Supporting Information

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SI Text 1: Advantageous Properties of Cortical Thickness as an Anatomical Metric

Cortical thickness is an informative metric of cortical anatomy that has shown sex differences in existing postmortem and cross-sectional neuroimaging studies of humans (1) and is known to be a sensitive in vivo index of both typical (2, 3) and atypical cortical development (4). Furthermore, unlike the principal alternative spatially nonbiased measure of cortical anatomy—voxel-based measures of "gray matter density"—vertex-based measures of cortical thickness do not conflate cortical thickness and cortical surface area. This property is an important advantage, because cortical thickness and surface area capture very different sets of biological processes, as evidenced by their differing evolutionary histories (5), developmental trajectories (6, 7), and genetic determinants (8, 9).

SI Text 2: Methodological Details

Genotyping. For each participant, DNA was extracted from previously prepared lymphoblastoid cell lines using standard methods (Qiagen). Lymphoblastoid cell lines were grown in culture for approximately 2 mo before DNA extraction. Genotyping of AR-CAG length was performed by Prevention Genetics, using a slightly modified Marshfield set (13) (http://research.marshfieldclinic.org/genetics/GeneticResearch/sets/Set%2013.xls). This screening set is comprised of 405 STRPs that cover the autosomal, X, and Y chromosomes at a density of ~10 cM. PCR was performed in 96-well plates in 6-μL reactions containing ~45 ng DNA, 0.075 μM forward (5'-ACCGAGGAGCTTTCCAGAAT-3') and reverse (5'-AGAACCATCCTCACCCTGCT-3') primers, 0.03 U Platinum Taq, 100 μM each dNTP, and 1.5 mM $MgCl_2$. All markers were multiplexed at the PCR stage. Multiplexes were put together based on nonoverlapping marker size ranges and/or unique fluorescent dyes. PCR reactions were incubated for 2 min at 95 °C, followed by 27 cycles of denaturation (95 °C for 40 s), annealing (55 °C for 75 s), and elongation (72 °C for 40 s). A final extension (72 °C for 6 min) completed the PCR profile. PCR products were run on a polyacrylamide gel, and product length was determined in comparison to a standard DNA ladder. DNA sequencing of positive controls and correlation analyses of CAG length call for duplicate samples were conducted to ensure reliability and accuracy of genotype assignment. The distribution of CAG repeats was similar to that reported by available reference data (13), with 90% of AR alleles having between 19 and 28 CAG repeats.

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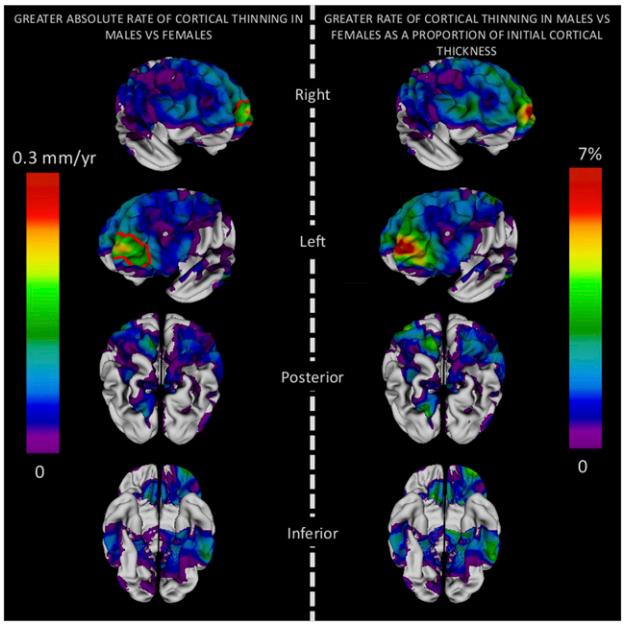

Fig. S1. Maps of difference in absolute (*Left*) and proportional (*Right*) rate of cortical thickness loss between ages 9 and 22 y in male and female subjects. (*Left*) Map of absolute difference between estimated mean rate of cortical thickness change in male subjects and estimated mean rate of cortical thickness change in female subjects (ie, coefficient magnitude for the age-by-sex interaction term in predicting cortical thickness). Colored vertices are those where cortical thickness loss is faster in male than female subjects. "Warmer" colors denote a greater acceleration of cortical thinning in males relative to females. The red "isobar" encompasses regions where the *t* statistic associated with this age-by-sex interaction term was statistically significant ($P < 0.05$). (*Right*) Map of percentage difference between rate of cortical thickness loss between ages 9 and 22 y in male compared with female subjects, where rate of cortical thickness loss in each sex is expressed as a proportion of initial cortical thickness at age 9 y. The equivalence of absolute and proportional maps indicates that sex differences in the rate of cortical thickness loss during adolescence are not explained by the fact that males have thicker cortices to begin with. Therefore, our findings regarding sex differences in the rate of cortical thickness loss hold regardless of any effect sex differences in overall brain size may have on sex differences in cortical thickness.

Table S1. Basis for nomination of cortical regions where distinct patterns of sexually dimorphic cortical maturation were hypothesized to exist

Domain of cognitive-behavioral sex difference	Evidence for sex difference	Cortical regions sub-serving cognitive-behavioral domain	Evidence for nomination of cortical regions	Evidence for regional structural and functional cortical sex differences
Language	Refs. 1, 2	TempPole, STS, transverse temporal sulcus, IFG, SMG	Refs. 3, 4	Refs. 5, 6
Visuospatial	Refs. 7, 8	SFG, MFG, IFG, PostCG, PreCG, SPL, IPS, IPL, ITG	Ref. 9	Refs. 10, 11
Social cognition	Refs. 12, 13	SFG, MFG, MedFG, OFC, AntCC, IFG, STS, vlPFC, vmPFC	Refs. 14	Refs. 15–18
Sensation seeking	Refs. 19, 20	MedFG, AntCC, IFG, insula	Refs. 21, 22	Ref. 23
Hyperactivity/impulsivity	Ref. 24	AntCC, DLPFC, vmPFC, OFC	Refs. 25–29	Ref. 30
Reward-related behaviors	Ref. 31	avPFC, vlPFC	Ref. 32	Ref. 33
Aggression	Ref. 34	FPC, vmPFC, dmPFC, AntCC	Refs. 27, 35, 36	–

avPFC, anterioventral prefrontal cortex; dmPFC, dorsomedial prefrontal cortex; FPC, frontopolar cortex; ITG, inferior temporal gyrus; MedFG, medial frontal gyrus; PostCG, post central gyrus; PreCG, pre central gyrus; SPL, superior parietal lobule; TempPole, temporal pole. For each principle domain of cognitive-behavioral sex difference (first column), references providing details of how male and female subjects differ at the cognitive behavioral level. Then, the set of cortical regions most consistently linked to each cognitive behavioral domain is listed, alongside references justifying the composition of each list.

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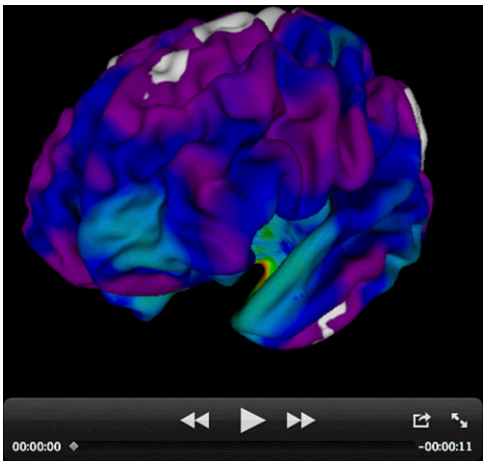
Table S2. Participant characteristics

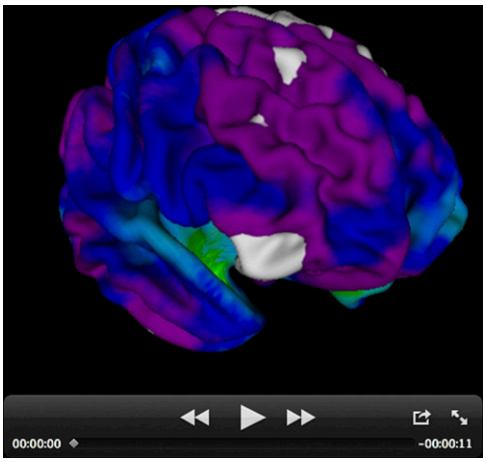
Characteristic	Group		Difference
	Male	Female	
No. of individuals	153	131	
Handedness, no.			NS
L	21	18	
R	132	113	
Race, no.			NS
White	138	107	
Black	7	12	
Asian	4	3	
Hispanic	2	7	
Other	2	2	
IQ, mean (SD)	113 (10.8)	111 (11.6)	NS
SES	42 (19.5)	43 (18.9)	NS
Total no. of scans	363	278	
Number of people by number of scans			
1 scan	47	40	
2 scans	36	50	
≥3 scans	70	41	
Mean age at each scan, y (SD)			
First scan	12.4 (2.7)	12.5 (3.0)	NS
Second scan	15.0 (2.5)	14.8 (2.8)	NS
Third scan	17.3 (2.5)	17.0 (2.5)	NS
Fourth scan	18.7 (2.0)	18.3 (1.8)	NS
Age distribution of scans, y			
Mean (SD)	14.6 (3.5)	14.3 (3.5)	
Range	9.0–22.8	9.0–22.8	
Genotype, no. individuals (no. of scans)			
AR-H	83 (192)	31 (66)	
AR-M	—	69 (152)	
AR-L	70 (171)	31 (60)	
Test for difference between genotype groups			
Handedness	NS	NS	
Race	NS	NS	
IQ	NS	NS	
SES	NS	NS	
Age at each scan			
First scan	NS	NS	
Second scan	NS	NS	
Third scan	NS	NS	

NS, not statistically significant; SES, socioeconomic status.



Movie S1. Time-lapse sequences show how spatial distribution of greater cortical thickness in males compared with females changes between ages 9 and 22 y for anterior-oblique left views of the cortical surface. Colored regions indicate a larger estimated mean group cortical thickness in male compared with female subjects. Color variation represents variation in the absolute magnitude of estimated difference in sex-group average cortical thickness. The transition from purple to dark blue to light blue to green to yellow to red represents grades of sex-group cortical thickness difference ranging from just above 0 mm to 0.5 mm greater cortical thickness in male than female subjects. White regions are where cortical thickness is greater in female than male subjects. At age 9 y, cortical thickness is greater in males than females over most of the cortex with the exception of small regions in bilateral supplementary motor (SMot) and inferior temporal (ITG) gyri, and right dorsolateral prefrontal (DLPF) regions. Then, as adolescence advances, frontal cortical thickness differences are lost in a bilateral wave that starts in posteriodorsal superior frontal gyrus and spreads in an anterioventral direction. This is driven by (*i*) cortical thinning with age in both male and female subjects, (*ii*) this occurring more rapidly in males, (*iii*) regional differences within the frontal lobe in the magnitude and sex difference in cortical thickness at age 9 y, and (*iv*) regional differences within the frontal lobe in the magnitude of sex difference in the rate of cortical thickness loss with age (Fig. 1 and Fig. S1). There is a striking similarity between these movies and those we previously published detailing the order at which frontal regions structurally mature relative to each other (http://www.pnas.org/content/suppl/2004/05/13/0402680101.DC1/02680Movie2.mpg). Therefore, the last regions in the frontal lobe to structurally mature are also the last where cortical thickness in males catches up with that in females. In contrast, beyond the frontal lobes, cortical thickness differences between male and female subjects generally increase over adolescence (with the exception of bilateral precuneus, superiodorsal parietal, and fusiform cortices). Divergence in cortical thickness between sex groups is most prominent in the temporal poles bilaterally.

Movie S1



Movie S2. Time-lapse sequences show how spatial distribution of greater cortical thickness in males compared with females changes between ages 9 and 22 y for anterior-oblique right views of the cortical surface. Colored regions indicate a larger estimated mean group cortical thickness in male compared with female subjects. Color variation represents variation in the absolute magnitude of estimated difference in sex-group average cortical thickness. The transition from purple to dark blue to light blue to green to yellow to red represents grades of sex-group cortical thickness difference ranging from just above 0 mm to 0.5 mm greater cortical thickness in male than female subjects. White regions are where cortical thickness is greater in female than male subjects. At age 9 y, cortical thickness is greater in males than females over most of the cortex with the exception of small regions in bilateral supplementary motor (SMot) and inferior temporal (ITG) gyri, and right dorsolateral prefrontal (DLPF) regions. Then, as adolescence advances, frontal cortical thickness differences are lost in a bilateral wave that starts in posteriodorsal superior frontal gyrus and spreads in an anterioventral direction. This is driven by (i) cortical thinning with age in both male and female subjects, (ii) this occurring more rapidly in males, (iii) regional differences within the frontal lobe in the magnitude and sex difference in cortical thickness at age 9 y, and (iv) regional differences within the frontal lobe in the magnitude of sex difference in the rate of cortical thickness loss with age (Fig. 1 and Fig. S1). There is a striking similarity between these movies and those we previously published detailing the order at which frontal regions structurally mature relative to each other (http://www.pnas.org/content/suppl/2004/05/13/0402680101.DC1/02680Movie2.mpg). Therefore, the last regions in the frontal lobe to structurally mature are also the last where cortical thickness in males catches up with that in females. In contrast, beyond the frontal lobes, cortical thickness differences between male and female subjects generally increase over adolescence (with the exception of bilateral precuneus, superiodorsal parietal, and fusiform cortices). Divergence in cortical thickness between sex groups is most prominent in the temporal poles bilaterally.

Movie S2