Investigating Biological and Brain Age in Children in the Adolescent Brain Cognitive Development (ABCD) Study

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INTRODUCTION

Whole person health involves considering multiple interconnected biological, behavioral, social, and environmental facets that affect the overall health and well-being of a person. Biological and brain aging, the quantification of the physiological deterioration of organ systems and the brain, has been shown to be an effective quantifiable tool that is predictive of a variety of diseases. We utilized blood-based biomarkers and gray matter volume biomarkers to calculate the acceleration of biological and brain age in a cohort of young children across the United States. In addition, we examined the relationship between biological and brain age acceleration (KDM Advance) with a multitude of physical, neurocognitive, and social health outcomes.
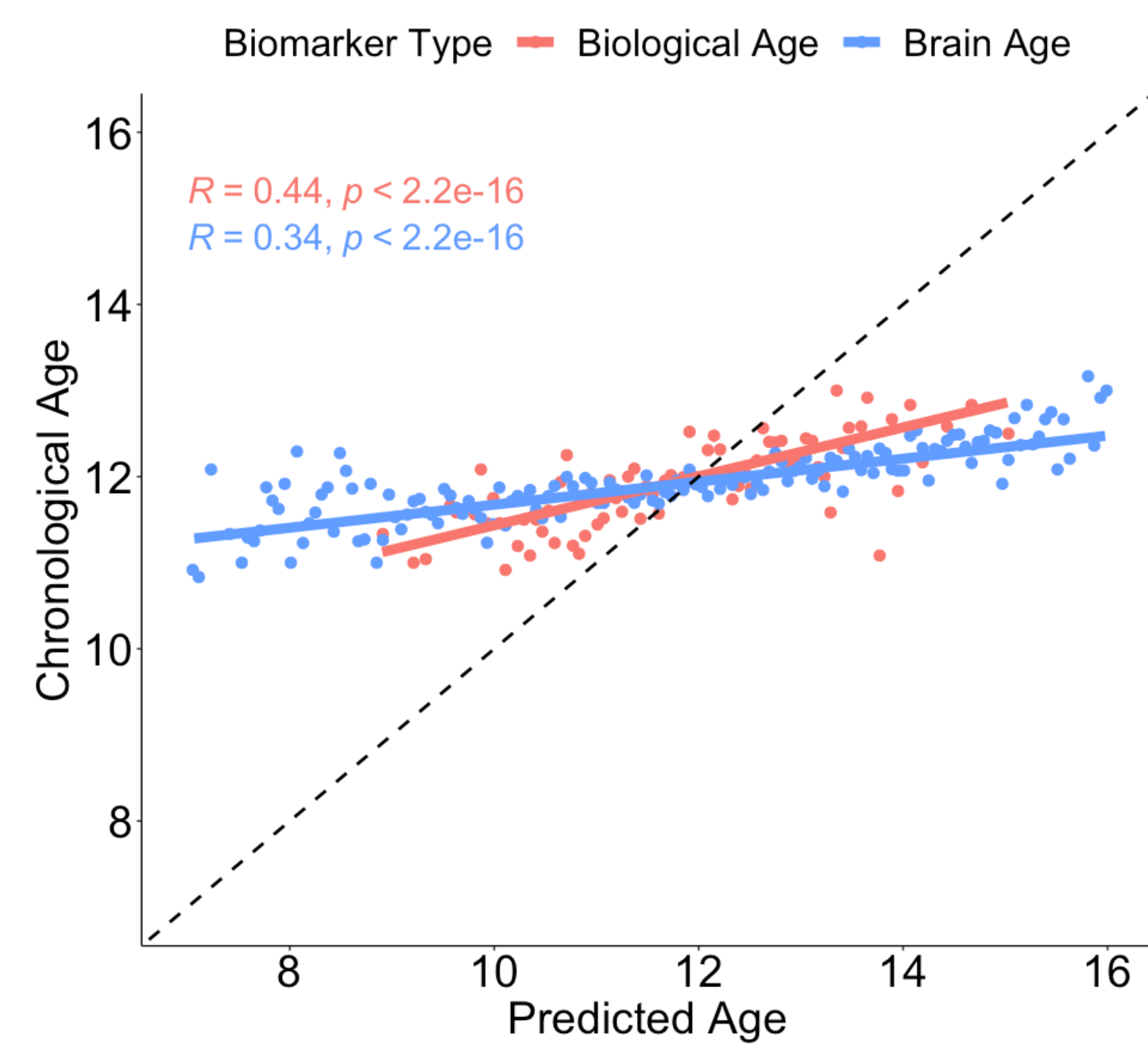
METHODS

Blood-based biomarkers and grey matter volume were selected from children from the ABCD study. The ABCD study is an ongoing longitudinal research study in the US undertaken by 21 data collection sites. The study aims to collect data on the behavior and brain development of over 11,500 children beginning at age 9-10 continuing into adulthood.

For this study, a subset of children were chosen for Biological Age and Brain Age depending on available biomarker data. Since Biological Age biomarkers are only available at year 2, Biological Age and Brain Age were both calculated with data from year 2.

	Biological Age Cohort	Brain Age Cohort
N	369	2117
Mean Age (SD)	11.94 (0.65)	11.93 (0.64)
Number of Males	214	1149

Biological Age Measures

Importance of Brain Regions for Brain Age Calculation

Standardized Regression Coefficient

BIOLOGICAL AND BRAIN AGE PREDICTION

The **Klemera-Doubal Method (KDM)** (Klemera et al., 2006) was used for Biological and Brain Age predictions.

$$BA_{EC} = \frac{\sum_{j=1}^{m} (x_j - q_j) \frac{k_j}{s_j^2} + \frac{CA}{s_{BA}^2}}{\sum_{j=1}^{m} \left(\frac{k_j}{s_j}\right)^2 + \frac{1}{s_{BA}^2}},$$

Pipeline

1. Split Cohorts by Healthy and Unhealthy
   1. Determined by CBCL scores and Physical Problems
2. Split Healthy Cohort into Training and Test set
3. Use Healthy Cohort to Train Model
4. Validate on Healthy Test set
   1. **RMSE = 0.91 years, MAE = 0.72 years** for KDM to Chronological Age (Healthy Test)
5. Use Healthy Test set plus Unhealthy Cohort (Outcome Cohort) to Predict Outcomes

RELATIONSHIP WITH HEALTH OUTCOMES

KDM Age Prediction Versus Chronological Age

$R = 0.44$, $p < 2.2e-16$
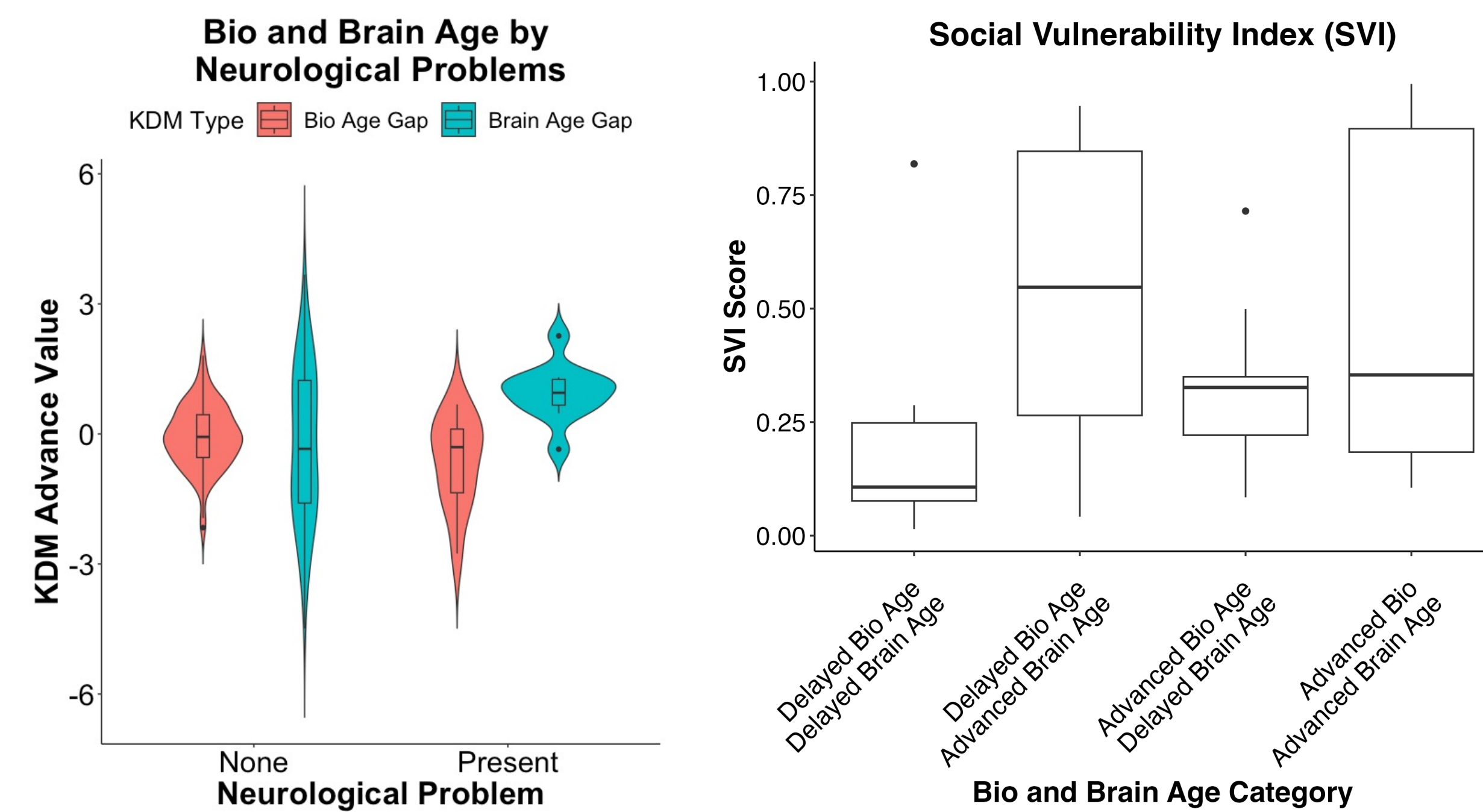$R = 0.34$, $p < 2.2e-16$

- The predicted age for the Biological Age Outcome Cohort is called **Biological Age**, and the predicted age for the Brain Age Outcome Cohort is called **Brain Age**.

- The **difference** between the Biological Age and Chronological Age is called **Bio Age Gap** and **Brain Age Gap** for Brain Age and Chronological Age.
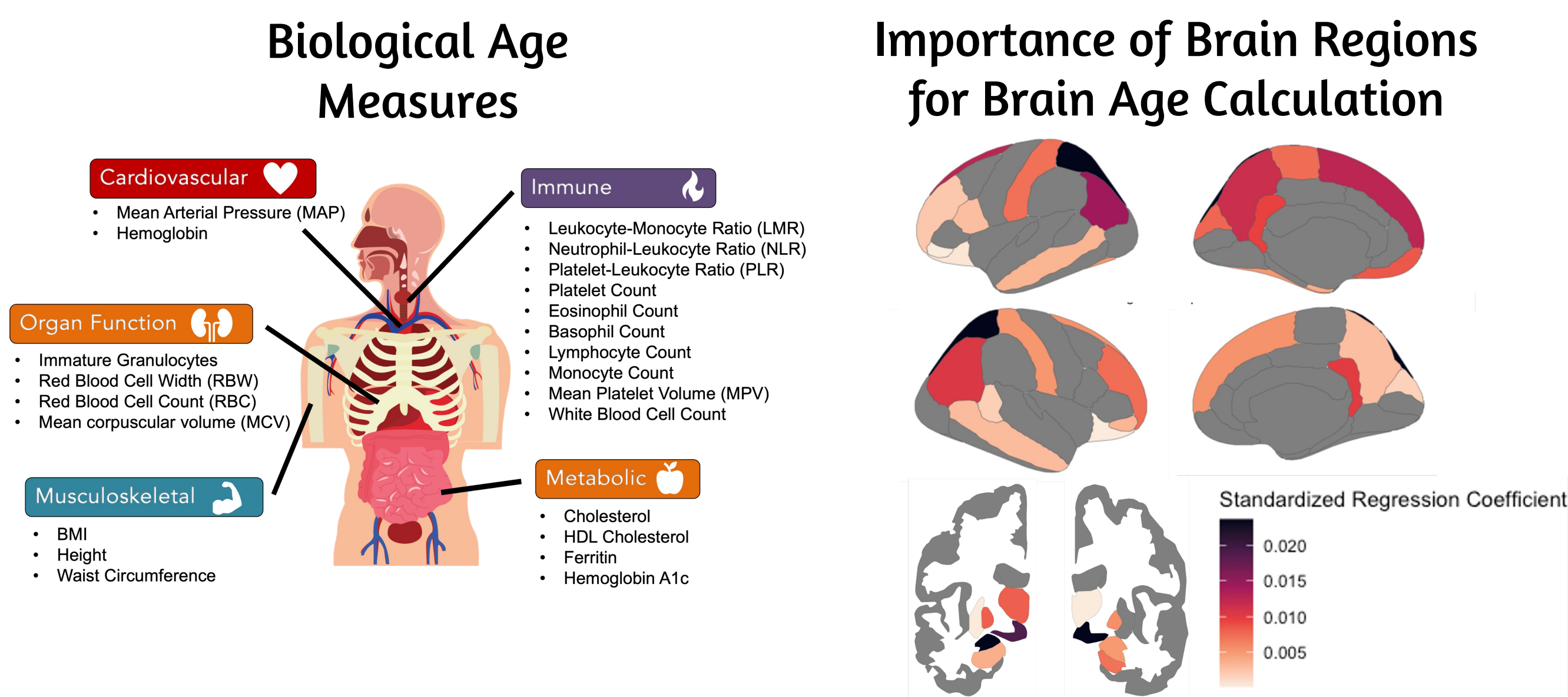
Regression Coefficients (Outcome ~ KDM Advance + Covariates)
2 Year Outcomes

b = .05
b = .50
b = 1.50
b = -.05
b = -.50
b = -1.50

Neurocognition
Social
Physical

Regression Coefficients (Outcome ~ KDM Advance + Year 2 Score + Covariates)
3 Year Outcomes
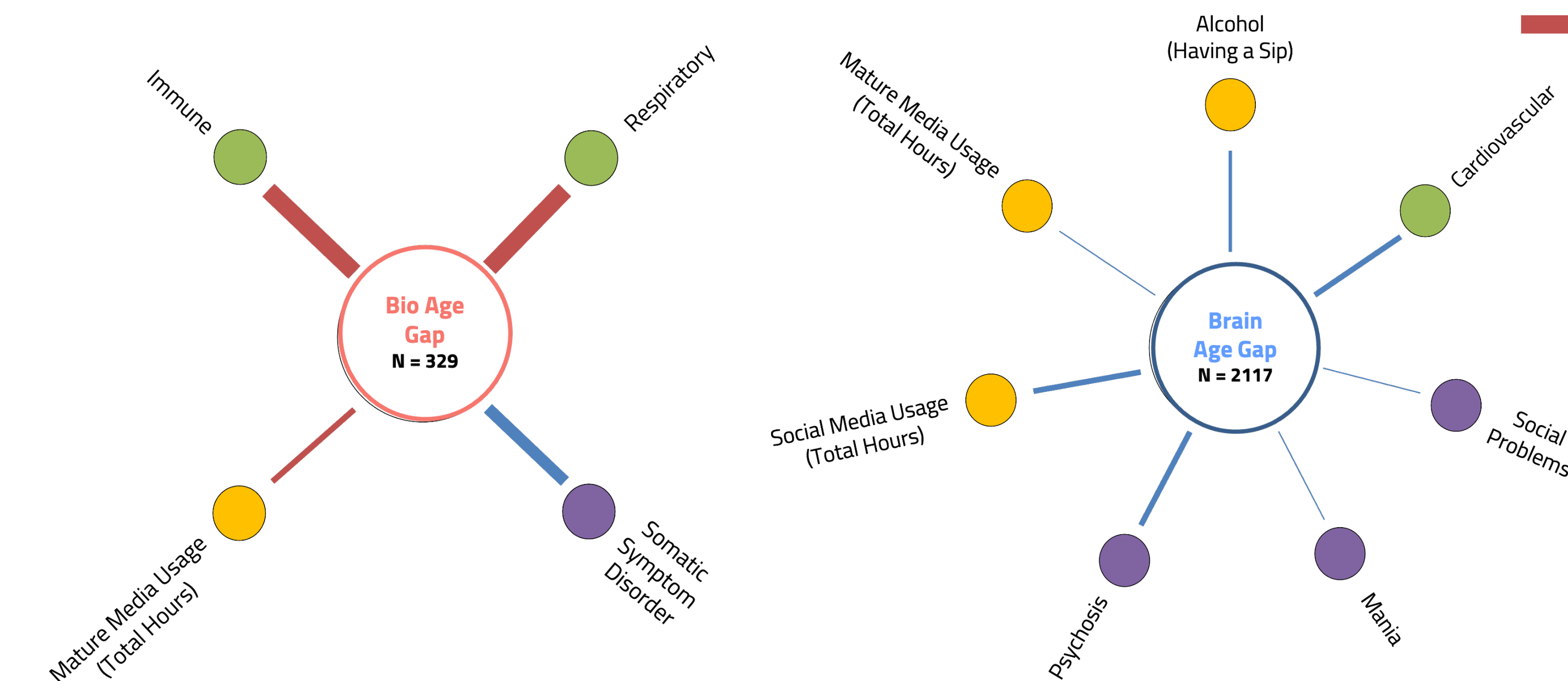
At the same time point (Year 2)
- A **greater Bio Age Gap** is generally associated with **less physical and social problems**.
- A **greater Brain Age Gap** is generally associated with **more neurocognitive, physical, and social problems**.

Future Prediction (Year 3)
- A **greater Bio Age Gap** is predictive of **less adverse health outcomes one year later.**
- A **greater Brain Age Gap** is predictive of **more adverse health outcomes on year later.**

RELATIONSHIP BETWEEN BIOLOGICAL AND BRAIN AGE

Proportion of Health Problems of Children with both Biological and Brain Age Data (N = 83)
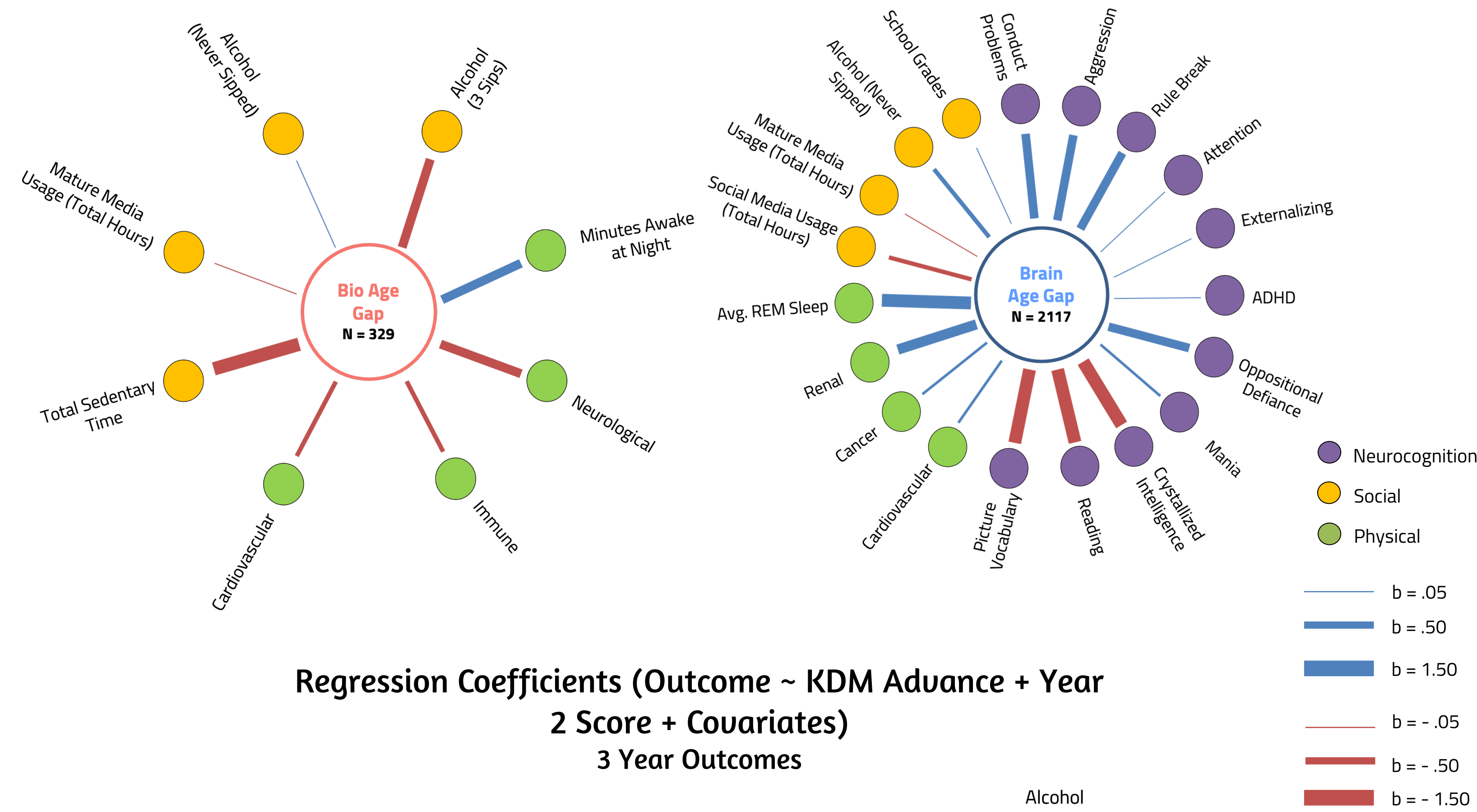
|	Cardiovascular	Immune	Neurological
Delayed Biological Age and Delayed Brain Age	14.29%	14.29%	0%
Delayed Biological Age and Advanced Brain Age	0%	9.1%	18.18%
Advanced Biological Age and Delayed Brain Age	11.11%	0%	0%
Advanced Biological Age and Advanced Brain Age	0%	0%	20%

- **Bio Age Gap** and **Brain Age Gap** may **be indicative of different health outcomes**.
- Furthermore, they may even show **different directionalities for the same health outcome** as shown by the interaction in neurological outcomes.

CONCLUSIONS

- We used the Klemera-Doubal Method (KDM) to estimate Biological and Brain age in children.
- A **greater Bio Age Gap** was associated with less adverse health outcomes.
- A **greater Brain Age Gap** was associated with more adverse health outcomes.
- Biological Age and Brain Age are predictive of different outcomes and may provide additional information when estimated together.
- More research is needed to understand the trajectories of biological and brain age in children.
- A larger sample size in a longitudinal study for are needed to study the true effects and interactions of Biological and Brain Age together across participants.

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