Exercise May Prevent the Development of Alzheimer's by Modulating Biomarkers in Rat Hippocampal Tissue

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Background

Alzheimer's Disease (AD)

- Progressive neurodegenerative disorder
- Main symptoms: Memory & executive function impairments
- Several leading hypotheses of Alzheimer's Disease development: (1) Aβ Hypothesis, (2) Oligomer Hypothesis, (3) Presenilin Hypothesis, (4) Tau Hypothesis [5]

Hippocampus

- Widely studied in AD research; exercise preserves hippocampal volume [3]
- Required for spatial learning in rodents and declarative memory in humans [2]

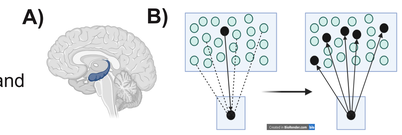

Figure 1: The Hippocampus. (A) Located deep within the medial temporal lobe (B) Critical for long-term memory consolidation, supporting the storage, organization, and expression of memories as both a memory encoder and index [12, 2]

Rise in Cases

- Number of cases are expected to double by 2060 [1]
- While somewhat effective in managing symptoms, current treatments lack the ability to completely reverse memory-impairing damage: 1) Cholinesterase inhibitors, (2) NMDA receptor antagonists, (3) Immunotherapy-based medications [6, 11, 10]
- **Accessible lifestyle-based preventative strategies must be further established**, such as exercise

Exercise

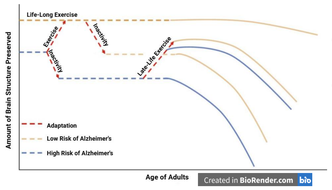

Figure 2: The Impact of Exercise According to the Adaptive Capacity Model. Exercise preserves hippocampal volume and alleviates Alzheimer's risk [Adapted from 10]

- Physically inactive people had a 36% higher risk of developing Alzheimer's Disease [4]
- Further research is needed to establish intervention guidelines and to clarify the molecular mechanisms underlying exercise's preventative effect

Pro-Inflammatory Cytokine IL-1β

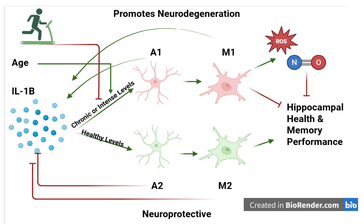

Figure 3: Exercise Regulates IL-1β, a Dose-Dependent Mediator of Harmful and Protective Effects [Adapted from 14]

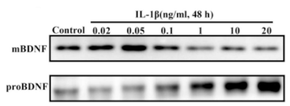

Figure 4: IL-1β May Mediate mBDNF/ proBDNF Ratio [7]

mBDNF/proBDNF

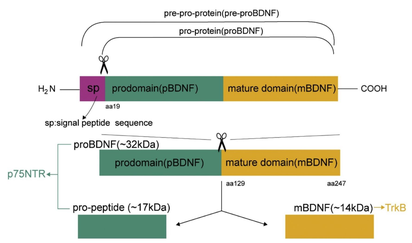

Figure 5: Different Isoforms of BDNF [13]

- ProBDNF: Promotes neuronal apoptosis (cell death); levels are reduced by exercise and increased in AD [8]
- Mature BDNF (mBDNF): Promotes neurogenesis and neuronal survival; levels are increased by exercise and decreased in AD [13]

Research Question: Can exercise prevent the development of Alzheimer's Disease by reducing IL-1β and increasing the mBDNF/proBDNF ratio?

Methods

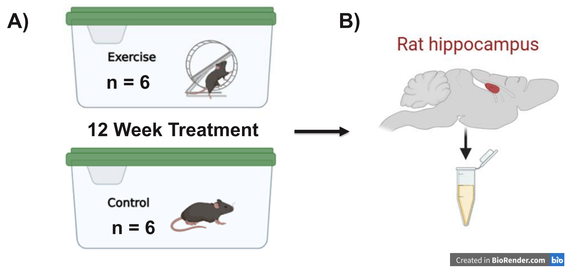

Figure 6. Sample Preparation (A) Male Spraque Dawley Rats are equally divided between an exercise and control group (B) Hippocampal tissue is extracted and prepared for analysis

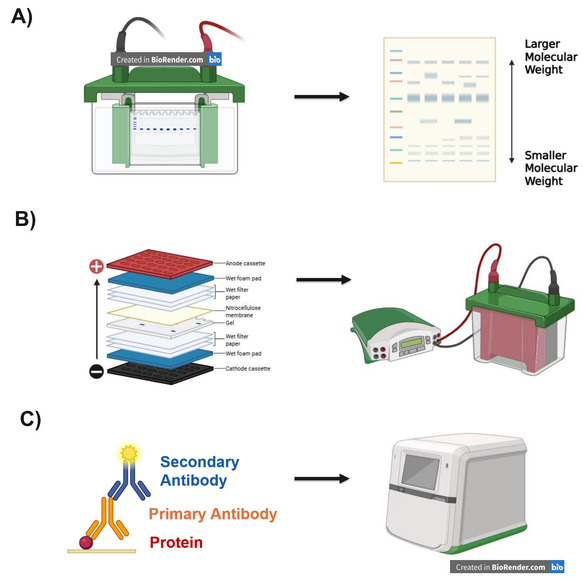

Figure 7. Western Blotting (A) Gel electrophoresis protein separation (B) Transfer to membrane (C) Visualization

Expected Final Results

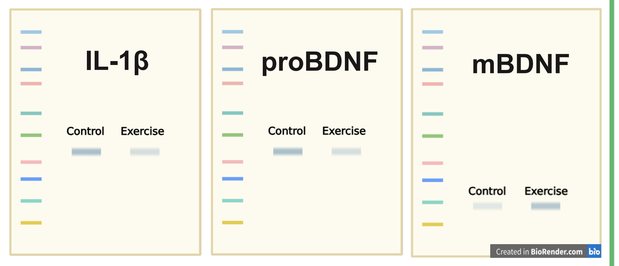

Figure 11: Hypothesis. Exercise may prevent the development of Alzheimer's by reducing IL-1β, lowering levels of proBDNF, and upregulating mBDNF expression

Bigger Picture

Figure 12: My Grandfather Patrick O'Malley, who was diagnosed with Alzheimer's Disease

- May contribute to the development of preventive guidelines to target at-risk populations before cognitive decline begins
- Should help clarify molecular mechanisms linking physical activity to hippocampal health and memory preservation
- Could support the development of future medical treatments utilizing biomarkers
- Reinforces the role of modifiable lifestyle factors in slowing or preventing neurodegenerative disease onset

Possible Methodological Next Steps

Figure 8: Current Results

Option #1: More Western Blot Troubleshooting

1) Increase antibody concentrations (e.g.,1:200)
2) Increase amount of total loading protein
3) Try a new BDNF antibody from Dr. Kelly!

Option #2: RT-qPCR to Quantify mRNA

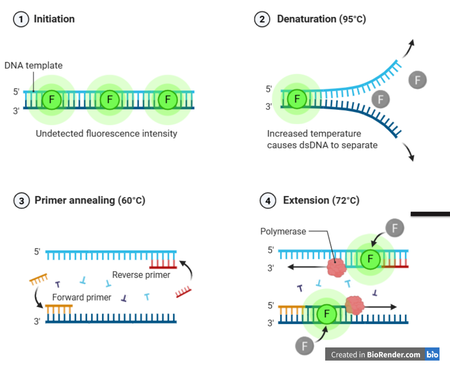

Figure 9: Steps for RT-qPCR

Option #3: Western Blot for NDMA Receptors

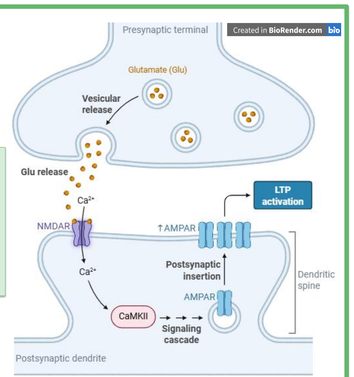

Figure 10: NDMA Receptors Underlie Memory

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References