

# The Effect of Exercise on the Cognitive Function of Patients with Alzheimer's Disease

Amanda Savitski

Interdisciplinary Health Services (Pre-PA track)

Fall 2018



# Introduction

- $\beta$ -amyloid plaques and tau proteins
- Unknown cause
  - Familial v. Sporadic
- Few treatments
- Diagnosis
  - Memory loss
  - Verbal and written tests
  - Scans
- Physical Exercise and brain plasticity
- Hippocampal volume, APOE, BDNF, VEGF, and IGF-1
- Animal studies



# Methodology

- ▶ Published, peer-reviewed articles
- ▶ WMU library databases
  - ▶ PubMed
  - ▶ Medline
  - ▶ ClinicalTrials.gov
  - ▶ National Institute of Health (NIH)
- ▶ Search Terms
  - ▶ “Alzheimer”
  - ▶ “Alzheimer’s Disease”
  - ▶ “neurodegeneration”
  - ▶ “aging brain”
  - ▶ “exercise”
  - ▶ “physical activity”

# What is Alzheimer's Disease?

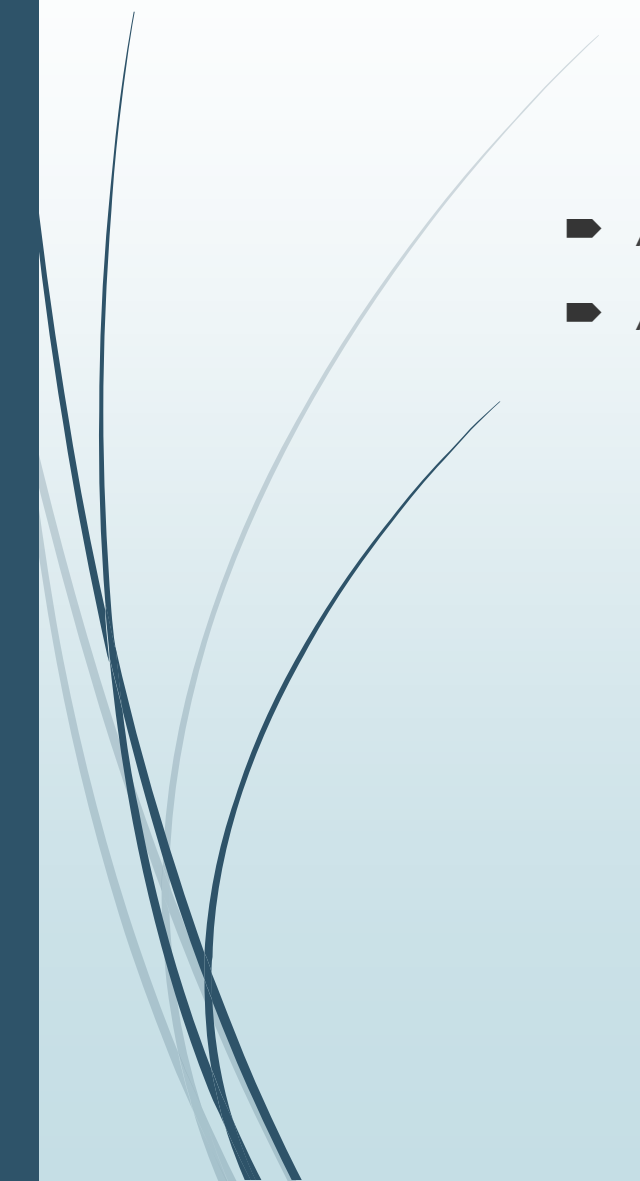
- Dementia characterized by neurofibrillary tangles and amyloid plaques
  - Amyloid plaques alone do not diagnose (Aizenstein et al., 2008)
- Crystallized intelligence v. Fluid intelligence
- Based primarily off observed symptoms
- APOE  $\epsilon$ 4 allele (Tyndall et al., 2018).
- APP, PSEN1, PSEN2, and MAPT genes



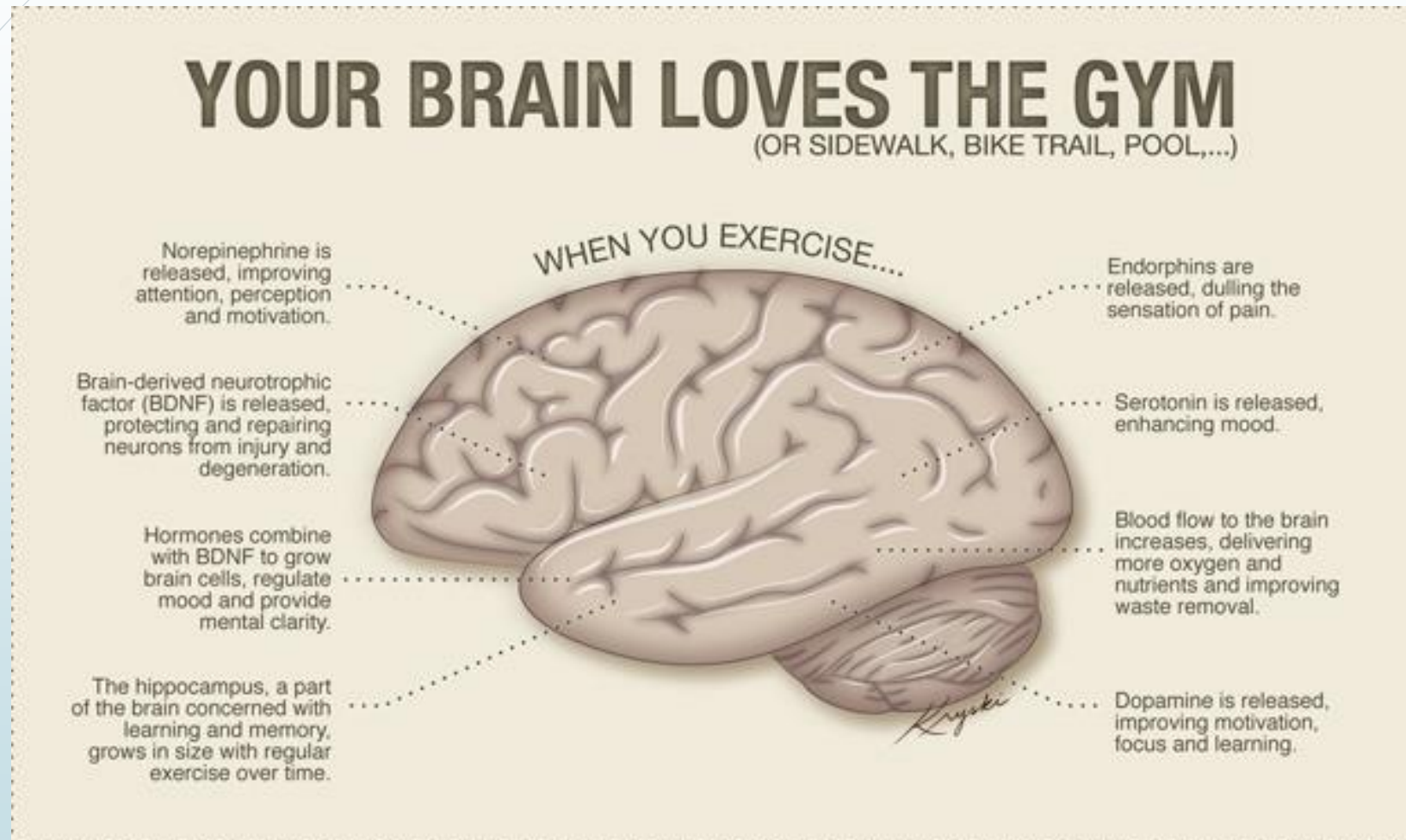
<https://www.dementiacarecentral.com/video/video-brain-changes/>



# Physical Exercise and the Brain

- Aerobic Exercise
  - Alternative Exercise
- 

# Aerobic Exercise and the Brain





# Aerobic Exercise and the Brain

- Dopamine, serotonin, and noradrenaline
  - Increase mood, attention span, focus, and memory
- BDNF, IGF-1, and VEGF in lateral and temporal lobes
  - Hippocampal volume (Voss et al., 2013, Tyndall et al., 2018, & Bernardo et al., 2016)
- Plasticity
  - Create new synapses while degrading old connections



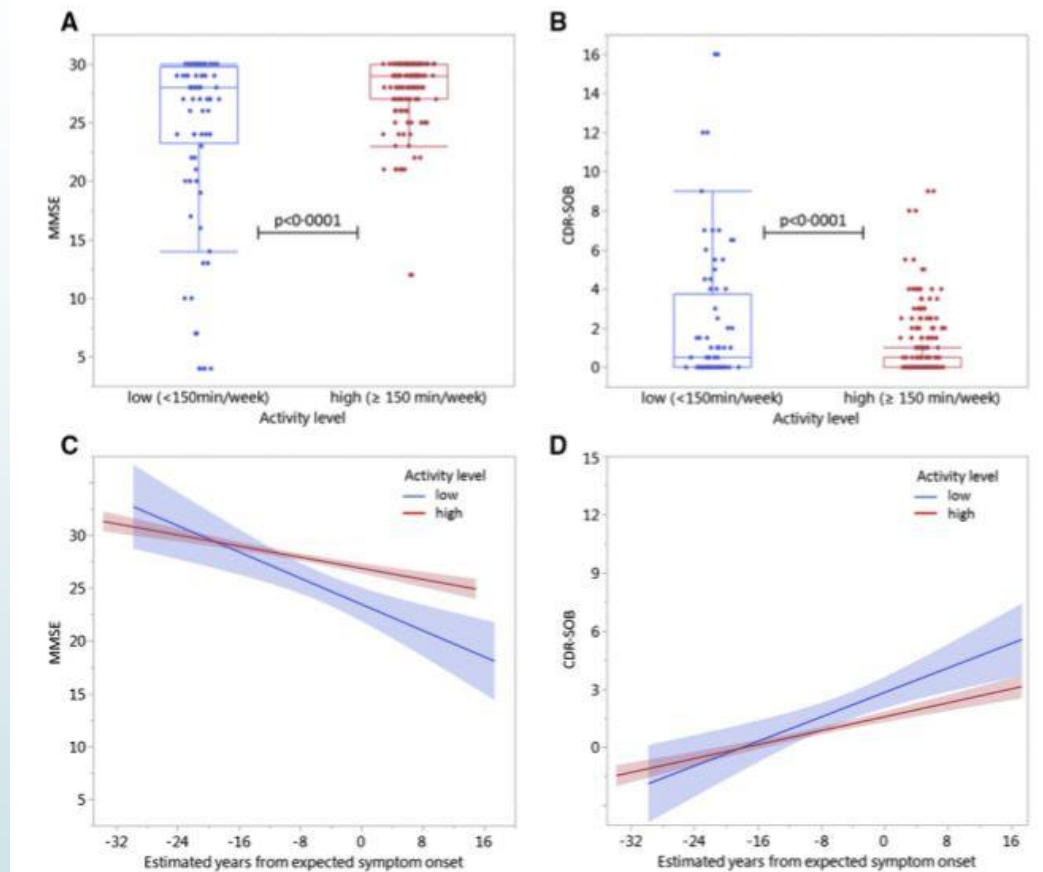
# Alternative Exercise and the Brain

- Mindfulness, tai chi, and yoga
  - Reduced depression states in dementia patients
- Sit 'N Fit chair yoga
  - Six-minute walk test, gait speed test, and Berg balance scale score
- NGF protecting basal forebrain neurons (Mooventhan & Nivethitha, 2017).
- Yoga and Curcumin ("Curcumin and Yoga Therapy for Those at Risk for Alzheimer's Disease," n.d.).
- Outdoor sunlight and socialization (Nelson & Tabet, 2015).



# Physical Exercise for Patients with AD

- Brain matter v. contractile skeletal muscles
- Mitochondrial health and BDNF levels (Bernardo et al., 2016).
- ADAD strongly affected by exercise. 150 minutes/week (Müller et al., 2018).



# Physical Exercise for Patients with AD

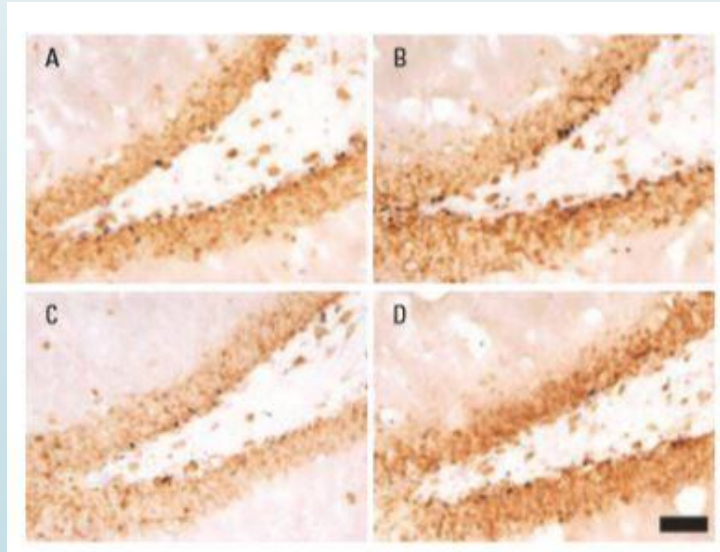
- Animal Studies
- Treatments



<https://newoldage.blogs.nytimes.com/2012/12/19/older-people-are-what-they-think-study-shows/>

# Animal Studies

- Questioned by some researchers
- Mouse study- absence of APOE (Soto et al., 2015)
- Enhancing neurogenesis with exercise after  $A\beta_{25-35}$  injection
  - Brains tested for BDNF, apical dendritic length, and hippocampal neurogenesis (Kim et al., 2014).



**Fig. 2.** Effect of treadmill exercise on neurogenesis in the hippocampal dentate gyrus. Upper: Photomicrographs of 5-bromo-2'-deoxyridine (BrdU)-positive cells in the dentate gyrus. The scale bar represents 50  $\mu$ m. Lower: The number of BrdU-positive cells in the hippocampus. (A) Sham-operation group, (B) sham-operation and treadmill exercise group, (C)  $A\beta_{25-35}$ -injection group, and (D)  $A\beta_{25-35}$ -injection and treadmill exercise group. \*Represents  $P < 0.05$  compared to the sham-operation group. #Represents  $P < 0.05$  compared to the  $A\beta_{25-35}$ -injection group.



# Treatments

- No cure
- Pre-symptomatic stages (Ryman et al., 2014)
- EXERT trial
  - Aerobic v. stretching-balance-ROM group
  - 70-80% Max HR for 30 min v. 35% Max HR for 30 min ("Exercise in Adults with Mild Memory Problems (EXERT)," n.d.).
- Acetylcholinesterase inhibitors (Knowles, 2006).
- Glutamate regulation for more severe cases
  - Namzaric- combination of Namenda and Aricept ("How Is Alzheimer's Disease Treated?," n.d.).



# Future

- Future Study
  - PET scan and MMSE at baseline and 16 weeks.
  - Aerobic exercise v. yoga v. control group
    - Aerobic: 60% Max HR
    - Yoga: poses
    - Control: video
    - 30 minutes 3X/week



# Current Studies (Appendix A)

- ▶ “Effects of Aerobic Exercise for Treating Alzheimer’s” by Fang Yu, PhD
- ▶ “Dose Response Study of Aerobic Exercise in Older Adults” by Jeff Burns, MD
- ▶ “Alzheimer’s Disease and Physiological, Cognitive Function and BDNF Levels of Plasma Adaptation After Exercise Training”



# Any exercise is better than no exercise

- Individualized to the patient
- Socialization (Nelson & Tabet, 2015)
- Lifetime activity



# Questions?





# References

- Aizenstein, H. J., Nebes, R. D., Saxton, J. A., Price, J. C., Mathis, C. A., Tsopelas, N. D., ... Klunk, W. E. (2008). Frequent Amyloid Deposition Without Significant Cognitive Impairment Among the Elderly. *Archives of Neurology*, 65(11), 1509–1517. <https://doi.org/10.1001/archneur.65.11.1509>
- Alzheimer's Disease and Physiological, Cognitive Function and BDNF Levels of Plasma Adaptation After Exercise Training - ClinicalTrials.gov. (n.d.). Retrieved from <https://clinicaltrials.gov/ct2/show/NCT02968875>
- Bernardo, T. C., Marques-Aleixo, I., Beleza, J., Oliveira, P. J., Ascensão, A., & Magalhães, J. (2016). Physical Exercise and Brain Mitochondrial Fitness: The Possible Role Against Alzheimer's Disease. *Brain Pathology*, 26(5), 648–663. <https://doi.org/10.1111/bpa.12403>
- Curcumin and Yoga Therapy for Those at Risk for Alzheimer's Disease - Full Text View - ClinicalTrials.gov. (n.d.). Retrieved October 14, 2018, from <https://clinicaltrials.gov/ct2/show/NCT01811381>
- Dose Response Study of Aerobic Exercise in Older Adults - ClinicalTrials.gov. (n.d.). Retrieved from <https://clinicaltrials.gov/ct2/show/results/NCT01129115>
- Effects of Aerobic Exercise for Treating Alzheimer's Disease- ClinicalTrials.gov. (n.d.). Retrieved from <https://clinicaltrials.gov/ct2/show/NCT01954550>
- Exercise in Adults with Mild Memory Problems (EXERT). (n.d.). Retrieved from <https://www.nia.nih.gov/alzheimers/clinical-trials/exercise-adults-mild-memory-problems-exert>
- How Is Alzheimer's Disease Treated? (n.d.). Retrieved from <https://www.nia.nih.gov/health/how-alzheimers-disease-treated>

# References

- Kim, B.-K., Shin, M.-S., Kim, C.-J., Baek, S.-B., Ko, Y.-C., & Kim, Y.-P. (2014). Treadmill exercise improves short-term memory by enhancing neurogenesis in amyloid beta-induced Alzheimer disease rats. *Journal of Exercise Rehabilitation*, 10(1), 2–8. <https://doi.org/10.12965/jer.140086>
- Knowles, J. (2006). Donepezil in Alzheimer's disease: an evidence-based review of its impact on clinical and economic outcomes. *Core Evidence*, 1(3), 195–219.
- Mooventhana, A., & Nivethitha, L. (2017). Evidence based effects of yoga in neurological disorders. *Journal of Clinical Neuroscience*, 43, 61–67. <https://doi.org/10.1016/j.jocn.2017.05.012>
- Müller, S., Preische, O., Sohrabi, H. R., Gräber, S., Jucker, M., Ringman, J. M., ... Laske, C. (2018). Relationship between physical activity, cognition, and Alzheimer pathology in autosomal dominant Alzheimer's disease. *Alzheimer's & Dementia*. <https://doi.org/10.1016/j.jalz.2018.06.3059>
- Nelson, L., & Tabet, N. (2015). Slowing the progression of Alzheimer's disease; what works? *Ageing Research Reviews*, 23, 193–209. <https://doi.org/10.1016/j.arr.2015.07.002>
- Soto, I., Graham, L. C., Richter, H. J., Simeone, S. N., Radell, J. E., Grabowska, W., ... Howell, G. R. (2015). APOE Stabilization by Exercise Prevents Aging Neurovascular Dysfunction and Complement Induction. *PLOS Biology*, 13(10), e1002279. <https://doi.org/10.1371/journal.pbio.1002279>
- Tyndall, A. V., Clark, C. M., Anderson, T. J., Hogan, D. B., Hill, M. D., Longman, R. S., & Poulin, M. J. (2018). Protective Effects of Exercise on Cognition and Brain Health in Older Adults. *Exercise and Sport Sciences Reviews*, 46(4), 215. <https://doi.org/10.1249/JES.0000000000000161>
- Voss, M. W., Erickson, K. I., Prakash, R. S., Chaddock, L., Kim, J. S., Alves, H., ... Kramer, A. F. (2013). Neurobiological markers of exercise-related brain plasticity in older adults. *Brain, Behavior, and Immunity*, 28, 90–99. <https://doi.org/10.1016/j.bbi.2012.10.021>