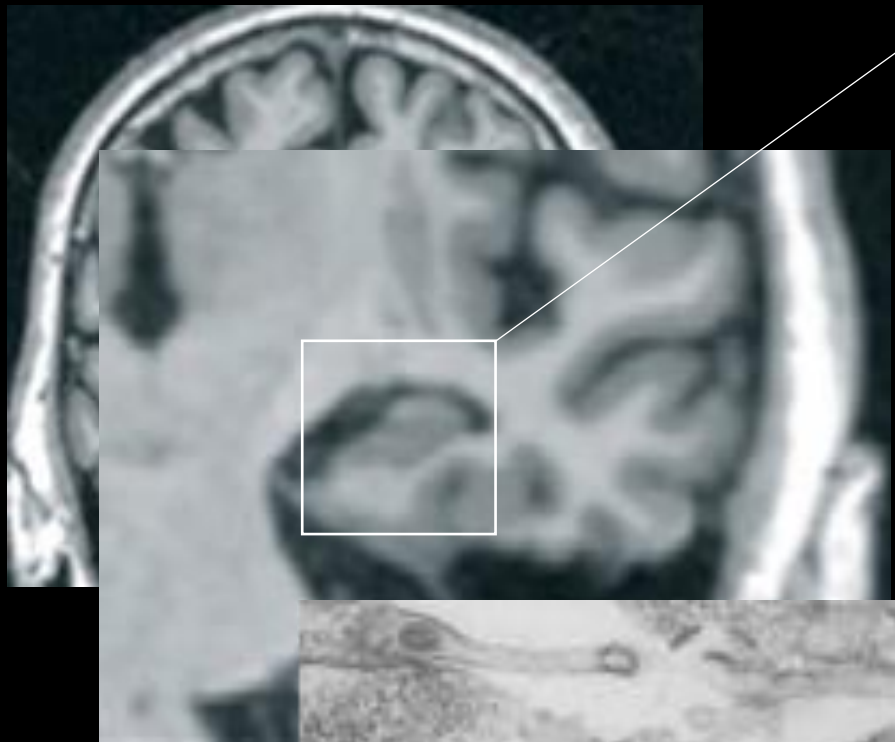
MAY 22, 2021

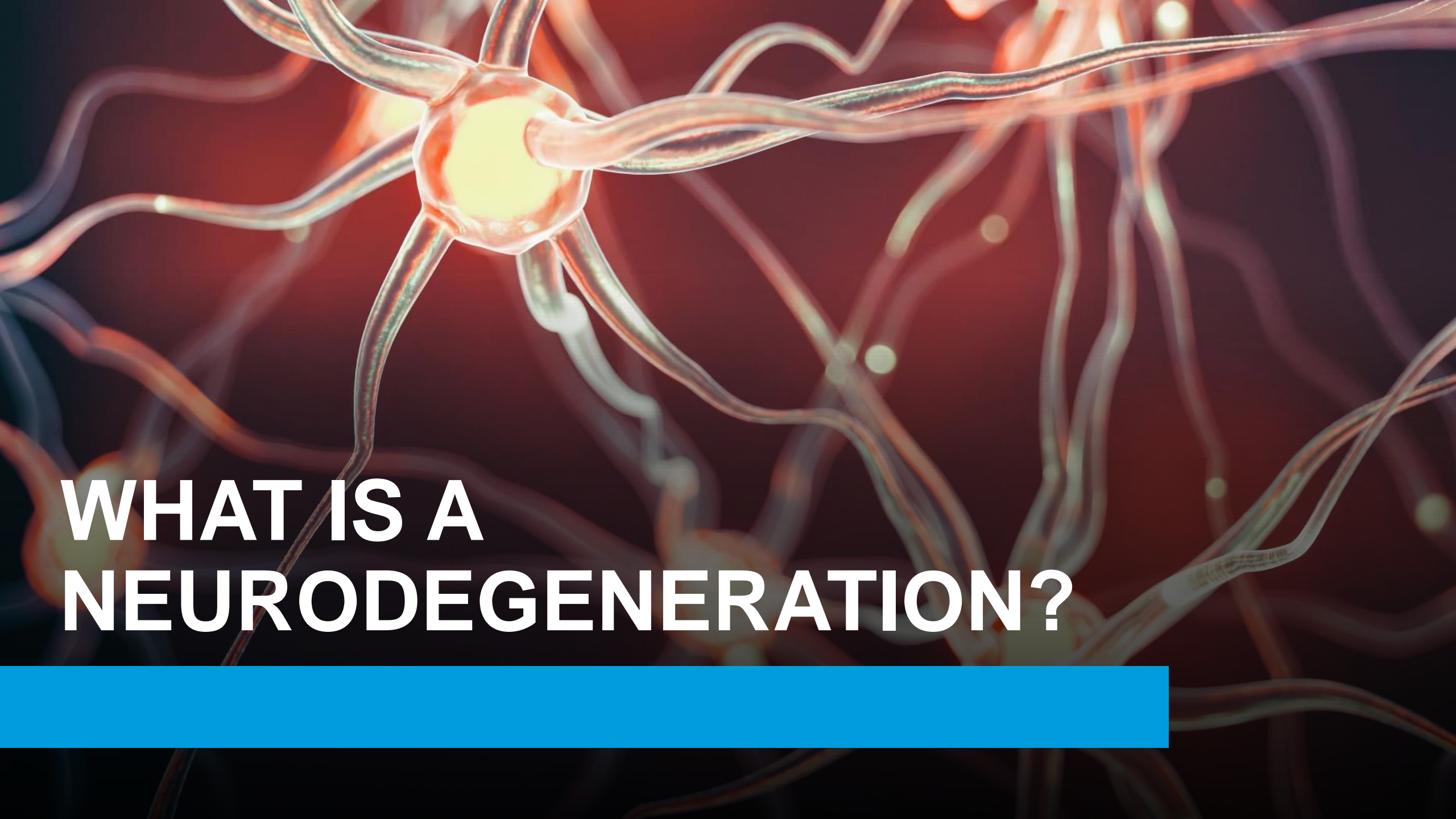


1. Rapid review & summary of evidence
2. Call to action

INTRODUCTION TO THE NERVOUS SYSTEM

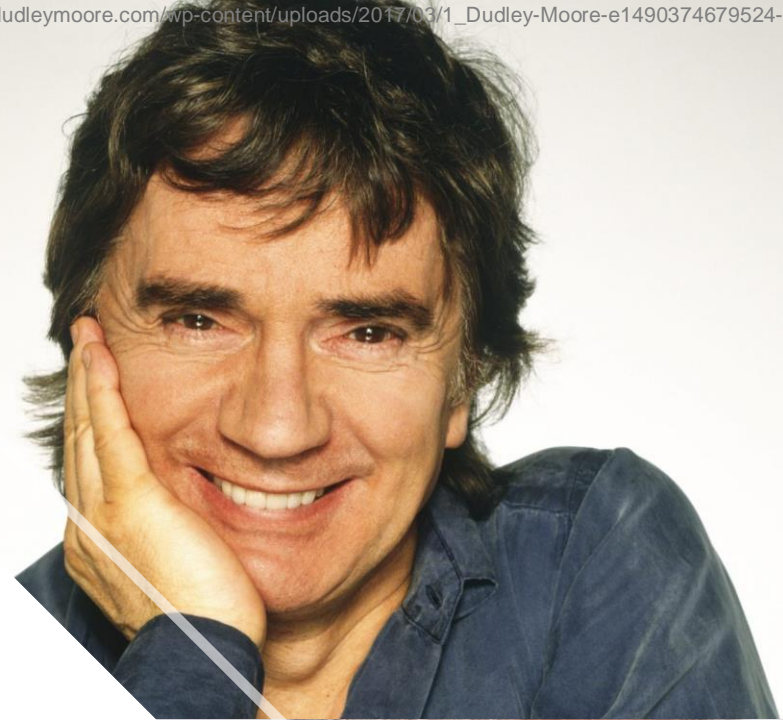
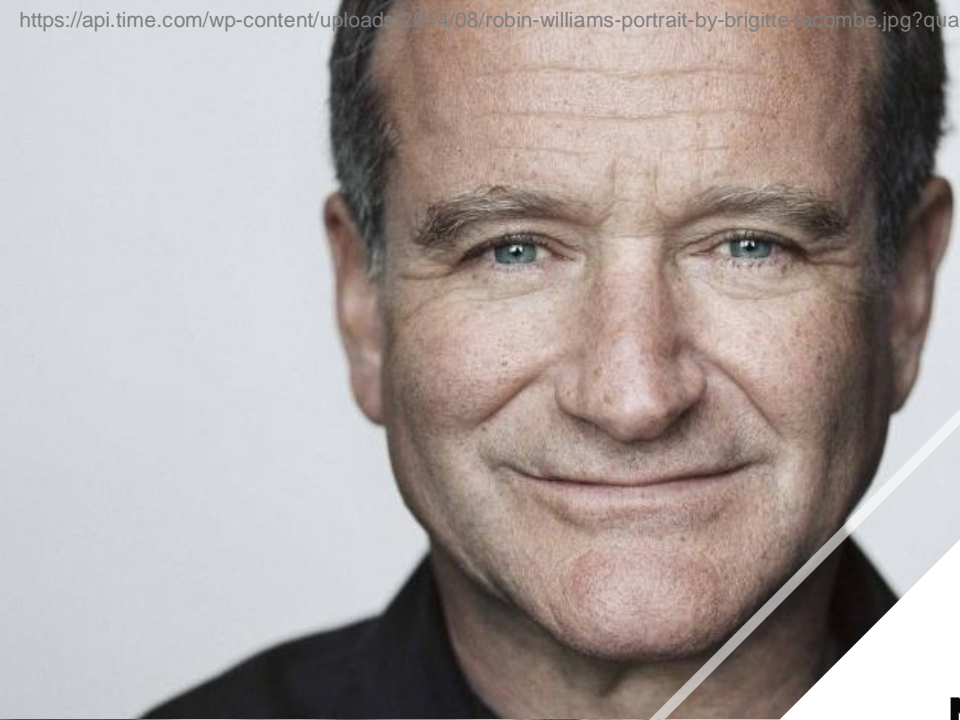




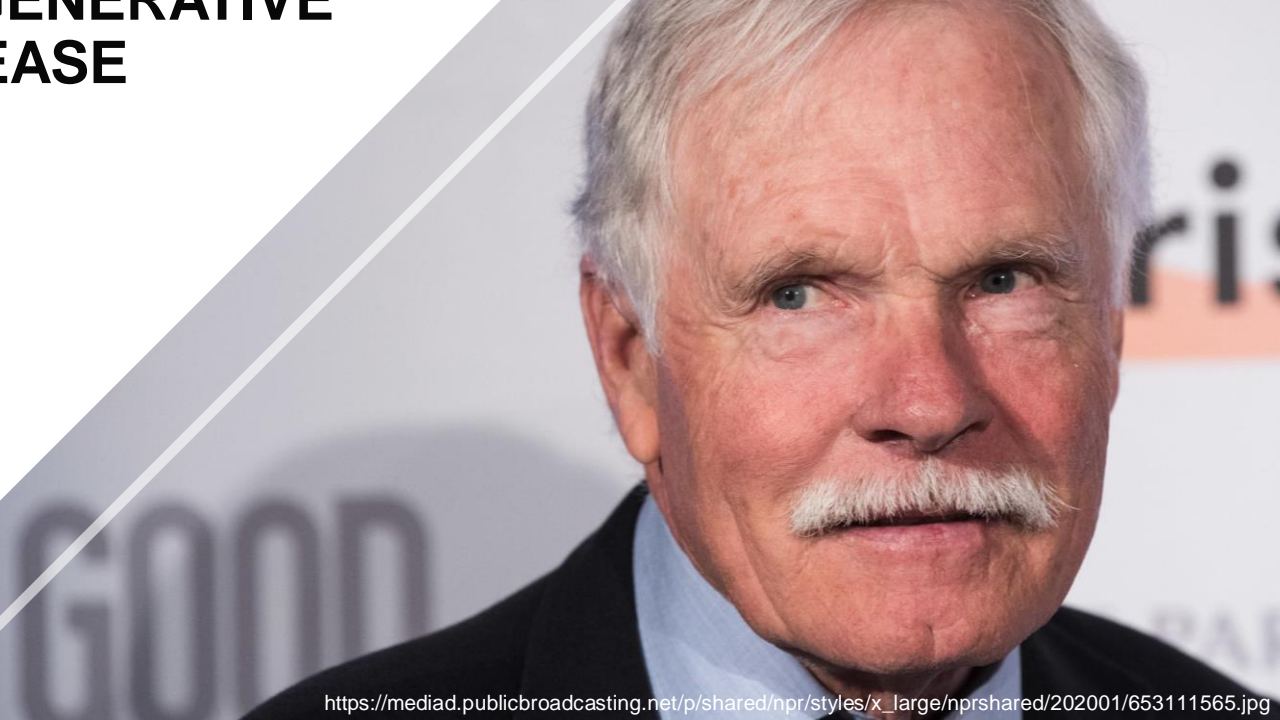


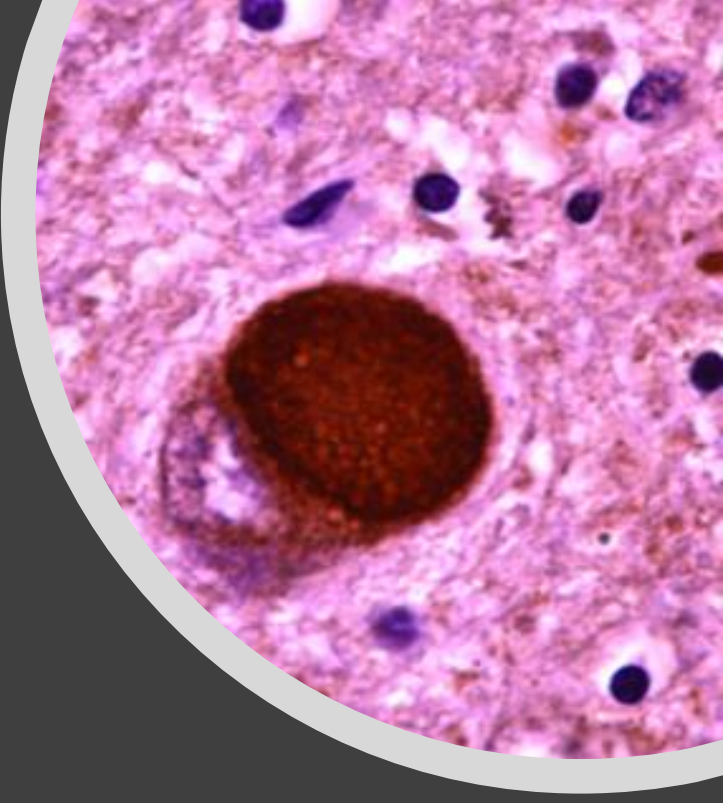
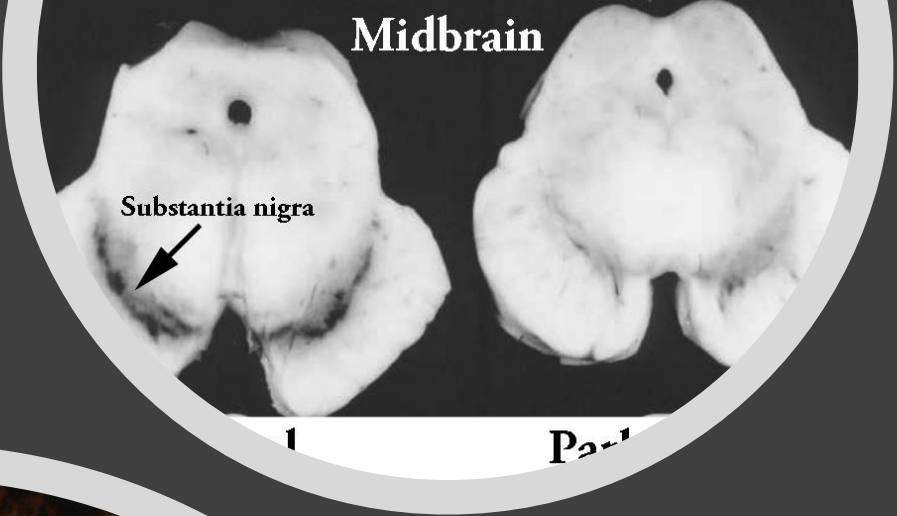
WHAT IS A NEURODEGENERATION?





THE FACES OF NEURODEGENERATIVE DISEASE

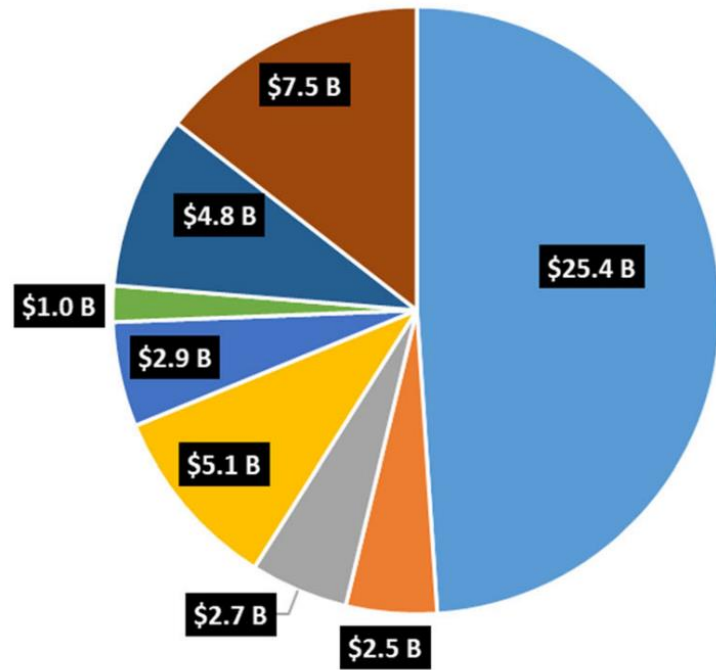




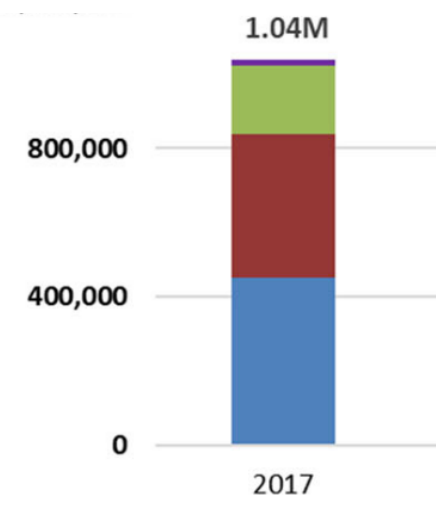
Parkinson's disease

Boxer Image from https://media1.s-nbcnews.com/i/newscms/2016_22/1564496/ali-liston_ce2b2d2917366a74628a579e283ad146.jpg
Olympics image from https://stillmed.olympic.org/media/Photos/2010/01/13/Opening%20Ceremony%20Atlanta%201996_112721.jpg
Brainstem section images from <https://scienceofparkinsons.com/tag/substantia-nigra/>
Lewy body image from <https://www.nia.nih.gov/health/what-lewy-body-dementia>

The Future of Parkinson's disease in the U.S.



- Direct Medical
- Reduced Employment
- Presenteeism
- Disability Income
- Premature Death
- Absenteeism
- Social Productivity Loss in Volunteer Work
- Non-Medical Costs

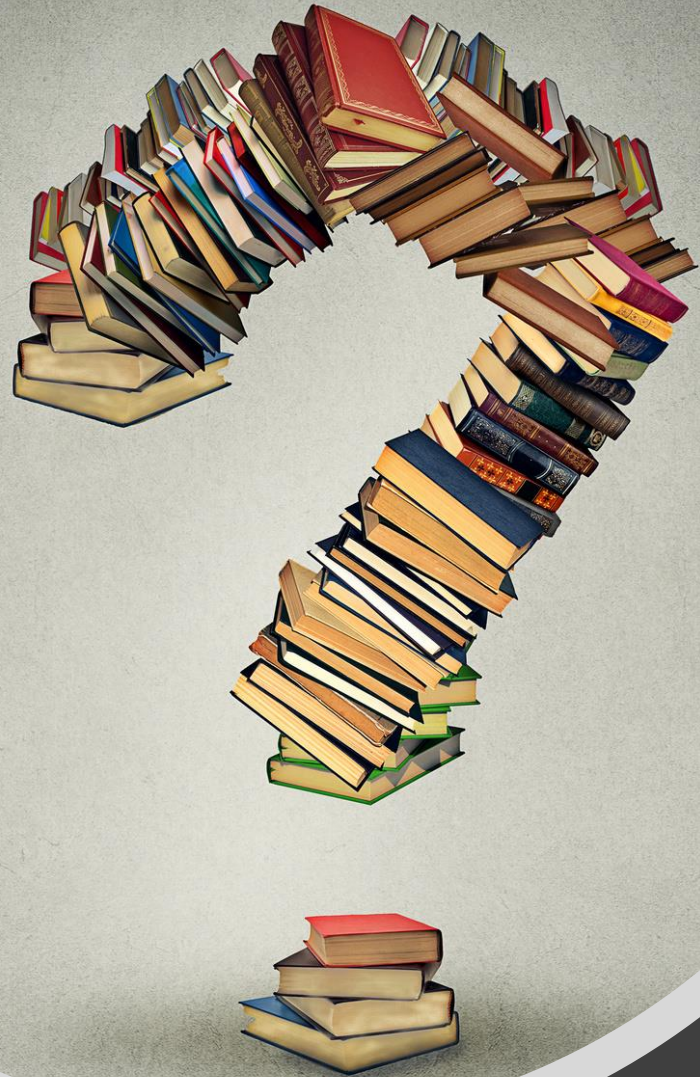


- >=75
- 65-74
- 50-64
- <=49

\$51,900,000,000.00

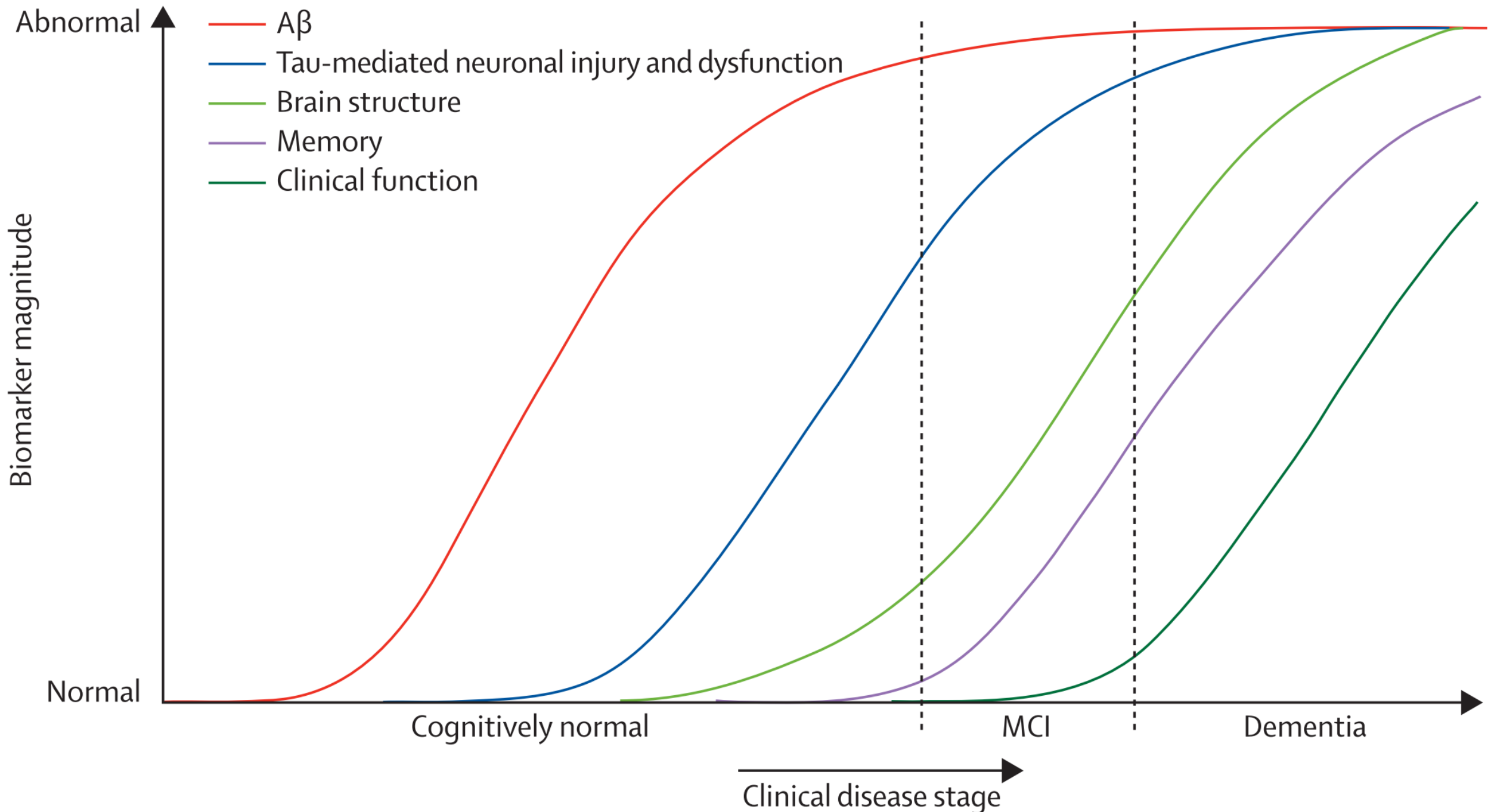
THE STUDY OF EXERCISE & NEURODEGENERATION





WHAT WE WANT TO KNOW...

- Does exercise prevent Parkinson's disease?
 - How early in life must one begin exercising?
 - What type of exercise is best?
- Does exercise slow progression of PD?
 - What type of exercise?
 - What symptoms are slowed?
 - How does it do this?
 - Are we replacing brain cells?
- Does exercise prevent PD-related cognitive decline?
 - If so, what type of exercise?
- Consider secondary benefits
 - Ex. Exercise to prevent deconditioning to prevent falls or other serious injury which may *appear* to accelerate the disease
 - Cardiovascular and cerebrovascular benefits





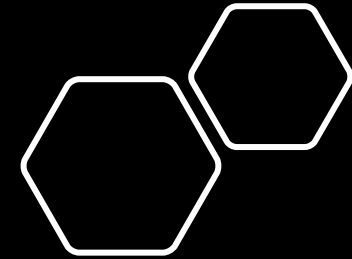
Aerobic Exercise: Evidence for a Direct Brain Effect to Slow Parkinson Disease Progression

J. Eric Ahlskog, PhD, MD

Abstract

No medications are proven to slow the progression of Parkinson disease (PD). Of special concern with longer-standing PD is cognitive decline, as well as motor symptoms unresponsive to dopamine replacement therapy. Not fully recognized is the substantial accumulating evidence that long-term aerobic exercise may attenuate PD progression. Randomized controlled trial proof will not be forthcoming due to many complicating methodological factors. However, extensive and diverse avenues of scientific investigation converge to argue that aerobic exercise and cardiovascular fitness directly influence cerebral mechanisms mediating PD progression. To objectively assess the evidence for a PD exercise benefit, a comprehensive PubMed literature search was conducted, with an unbiased focus on exercise influences on parkinsonism, cognition, brain structure, and brain function. This aggregate literature provides a compelling argument for regular aerobic-type exercise and cardiovascular fitness attenuating PD progression.

© 2017 Mayo Foundation for Medical Education and Research ■ Mayo Clin Proc. 2018;93(3):360-372



HURDLES

- How do we answer these questions?
 - Level of evidence
 - Anecdotal
 - Randomized control trials
- Considerations
 - PD is slow
 - Biomarkers are lacking
 - How to measure exercise
 - Reporting bias
- Cost (reality)
 - Exercise isn't profitable





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ANIMAL STUDIES

- Exercise facilitates neuroplasticity
- Exercised animals perform better on simple cognitive tests
- Microscopic and neuropsychologic evidence of exercise-related neuroplasticity
- Exercise facilitates biochemical markers of neuroplasticity
- Exercise influences on brain neurotrophic factors
- Brain neurotrophic factor levels increase with exercise in animals
- Animal models of neurotoxin-induced Parkinsonism Attenuated by Exercise
- Exercise Increases Neurotrophic factor levels and attenuates 6-OH-DA Nigrostriatal Neurotoxicity.
- Exercise tends to reduce MPTP Nigrostriatal Neurotoxicity



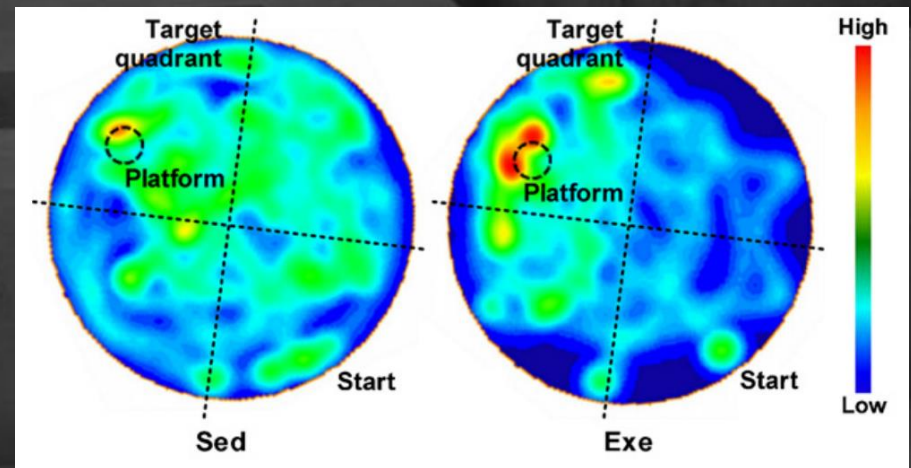
NEUROPLASTICITY

Ability for neural networks to change to suit the needs of the individual.



NEUROPLASTICTY

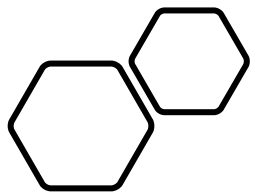
- Exercised animals perform better on simple cognitive tasks
 - Rats and mice show exercise-related improvement in spatial memory (maze) or object recognition



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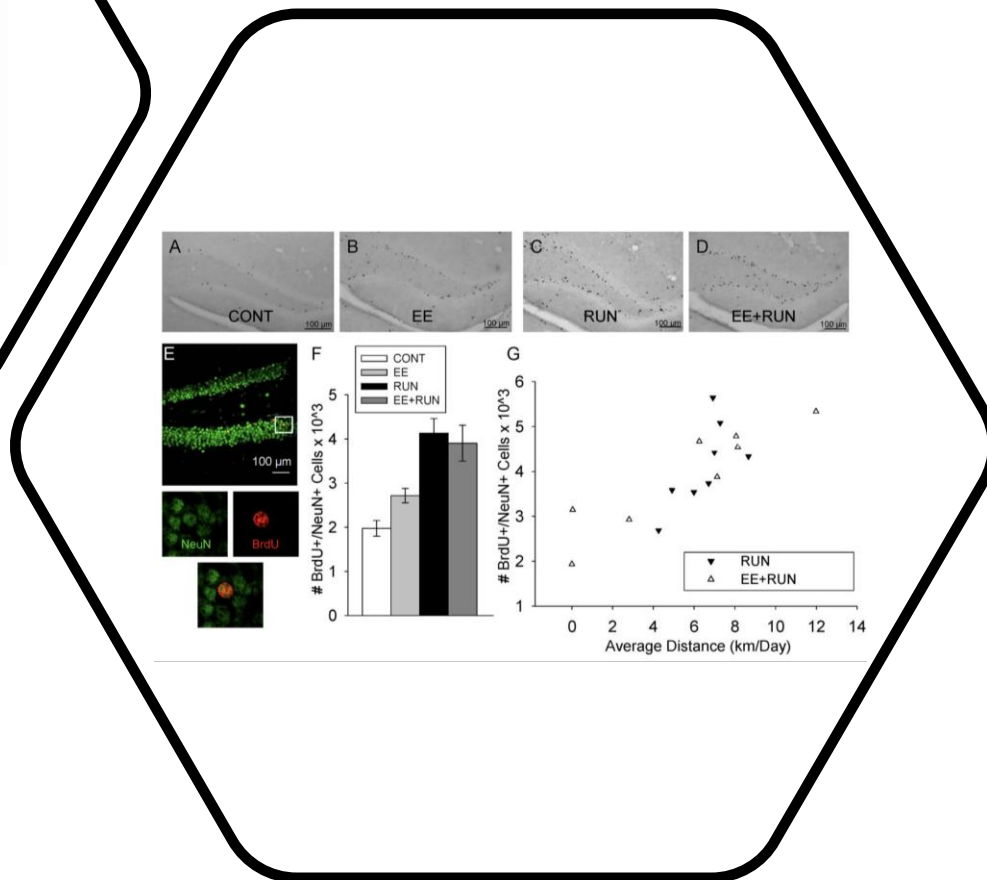
1. Ahlskog JE. Aerobic Exercise: Evidence for a Direct Brain Effect to Slow Parkinson Disease Progression. Mayo Clin. Proc. 2018;93(3):360–372.
2. Aguiar AS, Castro AA, Moreira EL, et al. Short bouts of mild-intensity physical exercise improve spatial learning and memory in aging rats: Involvement of hippocampal plasticity via AKT, CREB and BDNF signaling. Mech. Ageing Dev. 2011;132(11–12):560–567.

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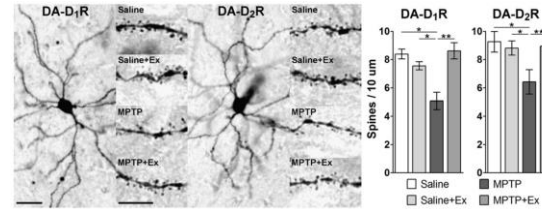
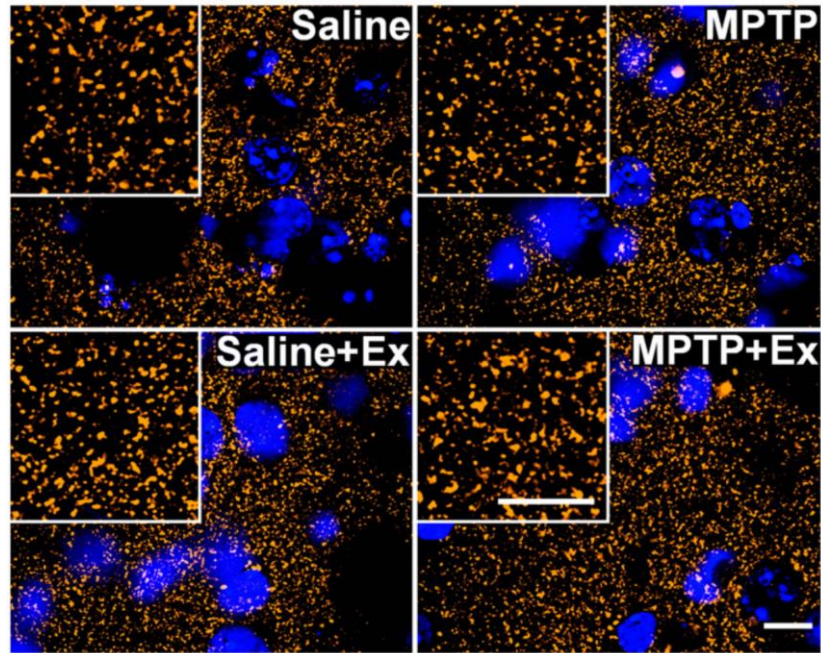


NEUROPLASTICTY

- Microscopic and neurophysiologic evidence of exercise-related neuroplasticity
- **Neurogenesis** occurs in the hippocampus
 - This may be enhanced with long-term running exercise in rodents.



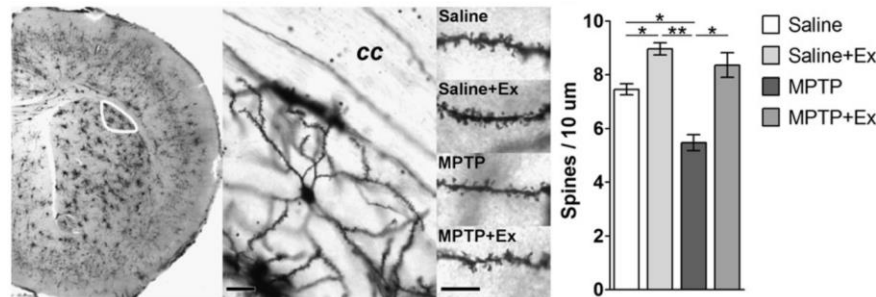
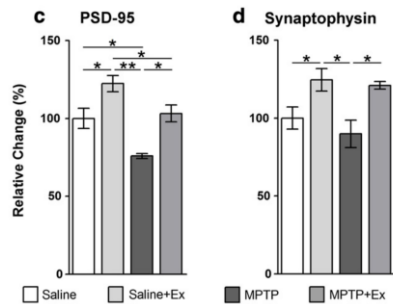
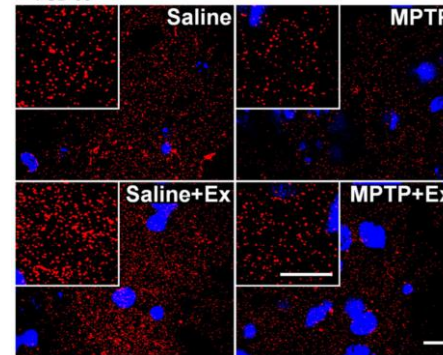
b Synaptophysin

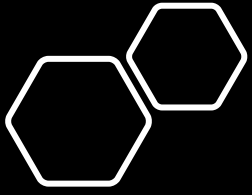


NEUROPLASTICTY

- Treadmill exercise **reverses dendritic spine loss** in mouse model of Parkinson's disease

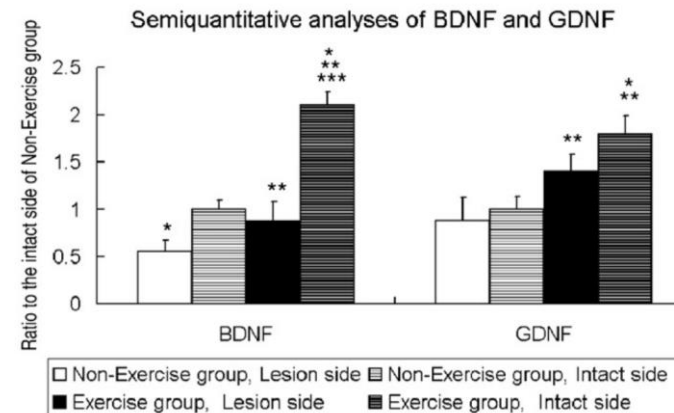
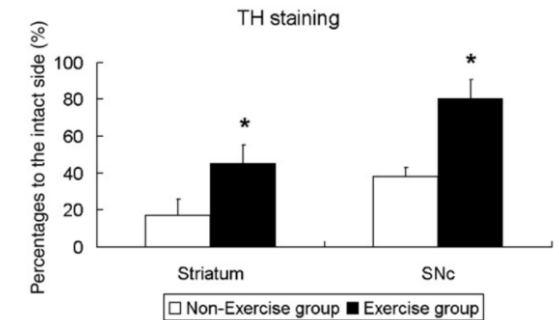
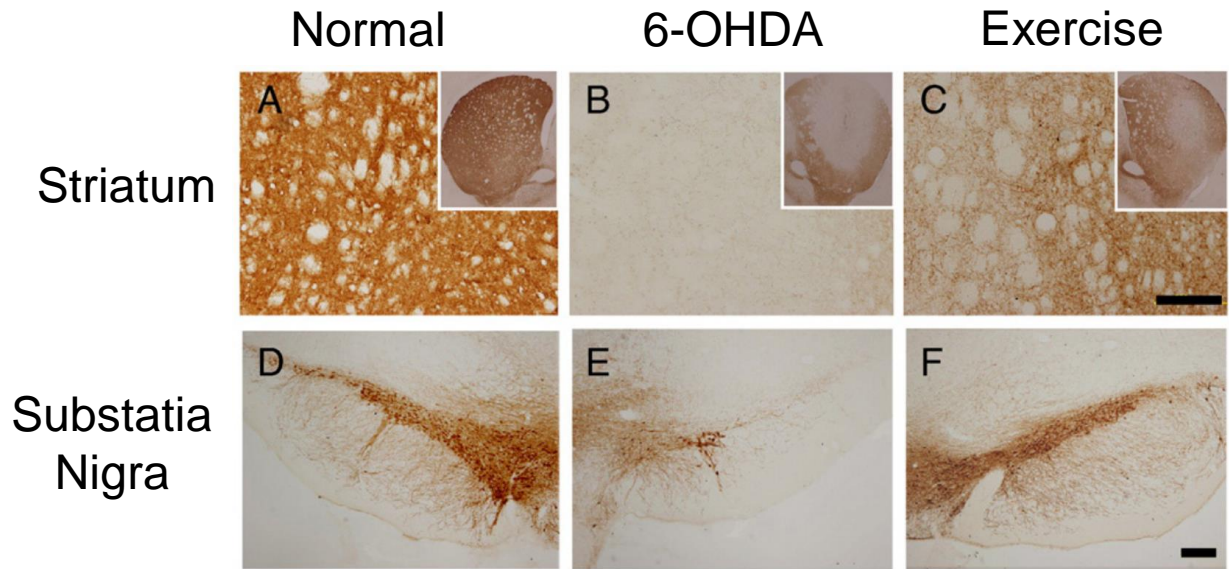
a PSD-95

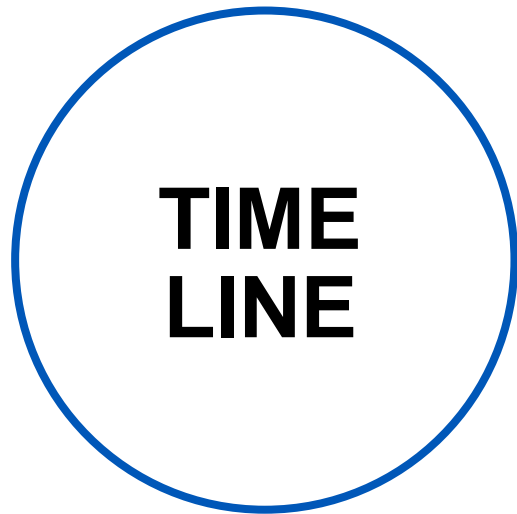




NEUROPLASTICTY

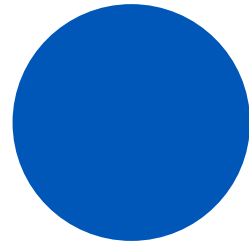
- PD rat model (6-OHDA)
- “Compulsive” Treadmill exercise 24 hours after 6-OHDA lesion
 - 5 days/wk, 30 min/day, 11 meters/min
- Preservation in dopamine signaling (TH)
- Increased neurotrophic factors (BDNF & GDNF)





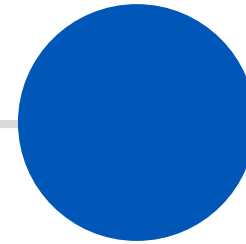
TIME LINE

NOVEMBER 14, 2020



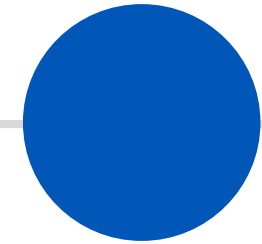
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4. Animal studies

MARCH 20, 2021



1. Rapid review
2. Human studies

MAY 22, 2021



1. Rapid review & summary of evidence
2. Call to action (Exercise & More)



QUESTIONS



**THANK
YOU**