A Translational Approach to a Therapeutic Intervention with Physical Activity for Neurological/Cognitive Dysfunction

**MOUSE: Alzheimer’s Disease**

**Background**
- Alzheimer’s Disease
  - AD is an age-related, neurodegenerative disease that causes neuronal damage and death and leads to cognitive impairment
  - High incident rate in women may be explained by loss of ovarian function during menopause
- Neuritrophic effects of exercise
  - Physical exercise has been associated with reduction in rates of cognitive decline

**Aims/Research Questions**
- Demonstrate how exercise can delay cognitive decline in AD
- Determine how progressive neuroinflammation in AD mouse model is influenced by exercise

**Exercise increased fitness of CVN-AD mice on a treadmill endurance test**
- Time to Exhaustion Endurance Test
  - For every 2 minutes, the speed of the treadmill increases by the same factor until mice are no longer able to run

**Exercise decreased neuroinflammation**
- IBA-1 Stain (Microglia marker)
  - Exercise increased thin microglia and decreased thick microglia, suggesting decreased neuroinflammation

**MOUSE: CVN-AD**

**Methodology**
- Female mouse model – CVN-AD
  - Develops human AD-like pathogenesis
  - Transitional menopause induced by ovariectomy VCD which kills ovarian follicles
- Design and Timeline
  - WOA: 8 10 12 14 16 20 24 28 32
  - Exercise: From 24-36 WOA mice ran on wheels for 6-8 hours/day, 5 days/week, and underwent forced treadmill training for 45 minutes, 2 days/week

**HUMAN: Post-Traumatic Stress Disorder**

**Background**
- Post-Traumatic Stress Disorder
  - PTSD is a mental health condition that is caused by an experienced traumatic event
- Neuroinflammation in neurological/cognitive dysfunctions
  - Is a non-invasive intervention to ameliorate cognitive impairment and neuroinflammation in neurological/cognitive dysfunctions?

**Aims/Research Questions**
- To explore the relationship between PTSD, inflammatory markers, physical activity, and cognitive function

**Methodology**
- Sample
  - 302 older patients with pre-diabetes (67 with PTSD)
- Enhanced Fitness Intervention
  - 12-month telephone physical activity counseling
- Systemic Inflammation
  - 9 serum cytokines collected for each individual
- Aerobic Fitness – 6 Minute Walk Test (6MWT)
  - Participants instructed to walk as far as they can in 6 minutes
- Statistics
  - Between-group comparisons (PTSD vs. No PTSD): t-tests
  - Associations between variables: bivariate correlations

**Results:**
- Cross-Sectional Associations
  - PTSD vs. Non on AD8
    - ΔPA: IL6 (r=-.13), TNFa (r=-.13), TNFR1 (r=-.11), TNFR2 (r=-.14); p<.10
    - ΔPA: IL6, 6MWT, HA, D-Dimer; p<.10
  - N.S.
- Longitudinal Associations
  - ΔPA w/ changes in 6MWT, PA (PTSD only)
    - ΔPA w/ changes in PA, 6MWT
    - ΔPA w/ changes in BM (PTSD only)
- Conclusion:
  - PTSD: AD8 w/ 6MWT, PA (PTSD only)
  - PTSD vs. Non on AD8: ΔPA w/ 6MWT, PA (PTSD only)
  - PTSD vs. Non on Inflammatory markers (BM)
  - ΔPA w/ changes in 6MWT

**CONCLUSION:** Physical activity is a non-invasive intervention to ameliorate cognitive impairment in neurological/cognitive dysfunctions.