Independent effects of socioeconomic status and genetics on adolescent brain development and working memory

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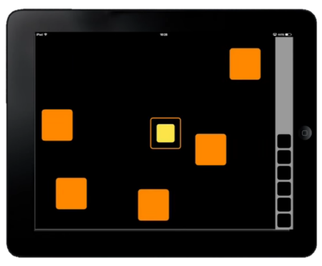
Introduction

Genetic and socioeconomic (SES) factors play a large role in educational attainment, and both have been associated with variations in brain structure. Even though these two factors are known to correlate, no prior study has assessed their neural effects independently. Here we used polygenic scores for educational attainment (EduYears-PGS) and SES to tease apart genetic and environmental effects on cognitive and brain development. 551 adolescents received structural MRI scans and working memory (WM) tasks at ages 14 and 19. This allowed us to measure the independent effects of EduYears-PGS and SES on global and regional measures of surface area and cortical thickness. We were also interested in how these causes impacted working memory (WM) at baseline and the development over five years.

Working Memory (WM)

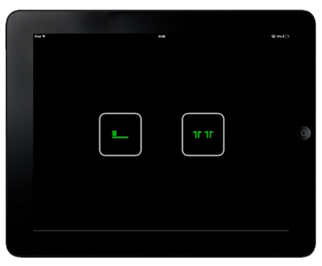
We estimated working memory from 3 cognitive tasks using the software CANTAB. We combined these into a latent factor that explained around 40% of the common variance.

Spatial Working Memory task (SWM)



Participants must search for a token hidden in one of many boxes. The token does not repeat location.
Measure: number of times participants returned to search a box that had a token.

Pattern Recognition Memory task (PRM)

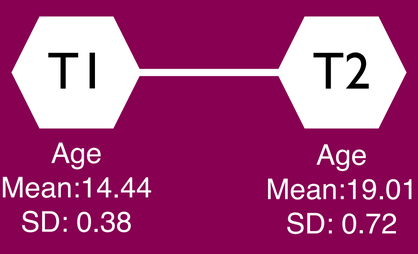


Participants must remember 12 abstract patterns.
Measure: correct choices on a two alternative forced choice task immediately after encoding.

Rapid Visual Information Processing task (RVP)

Participants must monitor for a 3-digit target sequence from a stream of 100 digits per minute.
Measure: correct responses to the target sequence.

The IMAGEN is a longitudinal study covering 8 sites in Germany, the UK, France, and Ireland. After exclusions from quality-control and missing data, we used 551 participants in total.



EduYears Polygenic Scores (PGS)

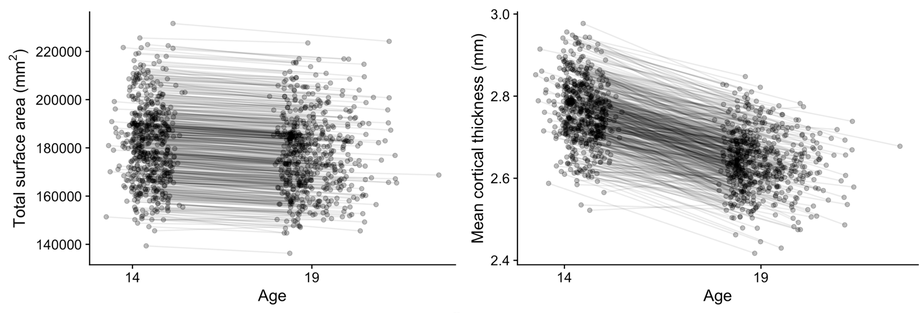
The genotype of IMAGEN was quality-controlled and imputed following standard procedures. We estimated polygenic scores for each participant using the software PRSice-2.
We identified the best p-value threshold to use by performing high-resolution scoring (with 1 million permutations to guard against over-fitting) on our sample's WM trait. This resulted in 5709 SNPs for estimating EduYears PGS. Empirical p = 0.009

Socioeconomic Status (SES)

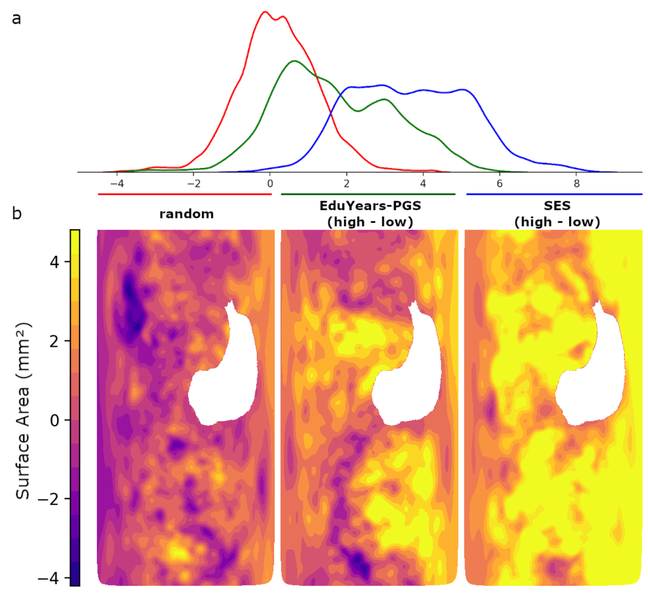
SES was obtained using the parent interview of DAWBA, and indexed by the sum of: Mother's Education Score, Father's Education Score, Family Stress Unemployment Score, Financial Difficulties Score, Home Inadequacy Score, Neighborhood Score, Financial Crisis Score, Mother Employed Score, and Father Employed Score.

Surface Area (SA) and Cortical Thickness (CT)

FreeSurfer was used to estimate SA and CT. ComBat was used to harmonize site effects independently of SES, PGS, gender, and age. In house QC specifically targeted skull strip errors.



Reduction in SA (-4057mm^2) and CT (-.12mm) over five years.



Global surface area of the left hemisphere displayed with **(a)** density histogram and, (**b**) flat maps. Data for EduYears-PGS (middle figure) and SES (right most) were calculated by vertex-wise averaging of subjects 1 SD above the mean subtracted from those 1 SD below. (n per group ~ 85)

Bivariate Latent Change Score Model

For the model, we set strict measurement invariance across T1 and T2 for variables of WM and SA. All observed variables were already controlled for age and gender differences at each time point. Circles indicate latent variables, and rectangles indicate observed variables. Single-headed arrows indicate regressions. Double-headed arrows indicate variance and covariance. A "1" indicates which values were constrained to unity. T1 = Timepoint 1, when participants were 14 years old. T2 = Timepoint 2, when the same participants were 19 years old. A Δ indicate change from T1 to T2. Intercepts are not shown for clarity. All values are standardized. ns: not significant. Parameters with values shown are significant (α = 0.05).

Total Surface Area

A bLCS model with strict measurement invariance for total surface area fit the data well (CFI = .99, RMSEA = .04).

Cross & Self feedback

- Higher WM at 14 led to more change (more reduction) in SA after 5 years yet it was also related to a lack in improvement in WM over 5 years.
- Higher SA at 14 led to more change (more reduction) in SA after 5 years yet it did not effect the change in WM over 5 years.

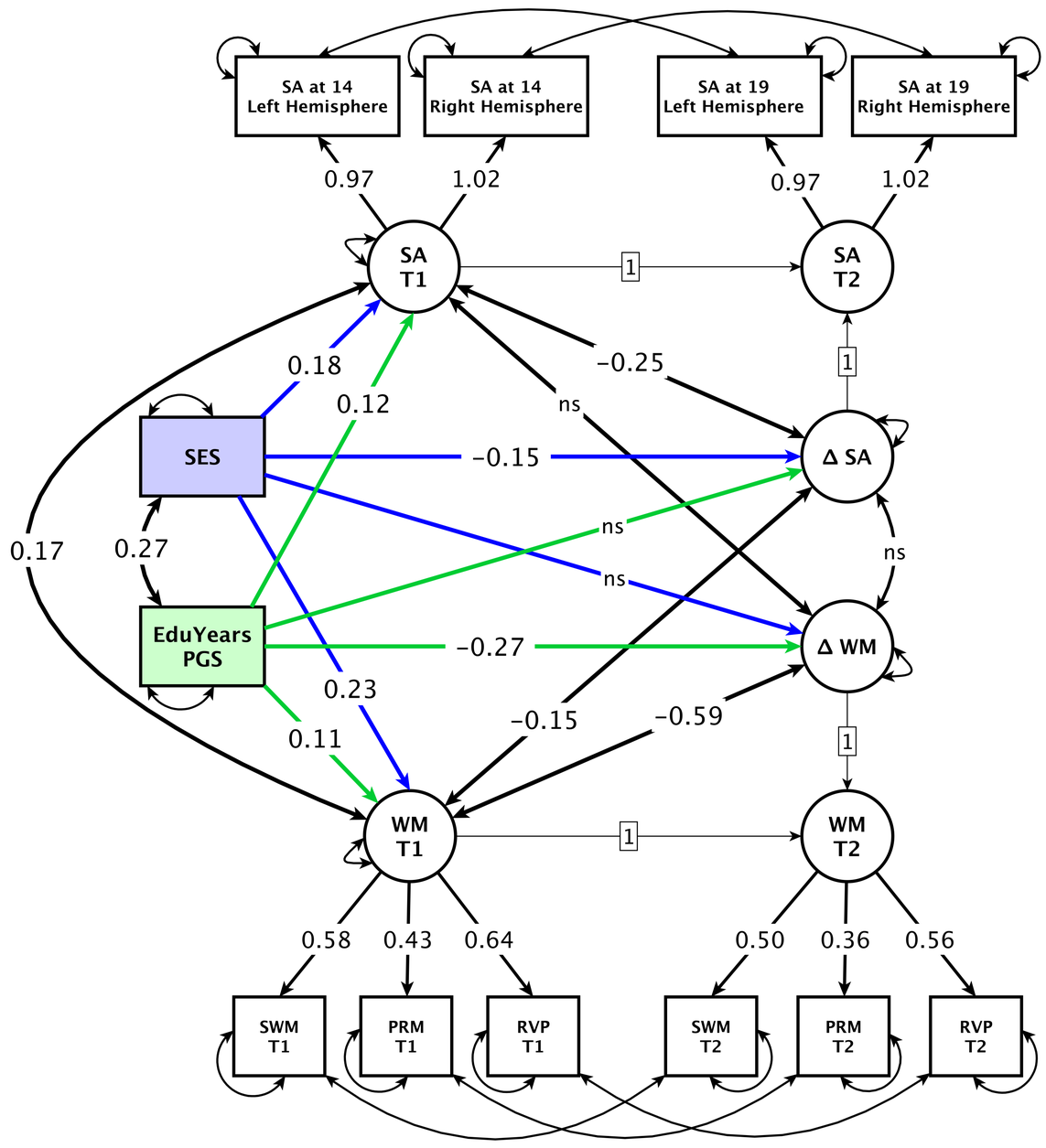
In fourteen year-old's

- Working memory at fourteen was independently related to SES (b = .23) and PGS (b = .11).
- Surface area at fourteen was also independently related to SES (b = .18) and PGS (b = .12).

Change over adolescence

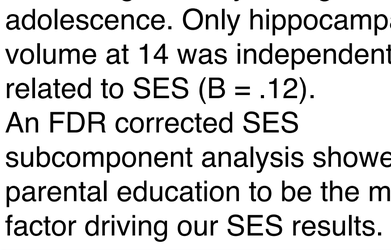
- The change of WM over five years was not related to SES yet did show a negative relationship with PGS (higher PGS less gains in WM).
- The change of SA over five years was was independently related to SES yet not PGS.

"In our reasonings concerning matter of fact, there are all imaginable degrees of assurance... A wise man, therefore, proportions his belief to the evidence."
- David Hume



Regional cortical effects

- Vertex-wise analyses (CFT < .001, CWP < .05) were run to identify regions independently associated to SES or PGS.
- Crucially total SA was covaried for allowing localization of regions.



- SA in the right intraparietal sulcus/supramarginal gyrus (309mm^2, [49, -42, 39]) was uniquely related to PGS.
- No clusters for SES, contrasting Noble et al., 2015; Nat. Neuro.
- No clusters for SES or PGS were present in the subtracted images.

Cortical Thickness

- bLCS model fit the data well, yet mean CT at age 14 and the change was not related to SES or PGS.
- No regional effects of SES or PGS (regardless of global correction).

Post hoc analyses

- Amygdala & Hippocampal volume did not significantly change over adolescence. Only hippocampal volume at 14 was independently related to SES (B = .12).
- An FDR corrected SES subcomponent analysis showed parental education to be the main factor driving our SES results.

Conclusions

EduYears-PGS and SES had both common and independent effects on brain structure and cognition. Specifically, lower SES was related to less total cortical surface area and lower WM at age 14. EduYears-PGS was also related to total cortical surface area, but in addition, had a regional effect on surface area in the right parietal lobe. SES, but not EduYears-PGS, affected the change in total cortical surface area from age 14 to 19.