

# Cardiometabolic Health in Individuals with Down Syndrome



**MET-DS**

Metabolic Health, Lifestyle, and Co-occurring  
Health Conditions in Down Syndrome



**School of Human Ecology**  
UNIVERSITY OF WISCONSIN-MADISON

**Sigan L. Hartley, PhD**

100 Women Distinguished Chair in Human Ecology  
Vilas Distinguished Achievement Professor  
Waisman Center Investigator  
School of Human Ecology  
University of Wisconsin-Madison



# Disclosures

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- Consultant: Alnylam Pharmaceuticals Inc.; Ionis Pharmaceuticals Inc.
- Chair: Alzheimer's Association ISTAART Down syndrome Professional Interest Area

# Metabolic Health and Down syndrome

| Physiological Changes in Down syndrome that impact energy Metabolism |                                                                                                                                |
|----------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------|
| Decreased energy expenditure                                         | Lower energy needs per day; lower basal metabolic rate (BMR), meaning they burn fewer calories at rest compared to peers,      |
| Altered appetite hormones                                            | Increased appetite, don't feel full                                                                                            |
| Hypotonia                                                            | Low fat free mass and higher fat mass (adiposity), lower energy expenditure                                                    |
| Chronotropic incompetence                                            | Lower maximal heart rate, low blood pressure, lower fitness, and lower energy expenditure of exercise                          |
| Dyslipidemia                                                         | ~50-60% children; commonly low HDL and high triglycerides                                                                      |
| Thyroid issues                                                       | Affects metabolism and can cause fatigue and weight gain                                                                       |
| Insulin Resistance                                                   | Insulin resistance, making it harder for the body to process sugar efficiently                                                 |
| Altered fat deposition and anatomical factors                        | High risk for obstructive sleep apnea due to midface hypoplasia, enlarged tonsils/adenoids, small airways, and low muscle tone |

# Cardiovascular Health and Down syndrome

- Congenital heart defects in ~40-60% of babies with Down syndrome, most commonly atrioventricular septal defects and ventricular septal defects
- Systemic hypertension less common, but pulmonary hypertension ~20-33% of children
- Traditional atherosclerosis (artery plaque) less common
- Cerebrovascular – increased risk for ischemic and hemorrhagic stroke, moyamoya
- Hypotension and low heart rate (bradycardia) common
- High prevalence of obesity and dyslipidemia, but low heart disease, heart failure, and hypertension and often not associated with type 2 diabetes

| Health History of Adults with Down syndrome (N = 524) |             |
|-------------------------------------------------------|-------------|
| Hyperlipidemia                                        | 147 (28%)   |
| Hypertension                                          | 25 (4.8%)   |
| Congenital heart disease                              | 157 (30.0%) |
| Hypothyroidism                                        | 304 (58.0%) |
| Type 2 Diabetes                                       | 28 (5.3%)   |
| Obesity                                               | 235 (44.8%) |

# Lifestyle Considerations

- In addition to cardiometabolic conditions, musculoskeletal problems can make physical activity more difficult:
  - Hypotonia (low muscle tone)
  - Ligamentous laxity (loose joints)
  - Hypermobility, which cause instability, pain, and fatigue.
  - Atlantoaxial instability
  - Hip subluxation/dislocation
  - Patellar instability
  - Flat feet



# Metabolic Health and Lifestyle in Children with Down syndrome (MET-DS)



**Goal:** Understand how alterations in metabolic pathways influence the health of individuals with Down syndrome

**Who:** individuals with Down syndrome aged 6-24 years who are English or Spanish speakers

**What:** 4 hour study visit and home activities

- Health checkup
- Blood collection
- Cognitive tests
- Diet intake
- Home sleep test
- Activity monitoring



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## Welcome to Collaboration for Down syndrome Progress (CDP)!



We aim to improve the health and well-being of people with Down syndrome by building and coordinating strong community ties.

We want to learn more about people with Down syndrome by recruiting and enrolling people for research studies. We want to understand how to help everyone with Down syndrome stay healthy and happy from the time they are born all the way through their adult years.

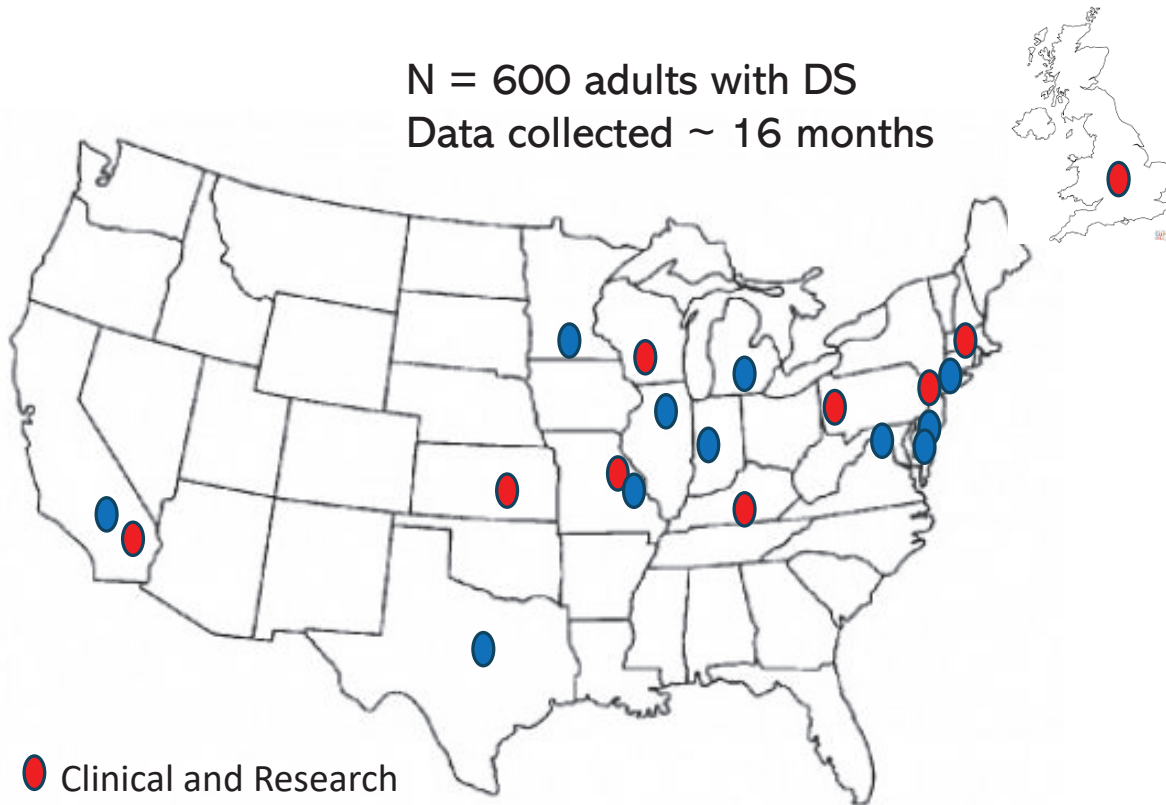
[hartleylab@waisman.wisc.edu](mailto:hartleylab@waisman.wisc.edu)



# Cardiometabolic Conditions and Aging in Down syndrome

# Alzheimer Biomarker Consortium- Down Syndrome (ABC-DS)

N = 600 adults with DS  
Data collected ~ 16 months



● Clinical and Research  
● Research

## Clinical and Research

- University of Pittsburgh (Handen & Cohen)
- University of Cambridge (Zaman)
- Washington University- St. Louis (Ances)
- University of WI-Madison (Christian & Hartley)
- University of California Irvine (Head & Mapstone)
- Massachusetts General Hospital (Lai & Rosas)
- University of Kentucky (Schmitt)
- Columbia University/New York Institute for Basic Research (Lee & Krinsky-McHale)
- Kansas University (Ptomey & Burns)

## Research

Georgetown University; University of North Texas; University of Michigan; Mayo Clinic; Washington University- St. Louis CSF Lab; NCRAD; ATRI & LONI; Johns Hopkins

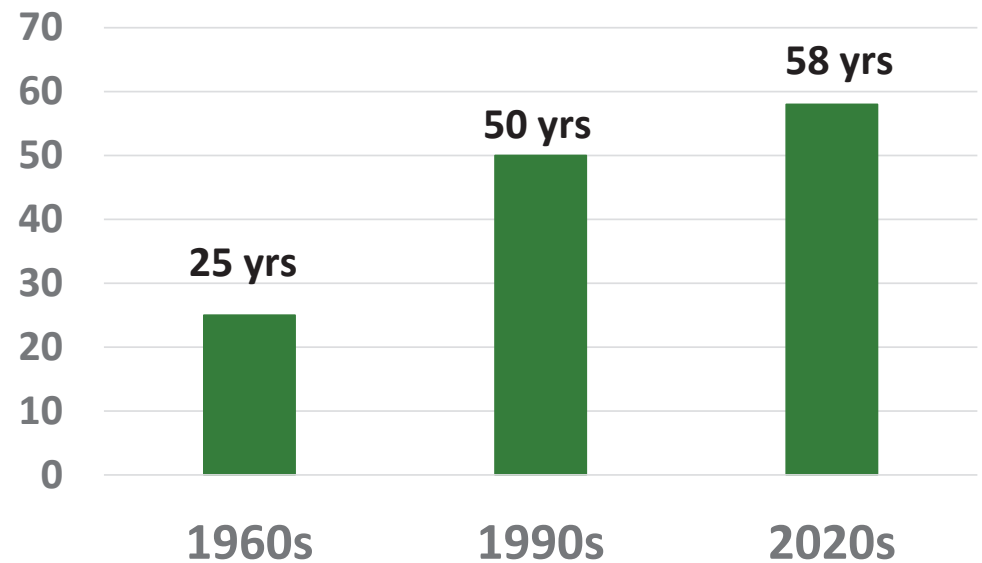
## NIH Partners

Laurie Ryan, Erika Tarver, Linda Garcia, Melissa Paris  
Nina Silverberg, Sujata Bardhan

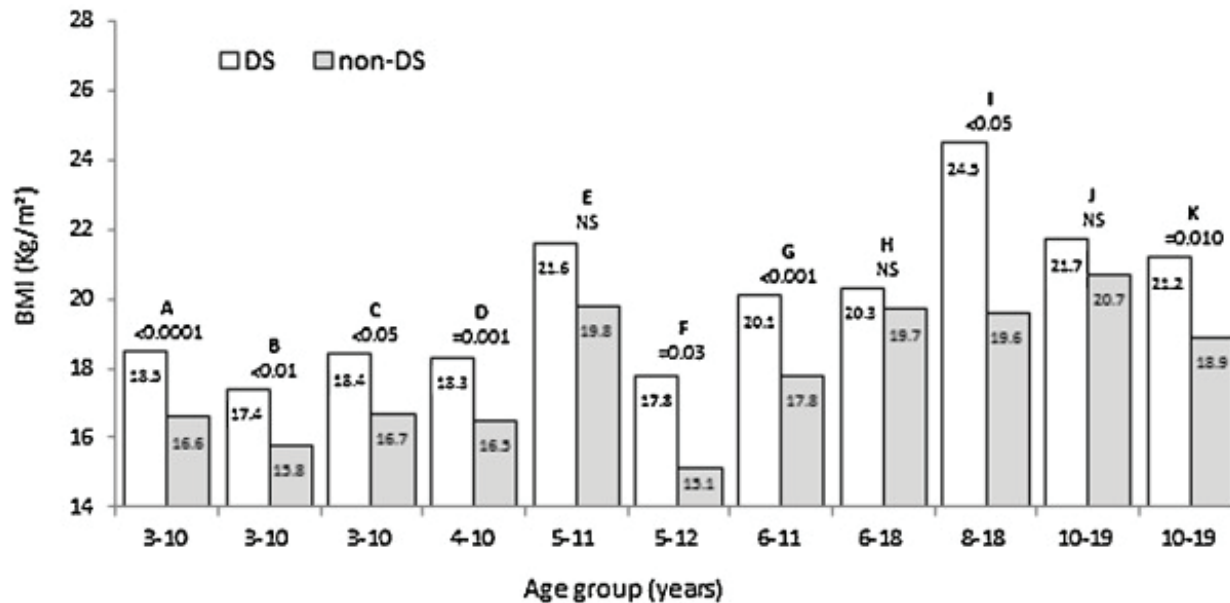
Funding: U01 AG051406; U01 AG051412; U19AG068064; MPIs: Handen, Christian, Mapstone, Head

# Aging and Down syndrome

- Early onset and increased prevalence of aging conditions:
  - Premature graying of the hair and wrinkles, hair loss
  - Hypothyroidism
  - Early age of menopause
  - Keratoconus and cataracts
  - osteoarthritis
  - hearing problems, hair loss



# Weight in adults with Down syndrome

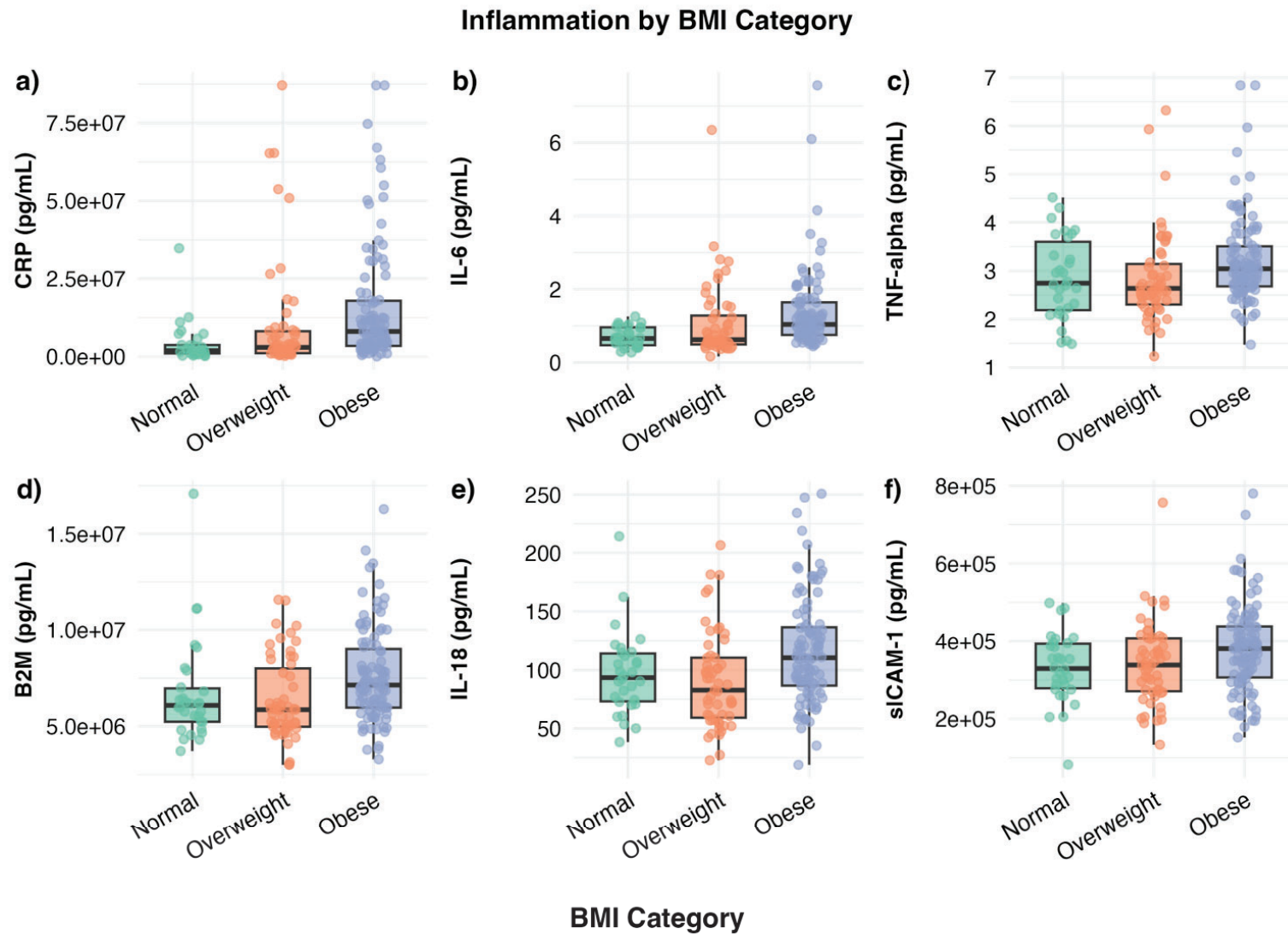


~45-60% of adults with Down syndrome are overweight or obese

Bertapelli et al., 2016  
Bell et al., 1992  
Stancliffe et al., 212

# Inflammation and weight

N = 199 adults with  
Down syndrome aged  
25-67 years



## Alzheimer's Disease

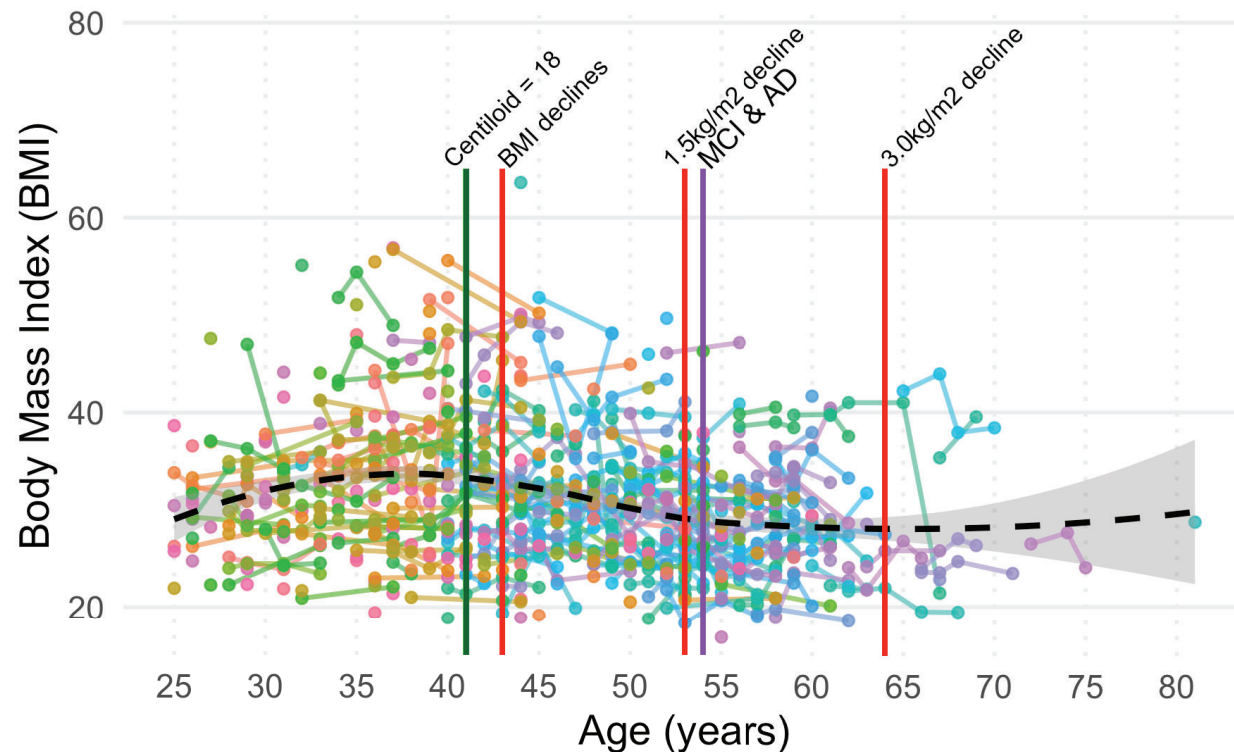
- Most common type of dementia
- Problems with memory, thinking and behavior. Develop slowly and get worse over time, eventually impacting everyday living tasks
- 6.7 million Americans have Alzheimer's disease
- 6<sup>th</sup> leading cause of death
- In the U.S.:
  - 10% people age 65+
  - 17% of people age 75-84
  - 32% of people age 85+

## Down syndrome associated Alzheimer's Disease

- **90%** lifetime prevalence for symptomatic Alzheimer's disease
- Average age of dementia onset = **52-54 years**
- Historically excluded from clinical AD trials; little known about AD in DS or medication efficacy

# Weight Across Adulthood in Down syndrome

**Body Mass Index and Age**



Green line = amyloid- $\beta$  reaches positivity (age=41 years)

First red line = BMI begins to decline (age=43 years)

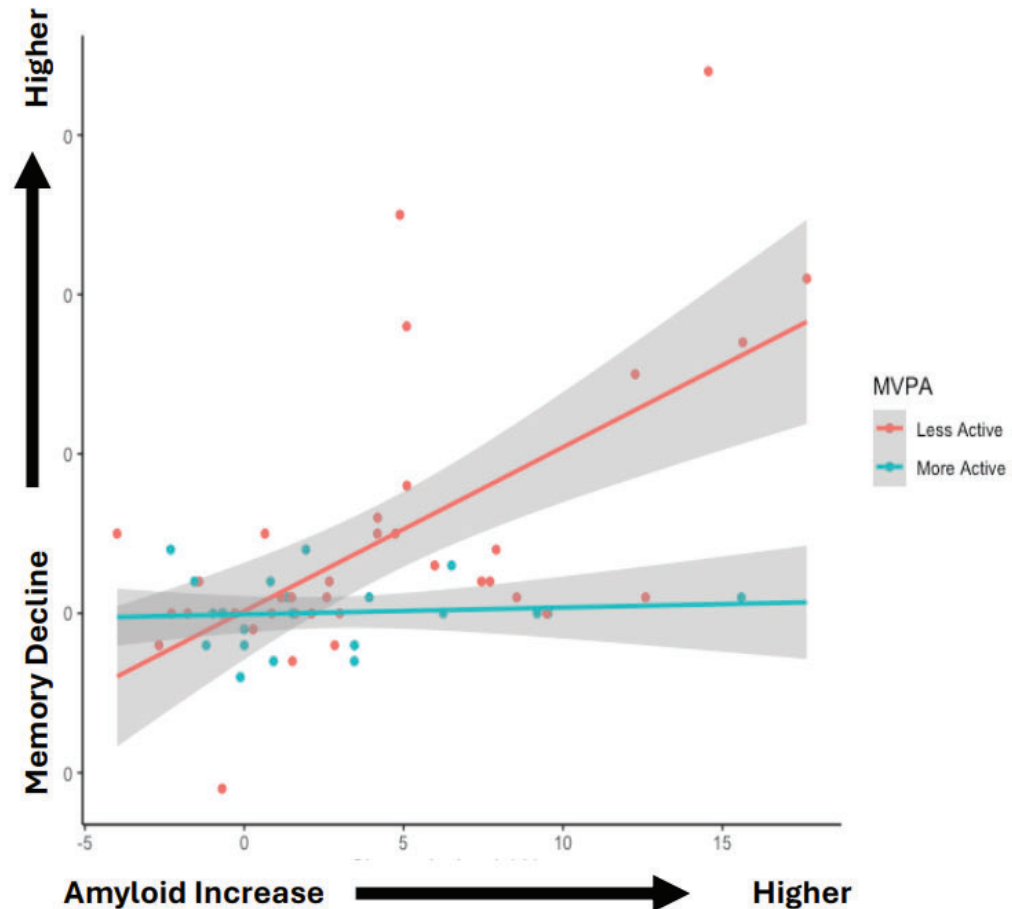
Second red line = 1.5 unit decline in BMI (age=53)

Third red line = 3.0 unit decline in BMI (age=64).

Purple line = average age of Mild Cognitive Impairment and dementia

# Physical Activity Benefits

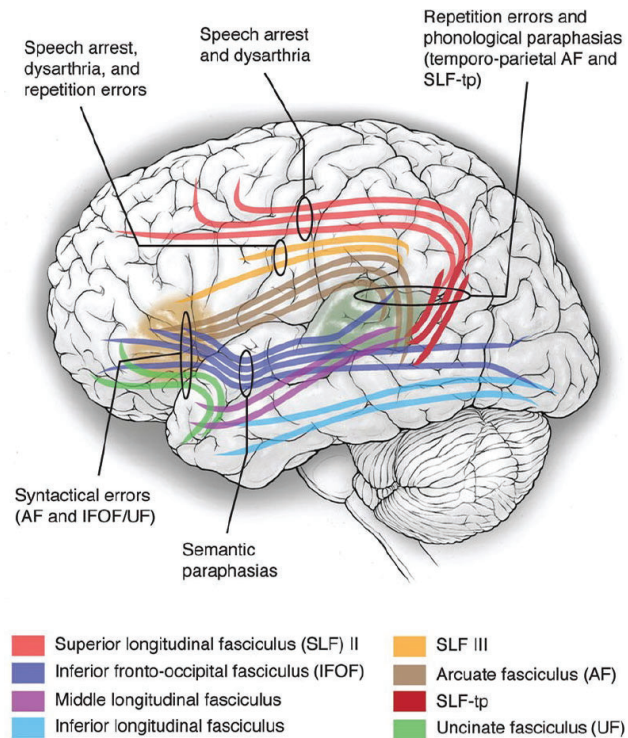
- Examined physical activity during a typical week
- Physical activity (% time in MVPA) was not related to baseline amyloid ( $\beta = -0.005$ ,  $p = 0.710$ ) or change in amyloid ( $\beta = 0.003$ ,  $p = 0.670$ )
- BUT, higher physical activity (% time in MVPA) was predicted less decline in memory across 32 months



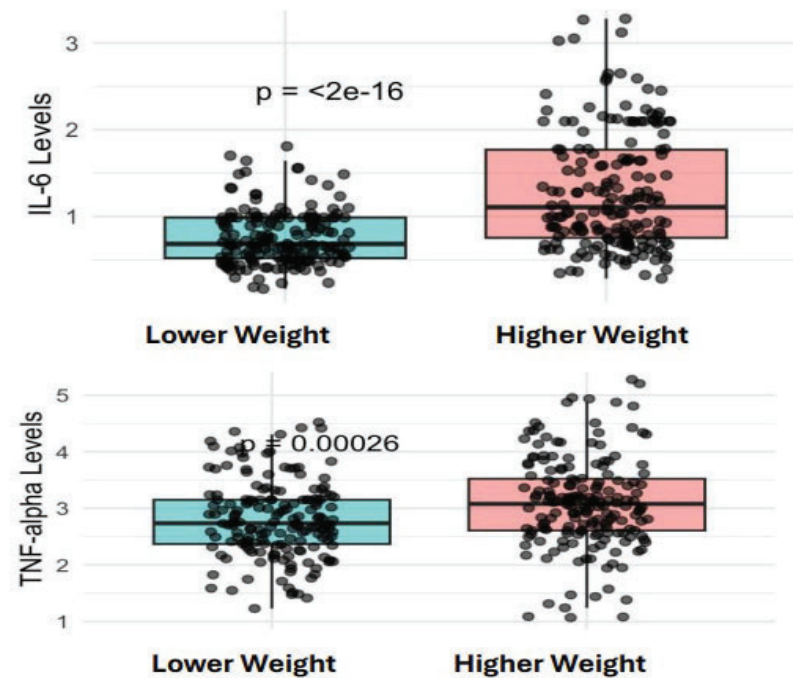
Fleming et al., 2025

# Physical Activity Benefits

- Improves brain white matter



- Reduces inflammation



Fleming et al., 2022; 2025

# Summary

- Children and adults with Down syndrome have a unique profile of metabolic and cardiovascular health
- Elevated weight is not related to some of the health outcomes observed outside of Down syndrome, it is related lipid levels and inflammation
- Lifestyles that foster healthy cardiometabolic functioning are important
  - Unique barriers
  - Physical activity may help maintain cognitive functioning
- Unintentional weight loss may be a sign of Alzheimer's disease



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