Exercise as a Therapy for Cognitive Aging and Alzheimer’s Disease

Researchers: Elizabeth M. Reynolds, M.S., Shayal Vashisth, Caitlin Grant, Emilia A. Grzesiak
Project Manager: Sara V. Maurer, B.S.
Faculty Advisors: Elizabeth A. Finch, Ph.D., & Christina L. Williams, Ph.D.

Introduction

Alzheimer’s Disease (AD)
- AD is a progressive, age-related neurodegenerative disease that causes neuronal damage and death, and leads to profound memory problems and cognitive impairment.
- AD is the 6th leading cause of death in the U.S. and 1/3 of seniors die with AD; AD is the only of the top 10 causes of death that can’t be prevented, slowed, or cured.

2/3rds of AD Patients are Women
- Women experience greater severity, more neuropathology, earlier onset and faster progression than men do.
- Loss of ovarian function during menopause may be a key factor in women’s increased risk and accelerated cognitive and neuropathological declines.

Hypothesis and Specific Aims

Hypothesis:
1. Menopause exacerbates AD
2. Exercise attenuates AD and its exacerbation by menopause

Specific Aims:
1. Determine the effects of transitional menopause (TM) on memory, neuropathogenesis, and gene expression in female AD and control mice.
2. Determine the effects of exercise experienced during pre-, peri-, and postmenopausal stages on cognitive function, neuropathogenesis, and gene expression in AD females.

Creating a mouse model of female physiology in AD

CVN-AD Mouse Model
Timeline for AD-like pathogenesis
Amyloid pathology

Transitional Menopause (TM) Mouse Model
Accelerated ovarian failure following treatment with the ovotoxin VCD

Outcome Measures

1. Cognitive Assessment: Memory task
2. Brain Pathology
3. Brain Pathways and Networks

Future Directions:
- To investigate underlying mechanisms using proteomic, metabolic, and other approaches
- To compare different types and timing of exercise interventions
- To investigate menopause and exercise effects in other mouse models of AD and neurodegenerative diseases

Summary and Potential Outcomes

- So far, our first hypothesis that TM worsens AD has been partially supported. Our second hypothesis on exercise and AD will be tested this coming summer
- These studies will:
  - Provide a proof-of-principle test for our hypothesis that menopause exacerbates and exercise attenuates AD pathogenesis
  - Create a foundational framework for more comprehensive and mechanistic future investigation on the impact of interactions among AD, menopause, aging, and exercise on female brain health

Acknowledgments:
We would like to thank Dr. Carol Colton for sharing her insight and Alzheimer’s mouse model. We would also like to thank the Bass Connections program for their funding.