Heritability of subcortical volumes in the adolescent brain

Christian Coffman Advised by: Dr. Saonli Basu and Dr. Eric Feczko

Division of Biostatistics, University of Minnesota

School of Public Health, University of Minnesota

University of Minnesota
Driven to Discover℠

Introduction and Objectives

Clinically diagonosoed psychological disorders are associated with heritable regional subcortical brain volumes (rSBVs) in adults [2, 4]. To see if the same regions are heritable in adolescents, we analyzed rSBVs in the Adolescent Brain Cognitive Development study (ABCD) whih has 10,000+ structural fMRI scans. Estimating Imaging derived phenotypes taken across multiple sites is complicated by confounding differences between sites [1]. In addition, sites have different distributions of subjects with respect to their genetic ancestries. Currently, no method of moments (MOM) estimator accounts for both influences which is important to get unbiased estimates.

Methods

1. AdjHE is closed form solution to 2nd moment [3]
2. Compared to existing methods for site effects theoretically and via simulations see (Figure 3)
3. Estimated on rSBV's in ABCD (see Figure 2)

Estimation Time

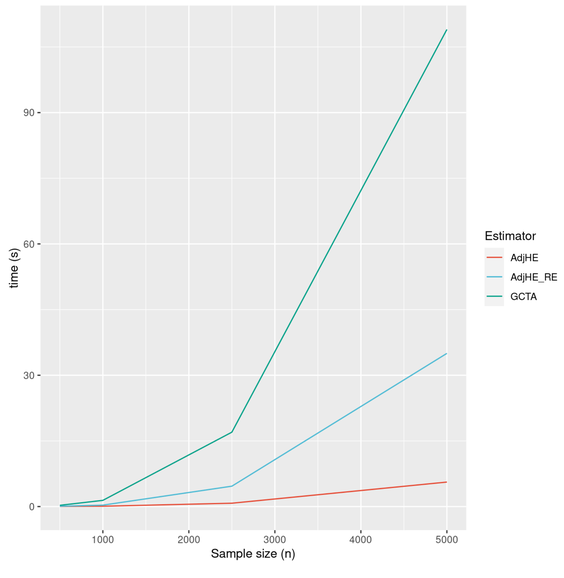

Figure 1:Time for estimation on increasinly large simulated datsets for AdjHE (blue), AdjHE with random site effects (light blue), and GCTA (red)

rSBV Heritability

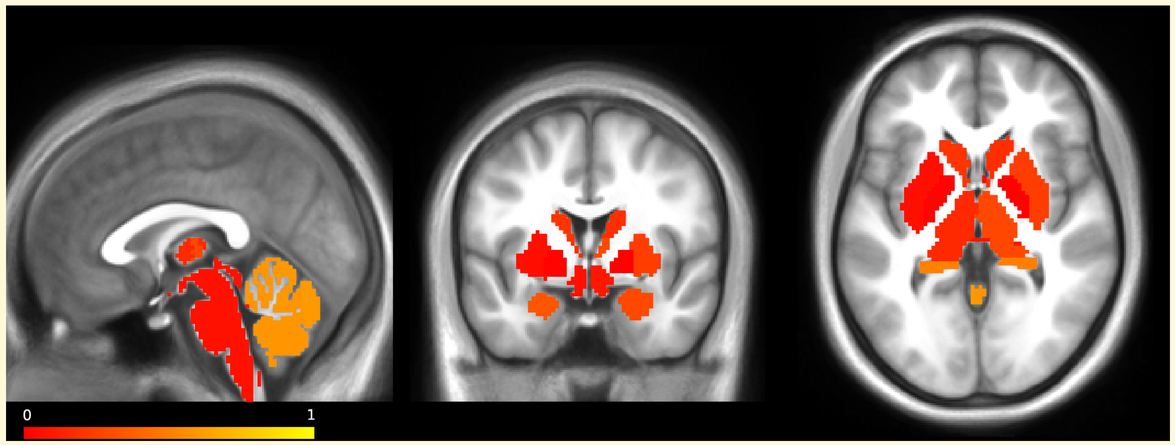

Figure 2:Heritability of rSBVs visualized on the Conte brain template. Yellow indicates high heritability, red indicates low.

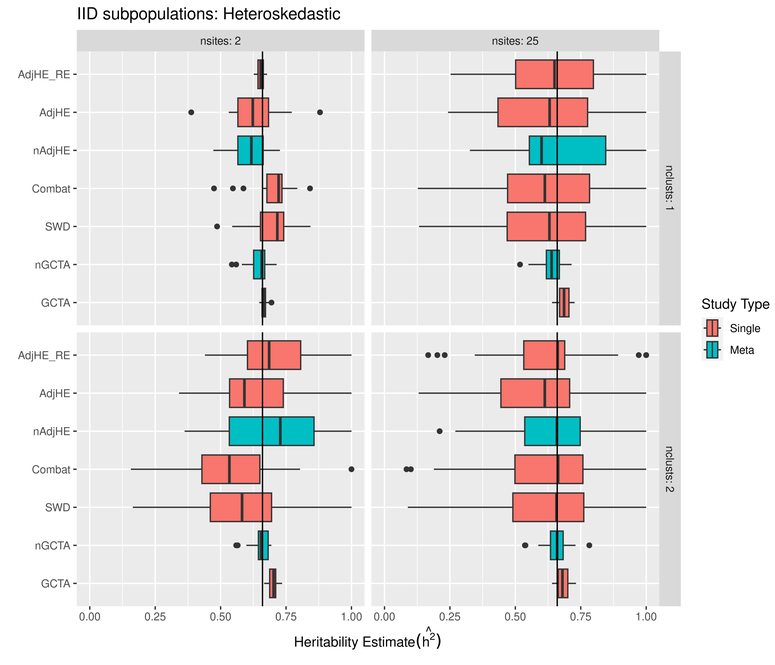

Figure 3:Simulation estimates under 2 and 25 sites (left and right columns) and 1 and 2 genetic ancestries (top and bottom rows). Estimates are compared between the proposed method "AdjHE_RE" and multiple other methods including GCTA.

Contact

Email: coffm049@umn.edu
Github: https://github.com/coffm049

Discussion

The new estimator broadens unbiased estimation to conditions where genetic ancestries and site effects vary between sites. We've shown the new estimator is unbiasedness theoretically and through simulations. In addition, we found multiple regions with significant heritability in the adolescent brain. We next hope to extend this method to multivariate traits.

ABCD Demographics

Characteristic	N = 11,878[1]
Household.Income	
<50k	3,224 (27%)
>=50k&<100k	3,071 (26%)
100k+	4,565 (38%)
Unknown	1,018 (8.6%)
Female	5,862 (49%)

[1] n (%)

Characteristic	N = 11,878[1]
Race	
Asian	252 (2.1%)
Black	1,784 (15%)
Hispanic	2,411 (20%)
Other	1,247 (10%)
Unknown	2 (<0.1%)
White	6,182 (52%)

[1] n (%)

Figure 4:Descriptions of key demographic variables in the ABCD dataset.

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