

Early life adversity and white matter development in the Healthy Brain Network dataset



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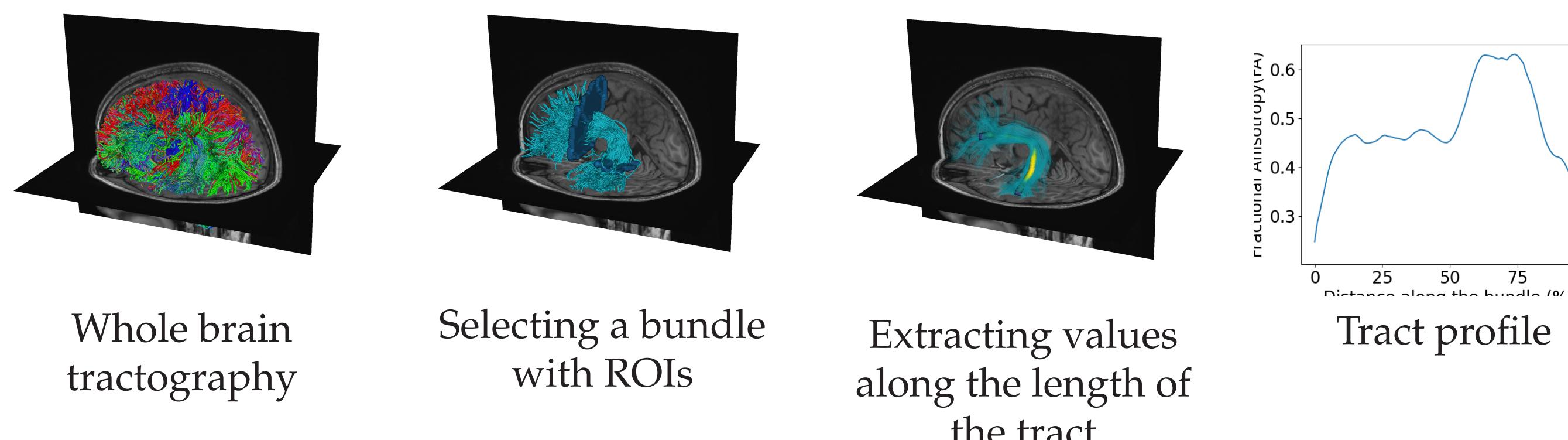
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Introduction

- Early life adversity (ELA) comprises negative environmental experiences that require significant adaptation by an average child.
- ELA is associated with depression, PTSD, low educational attainment, and deficits in language development and executive functioning[1].

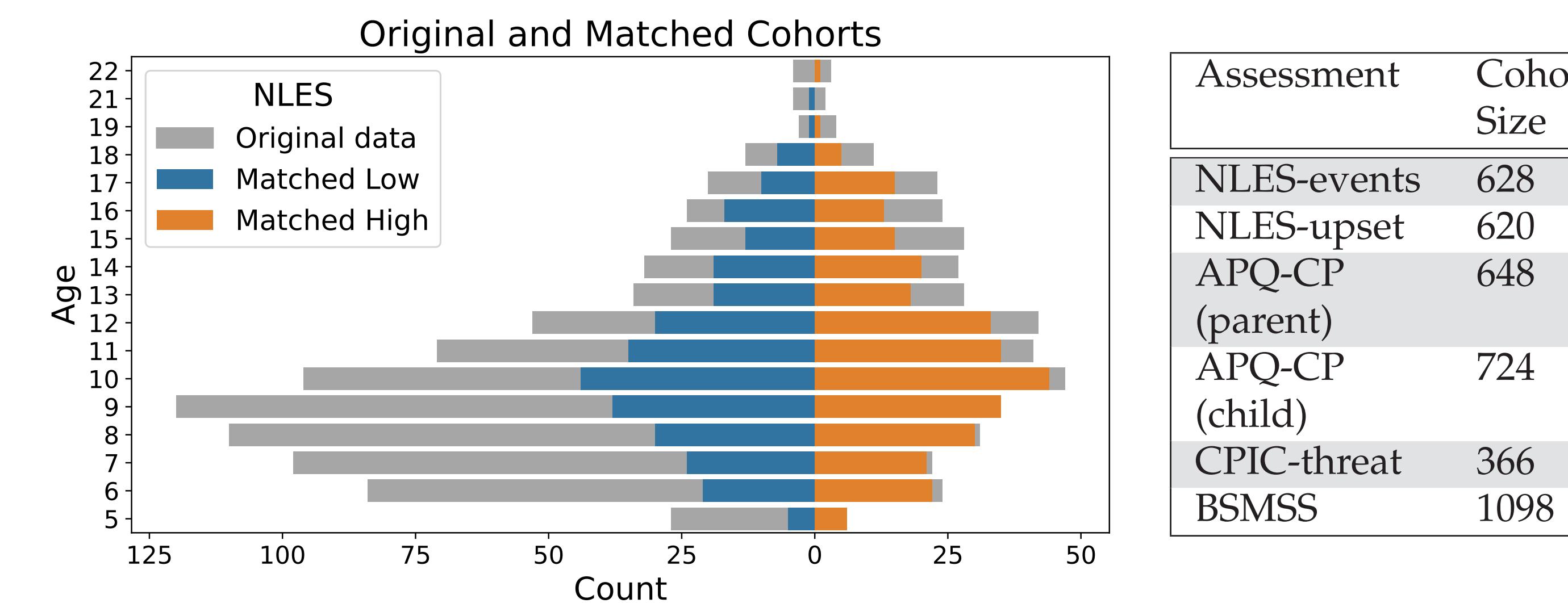
Question: How does early life adversity alter children's developing white matter, as assessed through diffusion MRI (dMRI)?

- There is some evidence that children exposed to adversity exhibit differences in the uncinate fasciculus, cingulum, and superior longitudinal fasciculus[2].
- We sought to test these findings in **tract profile** analysis of dMRI data from 1,817 participants in the Healthy Brain Network study[3], a large, heterogeneous dataset.

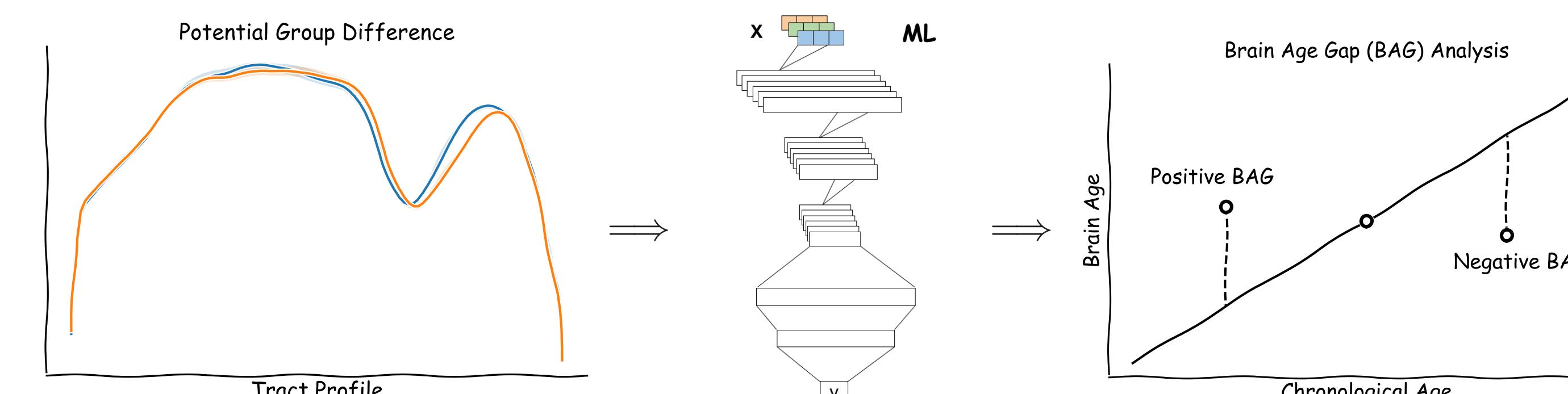


Methods

- ELA estimated using the self-reported negative life events scale (NLES).
- Threat dimension[4] assessed using child perception of interparental conflict threat (CPIC-threat), Alabama parenting questionnaire corporal punishment (APQ-CP) subscales.
- These were binarized into "low" (below median) and "high" (upper tertile) groups.
- SES assessed using the Barratt simplified measure of social status (BSMSS).
- Confounding variables were statistically matched between target and normative cohorts.



- Group difference assessed (1) as a classification task using linear and non-linear machine learning (ML) models and (2) using brain age gap analysis



References

- [1] Sinan Guloksuz, Jim van Os, and Bart P F Rutten. The Exposome Paradigm and the Complexities of Environmental Research in Psychiatry. *JAMA psychiatry*, 75(10):985–986, October 2018.
- [2] Raquel E Gur, Tyler M Moore, Adon F G Rosen, et al. Burden of Environmental Adversity Associated With Psychopathology, Maturation, and Brain Behavior Parameters in Youths. *JAMA psychiatry*, 76(9):966–975, May 2019.
- [3] Adam Richie-Halford, Matthew Cieslak, Lei Ai, et al. An analysis-ready and quality controlled resource for pediatric brain white-matter research. *Scientific data*, 9(1):616, October 2022.

Results

No differences found between statistically matched ELA groups: mass univariate paired t-tests for ELA~tract and per-bundle MANOVA for tract~ELA (both $p>0.05$, FDR corrected)

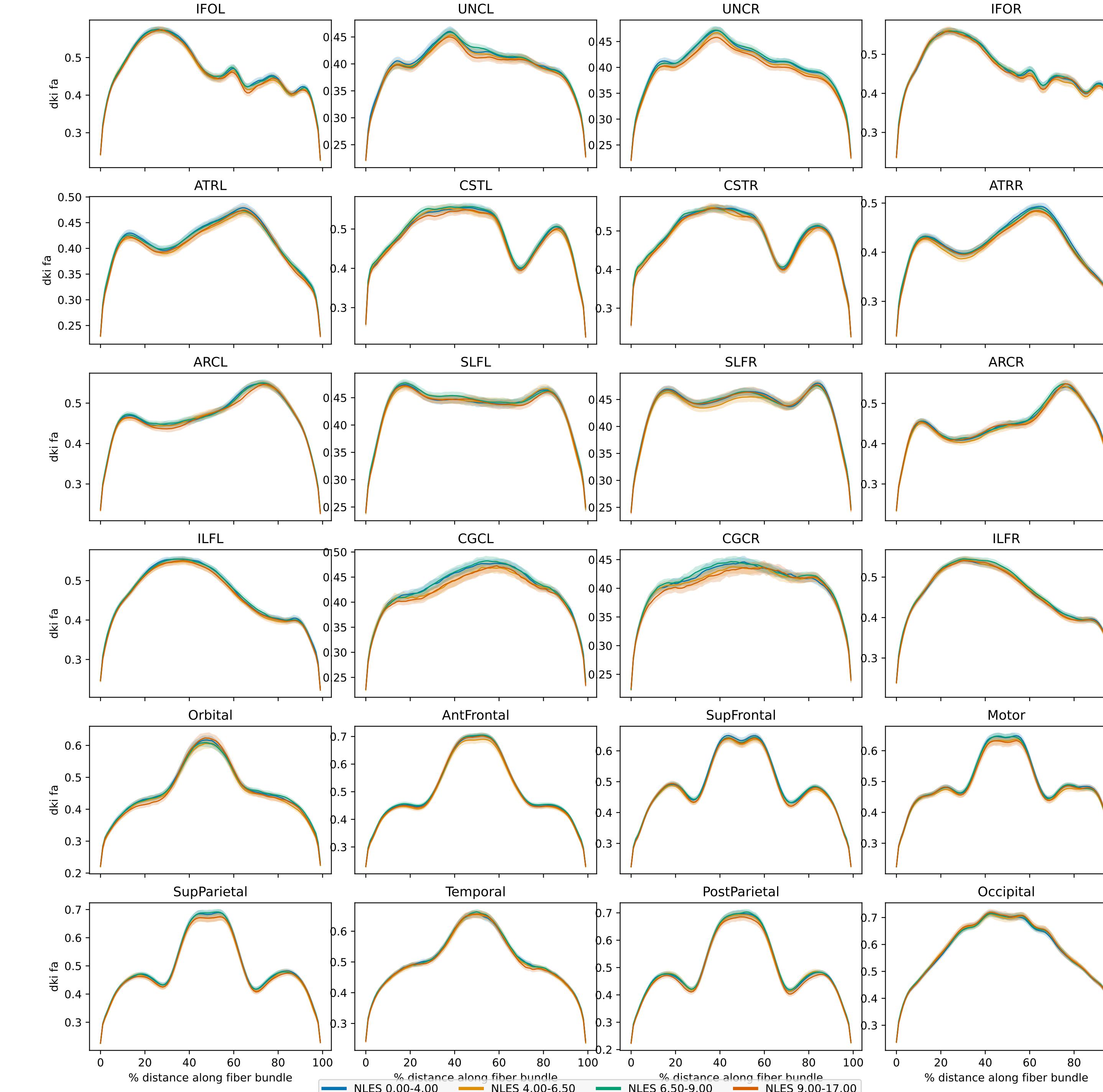


Figure 1: FA bundle profiles show no group differences between NLES quartiles. The x -axis is distance along the bundle. Error bands are 95% confidence intervals. Bundle abbreviations have a trailing "L" or "R" for the hemisphere. Bundle abbreviations: inferior fronto-occipital fasciculus (IFOF), uncinate (UNC), anterior thalamic radiation (ATR), corticospinal tract (CST), arcuate fasciculus (ARC), superior longitudinal fasciculus (SLF), inferior longitudinal fasciculus (ILF), cingulum cingulate (CGC), orbital corpus callosum (Orbital), anterior frontal corpus callosum (AntFrontal), superior frontal corpus callosum (SupFrontal), motor corpus callosum (Motor), superior parietal corpus callosum (SupParietal), temporal corpus callosum (Temporal), posterior parietal corpus callosum (PostParietal), and occipital corpus callosum (Occipital).

Discussion

- **Finding:** we find no associations between exposure to early life adversity and white matter structure in the HBN dataset using three distinct methods
 - statistical tests of group difference (paired t-test and MANOVA)
 - classification using advanced linear and non-linear models
 - brain age gap (BAG) analysis

- **Limitations**
 - As a self-reported, cumulative measure of ELA, NLES may be inadequate, however, threat measurements APQ-CP and CPIC-threat also yielded null results.
 - Due to HBN's recruitment protocol, comorbidity with other psychopathologies is high.
 - Cross-sectional data are inadequate to capture longitudinal changes due to ELA.

Machine learning models fail to classify ELA exposure groups.

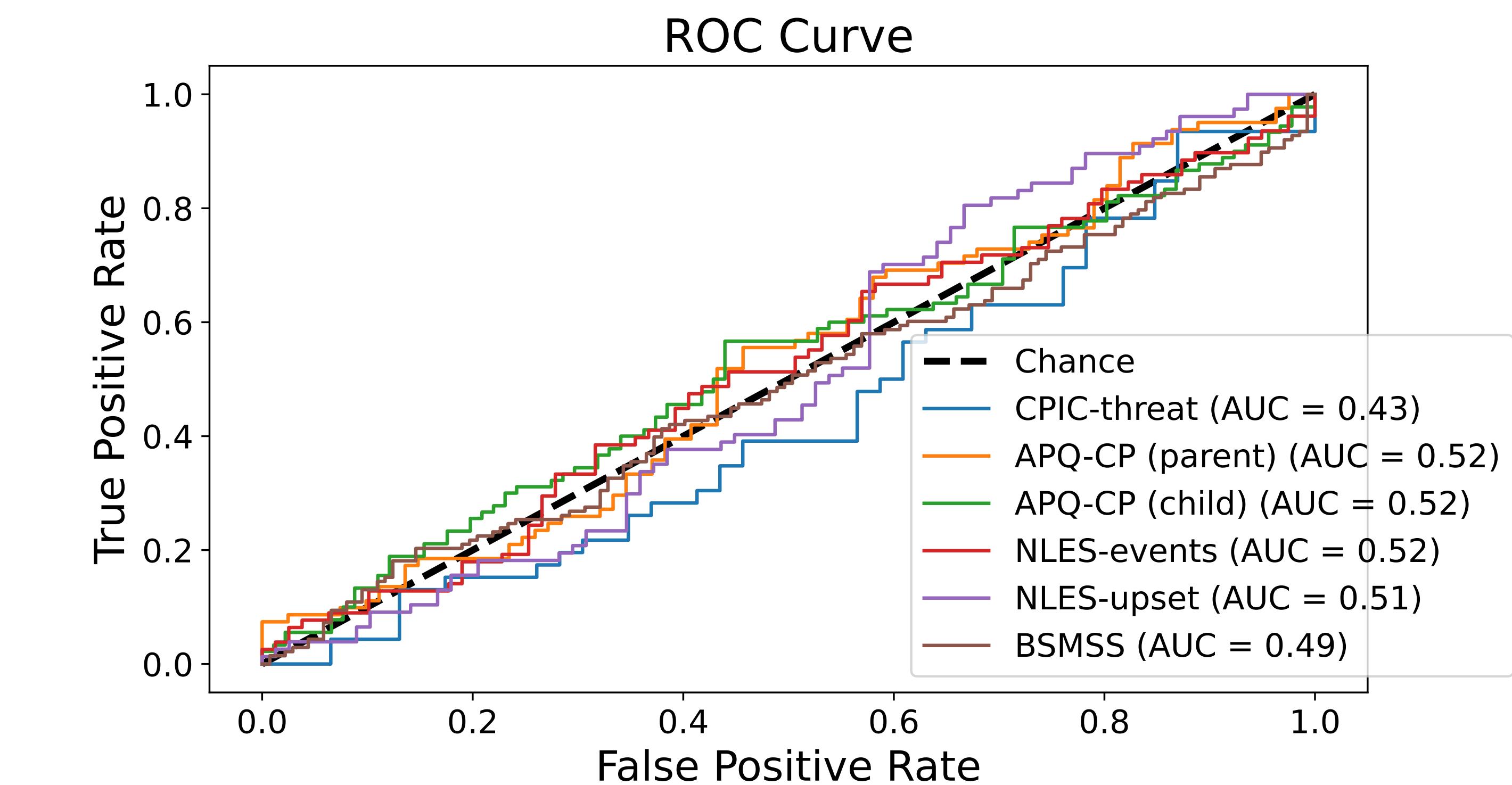


Figure 2: Machine learning models fail to classify ELA exposure groups, yielding ROC curves that are similar to random guessing.

There are no group differences in brain age gap.

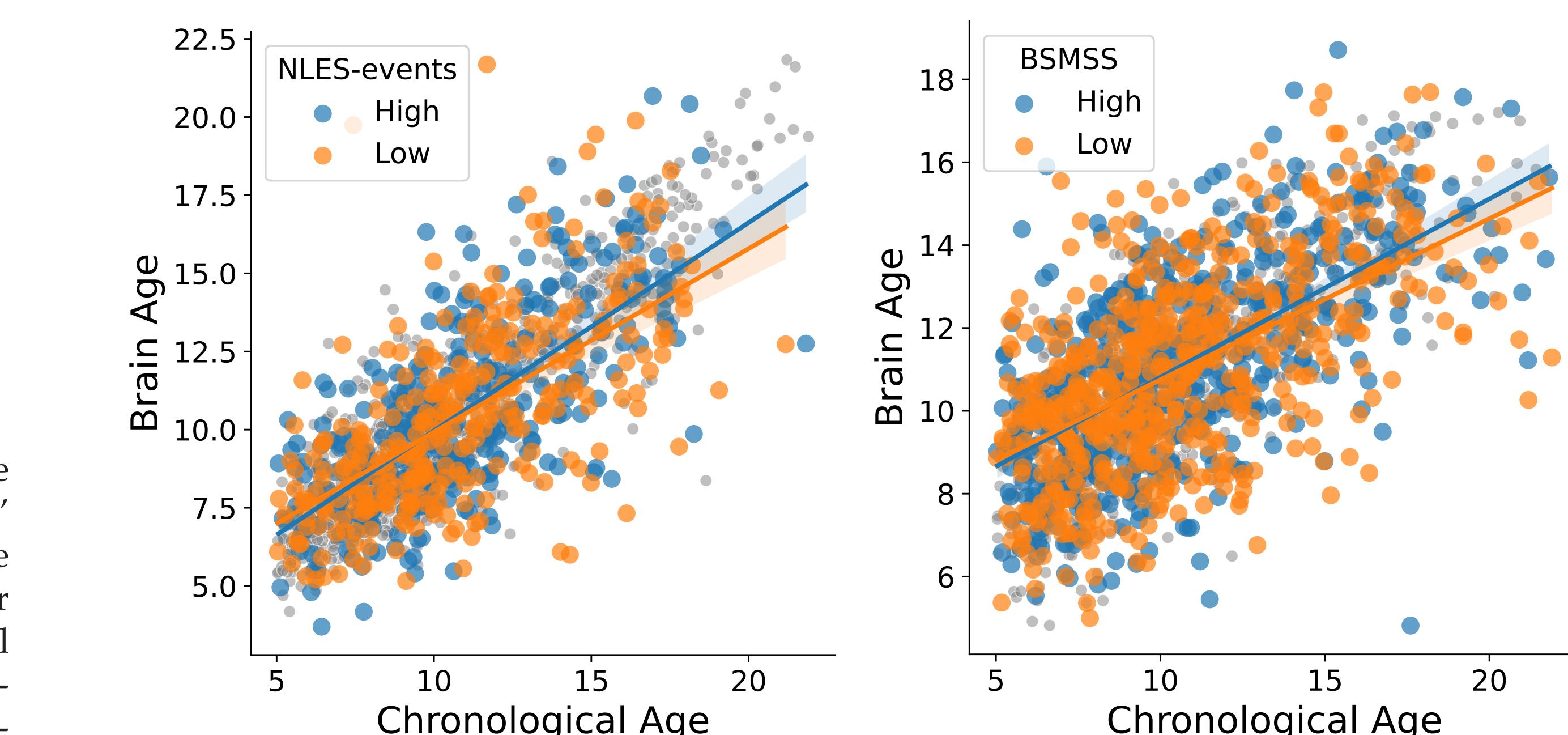
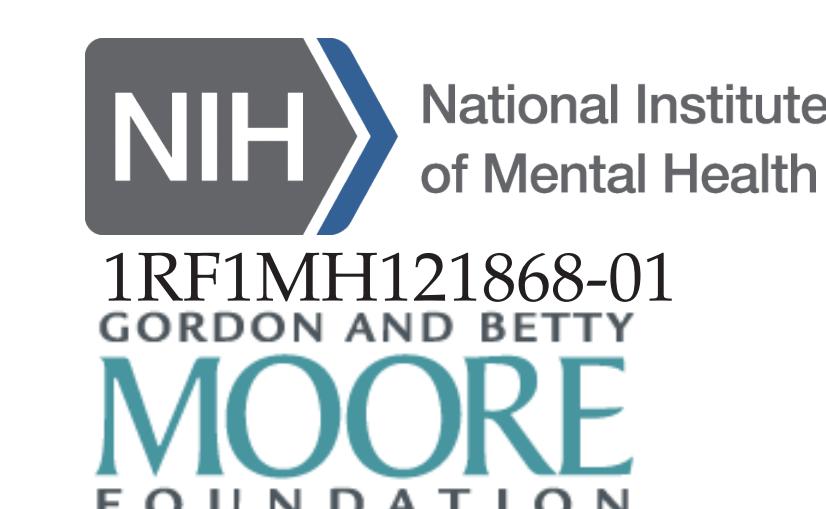


Figure 3: ELA and SES groups exhibit no differences in brain age gap.

Acknowledgments



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