

# Supporting Information

Raznahan et al. 10.1073/pnas.1203350109

## SI Methods

**Participant Recruitment and Screening.** All participants were recruited through local and national advertisement. The absence of neurological or psychiatric illness was established through completion of a screening questionnaire (Childhood Behavior Checklist) (1) and a screening interview administered by a child psychiatrist at intake (2). Participants were of mixed handedness (handedness established using Physical and Neurological Examination of Soft Signs) and race. SES was quantified using Hollingshead scales (3).

**Neuroimaging.** All sMRI brain scans were T-1 weighted images with contiguous 1.5-mm axial slices, obtained on the same 1.5-T General Electric Signa scanner using a 3D spoiled gradient recalled echo sequence with the following parameters: echo time, 5 ms; repetition time, 24 ms; flip angle, 45°; acquisition matrix, 256 × 192; number of excitations, 1; and field of view, 24 cm. Native sMRI scans were submitted to the well-validated (4, 5) CIVET pipeline\* for automated morphometric analysis. One set of algorithms within this pipeline estimates total GMV, WMV, and CSF volume using a validated neural net approach to voxel classification (6, 7). A separate set of algorithms models gray/white and pial cortical surfaces for each scan. Briefly, this process begins with linear transformation, correction of nonuniformity artifacts, and segmentation of each image into white matter, gray matter, and CSF (7). Next, each image is fitted with two deformable mesh models to extract the white/gray and pial surfaces. These surface representations are then used to calculate CT and SA at ~80,000 points (vertices) across the cortex (8) and aligned

with each other using a 2D surface-based registration algorithm to allow comparison of equivalent vertices across different scans (9). Surface area was calculated at the middle cortical surface, which lies at the geometric center between the inner and outer cortical surfaces (10).

**Statistical Analysis.** As an example of cross-sectional cognitive analysis, to relate the main effects of BW to FSIQ, we modeled FSIQ for the *i*th twin-pairs, *j*th member as follows:

$$\text{FSIQ}_{ij} = \text{Intercept} + d_i + \beta_1(\text{birth weight}) + e_{ij} \quad [\text{S1}]$$

As an example of longitudinal anatomical analysis, to relate the main effects of BW and linear age to TBV, we modeled TBV at *i*th twin-pairs, *j*th members, *k*th time point as follows:

$$\text{TBV}_{ijk} = \text{Intercept} + d_i + d_{ij} + \beta_1(\text{age}) + \beta_2(\text{birth weight}) + e_{ijk} \quad [\text{S2}]$$

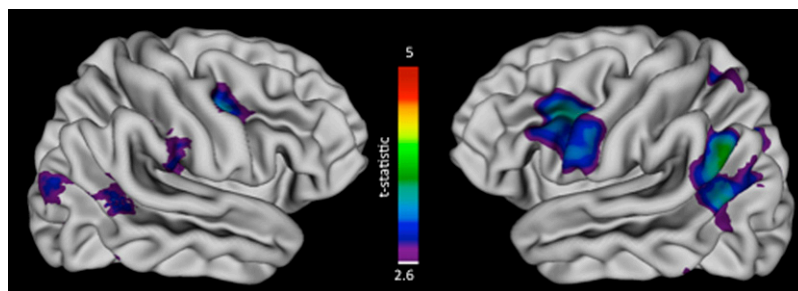
Building on above TBV example, interaction between zygosity and BW was modeled as:

$$\text{TBV}_{ijk} = \text{Intercept} + d_i + d_{ij} + \beta_1(\text{age}) + \beta_2(\text{birth weight}) + \beta_3(\text{zygosity}) + \beta_4(\text{birth weight} * \text{zygosity}) + e_{ijk} \quad [\text{S3}]$$

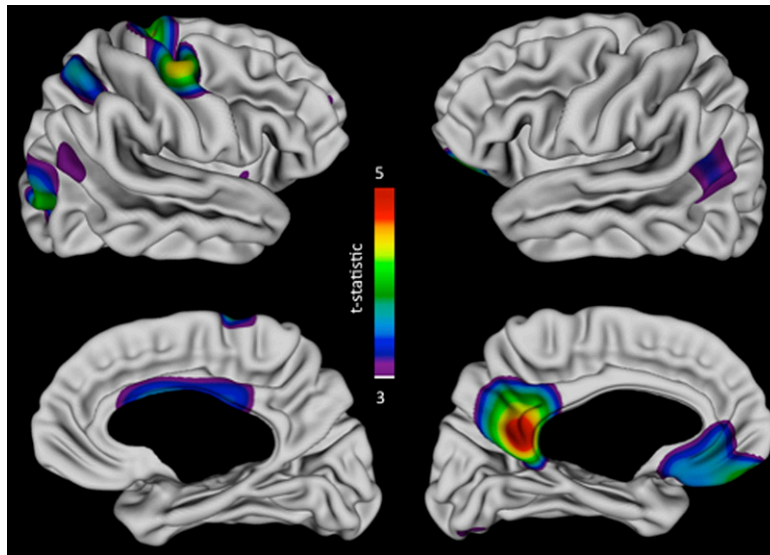
Use of a linear age term in Eqs. S2 and S3 is only for illustrative purposes. As explained in main body of our article (*Results*), age terms for most anatomical indices examined were nonlinear (i.e., cubic or quadratic) in nature. The best-fitting age model for each anatomical index was determined through a step-down approach that moved from cubic->quadratic-> linear until statistical significance was achieved.

\*Ad-Dab'bagh Y, et al., The CIVET image-processing environment: A fully automated comprehensive pipeline for anatomical neuroimaging research. Sixth Annual Meeting of the Organization for Human Brain Mapping (OHBM), June 11–15, 2006, Florence, Italy.

1. Achenbach TM, Howell CT, Quay HC, Conners CK (1991) National survey of problems and competencies among four- to sixteen-year-olds: Parents' reports for normative and clinical samples. *Monogr Soc Res Child Dev* 56:1–131.
2. Giedd JN, et al. (1999) Brain development during childhood and adolescence: A longitudinal MRI study. *Nat Neurosci* 2:861–863.
3. Hollingshead AB (1975) *Four-factor index for social status* (Yale UP, New Haven).
4. Shaw P, et al. (2008) Neurodevelopmental trajectories of the human cerebral cortex. *J Neurosci* 28:3586–3594.
5. Im K, et al. (2008) Brain size and cortical structure in the adult human brain. *Cereb Cortex* 18:2181–2191.
6. Cocosco CA, Zijdenbos AP, Evans AC (2003) A fully automatic and robust brain MRI tissue classification method. *Med Image Anal* 7:513–527.
7. Zijdenbos AP, Forghani R, Evans AC (2002) Automatic "pipeline" analysis of 3-D MRI data for clinical trials: Application to multiple sclerosis. *IEEE Trans Med Imaging* 21:1280–1291.
8. MacDonald D, Kabani N, Avis D, Evans AC (2000) Automated 3-D extraction of inner and outer surfaces of cerebral cortex from MRI. *Neuroimage* 12:340–356.
9. Lyttelton O, Boucher M, Robbins S, Evans A (2007) An unbiased iterative group registration template for cortical surface analysis. *Neuroimage* 34:1535–1544.
10. Lyttelton O, et al. (2009) Positional and surface area asymmetry of the human cerebral cortex. *Neuroimage* 46:895–903.



**Fig. S1.** Vertex maps showing the relationship between BW variation within MZ twin-pairs and postnatal differences in CT. Associations between BW and vertex-level measures of CT did not survive application of a FDR correction for multiple comparisons with *q* (the expected proportion of falsely rejected null hypotheses) set at 5%. However, as shown in this figure, at a nominal *t*-statistic threshold equivalent to a *P* value cutoff of 0.001, a number of cortical regions showed a significant positive association between BW and CT.



**Fig. S2.** Vertex maps showing the relationship between BW variation across singletons and postnatal differences in cortical SA. Associations between BW and vertex-level measures of SA are shown as t-statistic maps, after correction for multiple comparisons using False Discovery Rate with  $q = 0.05$ . The relationship between BW and SA was developmentally static over the age range considered and robust to inclusion of sex, gestation length, height, weight, and SES as covariates. As for MZ twins, BW variation across singletons was more strongly associated with SA variation in associative rather than primary sensory cortices, although the precise location and laterality of these effects showed some differences between groups.

**Table S1. BW and postnatal outcomes in singletons**

Measure	Effect of BW		Estimated change with 500-g BW increase	
	<i>t</i>	<i>P</i>	Absolute	Relative
IQ	0.6	0.6	0.7 points	0.05 SD
VIQ	0.2	0.8	0.3 points	0.02 SD
PIQ	0.3	0.8	0.3 points	0.02 SD
Total brain volume	2.6	0.01	28 cm <sup>3</sup>	2%, 0.25 SD
Gray matter volume	2.2	0.03	15 cm <sup>3</sup>	1.7%, 0.21 SD
White matter volume	2.2	0.03	11 cm <sup>3</sup>	2.1%, 0.19 SD
Total cortical volume	2.3	0.02	12.5	2%, 0.19 SD
Mean cortical thickness	0.04	0.9	0.0005 mm	0.01%, 0.004 SD
Total surface area	3	0.003	35.6 cm <sup>2</sup>	1.8%, 0.3 SD

Main effect of BW is shown for cognitive (IQ, VIQ, PIQ) and global anatomical outcomes.