

Ventral frontal cortex in children: morphology, social cognition and femininity/masculinity

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The ventral frontal cortex (VFC) has been shown to differ morphologically between sexes. Social cognition, which many studies demonstrate involves the VFC, also differs between sexes, with females being more adept than males. In a previous study of subregions of the VFC in our lab, in an adult population, size of the straight gyrus (SG) but not the orbitofrontal cortex (OFC), differed between sexes and correlated with better performance on a test of social cognition and with greater identification with feminine characteristics. To investigate the relationship between VFC structure and social cognition in children, VFC gray matter volumes were measured on MRIs from 37 boys and 37 girls aged 7 to 17. The VFC was subdivided into the OFC and SG. Subjects were also administered a test of social perceptiveness and a rating scale of femininity/masculinity. In contrast to our findings in adults, the SG was slightly smaller in girls than boys. In girls, but not boys, smaller SG volumes significantly correlated with better social perception and higher identification with feminine traits. No volume differences by sex or significant correlations were found with the OFC. These data suggest a complex relationship between femininity, social cognition and SG morphology.

Keywords: brain morphology; femininity; gender differences; social perception; straight gyrus

INTRODUCTION

Several decades of studies have demonstrated marked gender differences in social behavior and cognition. Boys and men tend to form larger social groups and be less accepting of non-group members, while girls and women tend to prefer dyadic interactions and are more compromising (Geary, 2002; Fabes *et al.*, 2003). Males make more frequent displays of physical aggression than females, though females are more likely to participate in relational aggression such as gossiping and back-stabbing (Maccoby *et al.*, 1980; Crick *et al.*, 1997; Geary, 1998, 2002; Christiansen, 2001). Girls and women also generally perform slightly better in tasks of social perception (Hall, 1984; Costanzo and Archer, 1989). In studies including over 4000 subjects including school-aged children and adults in several different countries, females consistently were more adept at interpreting non-verbal cues of emotion, such as vocal intonation, facial expressions and body language (Rosenthal *et al.*, 1979; Hall, 1984).

Differences of social cognition and behavior emerge early in childhood. For example, girls tend to be more fearful and exhibit more empathy and emotional support helping behavior than boys, while boys demonstrate more impulsivity and physical play even as young as 2 years old and across cultures (Maccoby *et al.*, 1980; Sanchez-Martin *et al.*, 2000; Geary, 2002; Cote *et al.*, 2003; Fabes *et al.*, 2003). At age 3,

girls perform better than boys on theory of mind tests (Walker, 2005). Gender differences in social behavior emerge early in infancy. Female infants at 3 months of age show more interest expressions, such as wider eyes and higher brow placement (Malatesta and Haviland, 1982). As young as a few days old, female infants make more eye contact than male infants (Malatesta and Haviland, 1982; Geary, 2002). At 1 day of age, boys look longer at a mobile than at a human face, while girls look longer at a human face (Connellan *et al.*, 2000). These data imply inherent biological differences in social behavior and cognition. This idea is supported by the observation that the majority of patients with Turner syndrome (45, X) have problems with social interactions and interpretation of social cues. Furthermore, impaired social cognition is associated with inheritance of the maternal X chromosome, suggesting that imprinting of the paternal chromosome may play a role in development of higher order executive functions necessary for social perception (Skuse *et al.*, 1997). In addition, heritability of social cognitive skills in children aged 5–17 has been estimated at 0.68 (Scourfield *et al.*, 1999).

Given the data suggesting biological and genetic components as well as differences in social behavior and cognition, sexual dimorphism in brain structure in regions mediating these faculties might be expected. In particular, the ventral frontal cortex (VFC), consisting of the orbitofrontal cortex (OFC) and straight gyrus (SG), is an important node in the neurocircuitry governing normal social behavior in humans (Figure 1) (Blair *et al.*, 1999; Brunet *et al.*, 2000; Farrow *et al.*, 2001; Moll *et al.*, 2002; Tranel *et al.*, 2002; Adolphs, 2003; Wicker *et al.*, 2003; Mah *et al.*, 2004, 2005; Amodio

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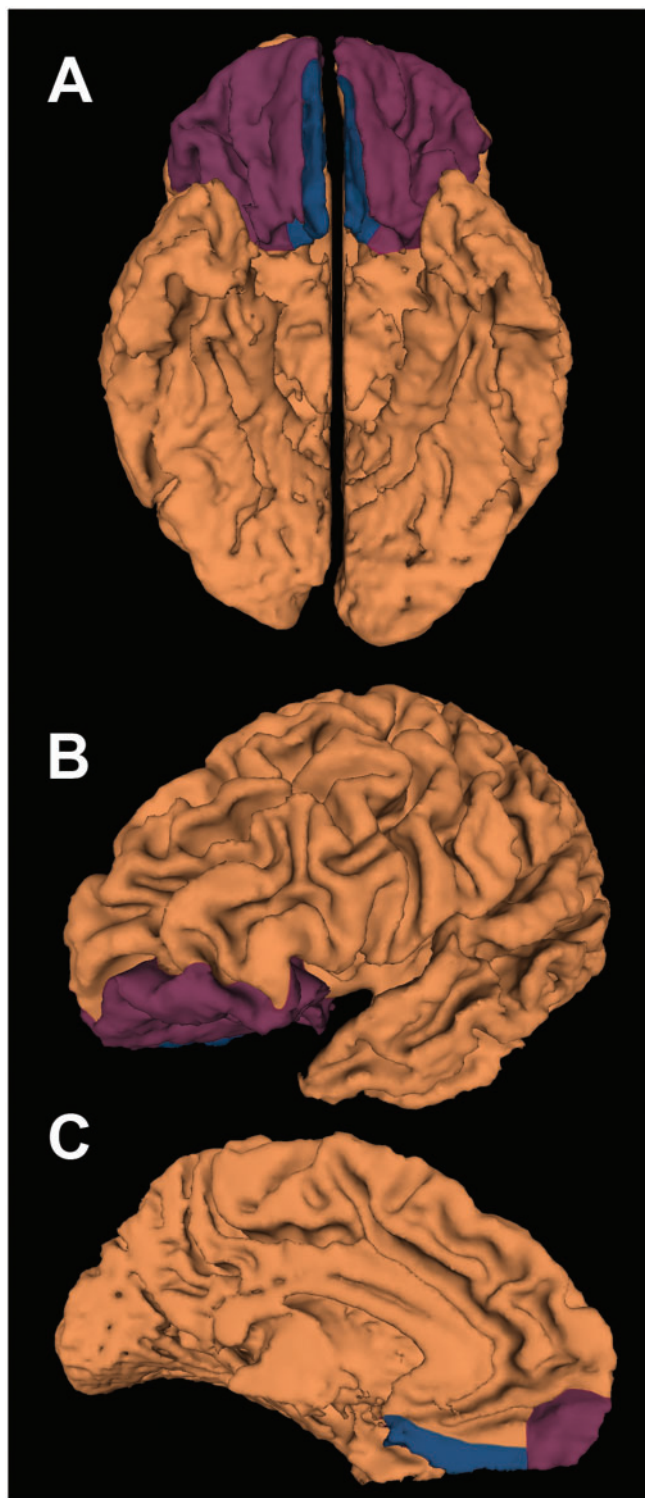


Fig. 1 The orbitofrontal cortex and straight gyrus. (A) ventral, (B) lateral and (C) medial views of the orbitofrontal cortex (purple) and straight gyrus (blue).

and Frith, 2006). In women, larger ventral frontal cortex (VFC) volumes relative to total cerebral or intracranial volume have been observed in two studies (Goldstein *et al.*, 2001; Gur *et al.*, 2002). Several lines of data implicate the VFC, as well as other areas, in social cognition and behavior,

Table 1 Demographic data

	Males ($n = 37$)		Females ($n = 37$)		p^a
	Mean (s.d.)	Range	Mean (s.d.)	Range	
Age (years)	12.46 (2.82)	7.8–17.0	12.60 (2.91)	7.1–17.6	0.83
Verbal IQ	112.11 (14.75)	89–147	109.81 (16.69)	83–155	0.53
Performance IQ	109.92 (16.27)	81–144	112.14 (13.11)	84–146	0.52
Full Scale IQ	112.05 (15.06)	87–146	111.86 (13.91)	86–150	0.96
Educational Performance	2.03 (1.08)	1–5	2.00 (0.87)	1–5	0.24
Parental social Class	2.24 (0.61)	1–4	2.26 (0.45)	2–3	0.13
Height (cm)	153.89 (18.52)	123–190	153.80 (14.25)	121–174	0.98

^aIndependent samples *t*-test, $\alpha = 0.05$.

suggesting that the larger VFC in women may be associated with better skills of social perception. In a previous MRI study in our lab in an adult population, we found no differences in OFC size between sexes. However, women had proportionally larger SG size compared to men. Furthermore, larger SG size correlated with higher identification with feminine characteristics and better performance on a test of social cognition (Wood *et al.*, in press).

The current study was designed to further investigate sexual dimorphism in ventral frontal brain morphology and its relationship with social cognition from a developmental perspective. VFC morphological measures in children and adolescents were compared between sexes and correlated with tests of social perception and identification with masculine/feminine characteristics. We hypothesized that, as in adults, SG size would differ between boys and girls and would be correlated with identification with feminine traits and performance on a test of social cognition.

MATERIALS AND METHODS

Subjects

The study population consisted of 74 healthy, right-handed Caucasian children ranging in age from 7 to 17 years recruited from the community by newspaper advertisements. Thirty-seven boys and thirty-seven girls were matched by age and IQ (Table 1). Subjects were excluded if significant (requiring medical intervention) medical, neurological, or psychiatric illness, including alcohol and other substance abuse, was reported by parents. Handedness was determined by the Physical and Neurologic Examination for Soft Signs [PANESS, (Denckla, 1985)]. IQ measures for children ages 7–16 were obtained using the Wechsler Intelligence Scale for Children III (WISC-III) without the similarities subtest (Wechsler, 1991). IQ measures for 17-year olds were obtained using the Wechsler Adult Intelligence Scale III (WAIS-III) without the similarities subtest (Wechsler, 1997). Parental social class was determined using a modified Hollingshead scale of 1–5, with the lower the number, the higher the socioeconomic status. Educational performance

was rated by parents according to the following scale: 1 = A, 2 = A-B, 3 = B, 4 = B-C, 5 = C, 6 = D, 7 = F. Mean age, full scale IQ, performance IQ, verbal IQ, parental socioeconomic status, educational performance and height are shown in Table 1. There were no significant differences between boys and girls in any of these measures.

Written informed consent was obtained from one parent and the child for all subjects prior to participation. The study was approved by the University of Iowa Human Subjects Institutional Review Board.

MRI acquisition

MRI scans were performed on a 1.5 Tesla General Electric SIGNA System (GE Medical Systems, Milwaukee, WI). Three different sequences were obtained for each subject. Three-dimensional (3D) T1-weighted images using a spoiled grass sequence (SPGR) were acquired in the coronal plane with the following parameters: echo time (TE) 5 ms, repetition time (TR) 24 ms, numbers of excitations (NEX) 2, rotation angle 45°, field of view (FOV) 26 × 24 × 18.8 cm, slice thickness 1.5 mm and a matrix of 256 × 192 × 124. Two-dimensional (2D) PD and T2 sequences were acquired with the following parameters: TE 36 ms for PD and 96 ms for T2, TR 3000 ms, NEX 1, FOV 26 × 26, coronal slice thickness 3 or 4 mm and a matrix of 256 × 192. The in-plane resolution was 1.016 × 1.016 mm for the three modalities.

Image processing

Image data were processed using the locally developed software BRAINS2 (Brain Research: Analysis of Images, Networks and Systems) as previously described (Magnotta *et al.*, 2002). Briefly, T1 images were realigned in a standard orientation to correct for head rotation, with the interhemispheric fissure determining alignment in axial and coronal planes and the anterior-posterior commissure line determining the horizontal in the sagittal plane. The T2 and proton density images were aligned to the realigned T1 image using an automated image coregistration program. A Talairach-based atlas coordinate system (Talairach and Tournoux, 1988) was overlaid onto each individual brain, aligning with anatomical landmarks of that brain without normalization to a standardized brain size. These coordinates were then used to generate automated measurements of frontal, temporal, parietal and occipital lobes, cerebellum and subcortical regions. This method permits morphological measurements to be made in non-normalized or 'raw' space.

Using multispectral data and a discriminant analysis method based on automated training class selection, the data sets were segmented (Harris *et al.*, 1999). Next, total cerebral gray and white matter were measured and the tissue-classified image was used to generate a triangle-based isosurface using a threshold of 130 representing pure gray matter that corresponded to the parametric center of the cortex (Magnotta *et al.*, 1999). This triangulated surface was

used in calculations of regional cortical volumes as well as total cerebral measures.

Gray matter volume and cortical surface measurements

Regions of interest (ROI) were hand-traced by 2 of the authors (JW and VM) who were blind to the age and gender of subjects. Tracing was randomly and approximately equally divided between the tracers. ROIs were drawn to surround contiguous areas of the gray matter triangle isosurface. On each 2D slice, the cortical surface was visualized as a continuous contour that represented the intersection between the 2D plane and the 3D triangulated surface. Using this contour as a guide, frontal regions of interest were defined on each 2D slice.

ROI definition

The procedures and anatomic boundaries utilized in the definition of the orbitofrontal cortex and straight gyrus have been previously described (Crespo-Facorro *et al.*, 1999; Chemerinski *et al.*, 2002). Briefly, the SG, which resides along the ventromedial margin of the frontal cortex, was traced in the axial plane. It is the portion of the ventral frontal cortex medial to the olfactory sulcus and was traced from the most inferior slice containing the SG superiorly to the last slice in which the olfactory sulcus was still identifiable. The OFC was traced in the coronal plane. First the lateral orbital sulcus (LOS), which is the most lateral and ventral sulcus below the horizontal ramus of the lateral fissure, was identified on the intermediate frontal lobe. Anteriorly, the lateral boundary of the OFC is the frontomarginal sulcus (FMS) until the LOS appears. Proceeding caudally through serial coronal slices, the lateral boundary of the OFC is the deepest part of the LOS until it disappears, then the inferior margin of the circular sulcus of the insula (CSI). The most posterior coronal slice containing some aspect of the posterior medial orbitofrontal gyrus marks the posterior OFC boundary. The medial boundary of the OFC consists of the deepest point of the olfactory sulcus posteriorly and the deepest point of the superior rostral sulcus (SRS) anteriorly.

Reliability

After practicing OFC and SG tracing on an independent set of scans, the raters (JW and VM) traced these ROIs on a set of 10 test scans for a reliability study. Interrater reliability was calculated for the raters' ROIs by comparison to ROI tracings performed by an experienced research assistant (the 'gold standard' tracings.) R coefficients were calculated for cortical gray matter volume and surface area measurements. Volume and surface area reliability scores for the left and right OFC and SG were all $R \geq 0.88$.

Social cognitive tasks

Subjects were administered the Interpersonal Perception Task 15 (IPT) and the short form of the Children's Sex Role Inventory (CI). The IPT was designed to measure social perception. It was validated in a study of over 400 undergraduate students (Costanzo and Archer, 1989) and has been previously used in adolescent populations (Racey *et al.*, 2000). It consists of a videotape of 15 short independent scenes showing from one to four individuals interacting and speaking. After each vignette, one multiple choice question with two or three foils is asked about relationships between individuals, truthfulness of an individual, victory of one individual in a sports match or status of individuals relative to one another. Scores for the IPT are the total number of questions answered correctly out of 15. Chance performance was estimated as 33% for seven questions with three foils and 50% for eight questions with two foils, for a score of 6/15 items by chance. Mean IPT scores for the study population divided into age groups 7–12 (boys = 8.35, girls = 8.42) and 13–18 (boys = 9.2, girls = 9.5) were statistically significantly better than chance (*t*-test, $P < 0.001$ in both age groups).

Several aspects of social cognition are stereotypically feminine, such as empathy, helpfulness and insight into others' feelings (Spence *et al.*, 1975; Boldizar, 1991). To explore masculinity/femininity and the relationship to social cognition and brain morphology, subjects were also administered the CI. The CI is a 20-item questionnaire asking subjects to rate on a scale from 1 (not at all true of me) to 4 (very true of me) their identification with statements of personality characteristics demonstrated to be stereotypically male or female (Boldizar, 1991). Items were scored such that +4 corresponded to very feminine and -4 to very masculine. For each individual, the mean score from the 20 items was calculated to yield an overall rating of masculinity-femininity with possible scores ranging from -30 (most masculine) to +30 (most feminine). Four boys and six girls from the study population were not administered the IPT because of time constraints on the day of testing. One boy omitted one question on the CI. These subjects were not included in analyses for the respective tests for which data were missing.

Statistical analyses

All analyses were performed using SPSS 14 for Windows. Independent samples *t*-tests were used to compare demographic, cognitive, behavioral and global morphological data between sexes. All tests assumed equal variance and were two-tailed with $\alpha = 0.05$. Levene's test for equality of variances showed no significant differences in variance between groups.

The general linear model (GLM) repeated measures procedure (type III sum of squares) was used to compare SG and OFC gray matter volumes between sexes with the within subject factor of hemisphere. To control for brain size, total frontal lobe volume was included as a covariate.

Similar results were obtained when the same analysis was performed with ventral frontal cortical subregion gray matter volumes corrected for total frontal lobe volume instead of using this variable as a covariate. Myelination and gray matter pruning continue through childhood and adolescence and differ between genders; thus, age was also included as a covariate and a sex by age interaction term added (Caviness *et al.*, 1996; Giedd *et al.*, 1996; De Bellis *et al.*, 2001; Reiss *et al.*, 2004). Significant multivariate findings were further evaluated with a simple contrast. Contrast results were not corrected for multiple comparisons, as there were only two variables (SG and OFC volume). Data were checked for outliers, normality, multicollinearity and sphericity and did not violate these preliminary assumptions. Box's test for equality of covariance matrices demonstrated no significant difference in covariance between dependent variables. Levene's test for equality of variances showed no significant differences in error variances between groups for dependent variables. Wilks' lambda was used for multivariate tests. GLM estimated marginal means was used to calculate VFC subregion volumes corrected for total frontal volume. Pearson correlations were used as a post hoc test to evaluate the relationship between age and total SG volume corrected for total frontal lobe volume, with Fisher's *r* to *z* transformation to compare independent correlations between boys and girls.

To evaluate relationships between VFC gray matter, IPT and CI scores, partial correlations were performed controlling for age, as gray matter volumes change with age as discussed above. To correct for brain size, subregion volumes were expressed as a proportion of the total frontal lobe volume. Pearson correlations were used to evaluate the relationship between IPT and CI score in boys and girls. Fisher's *r* to *Z* transformation was used to compare significant correlations of CI or IPT score and VFC subregion volumes for significant differences between groups. All tests assumed equal variance and were two-tailed with $\alpha = 0.05$.

RESULTS

Cerebral measures

Table 2 shows results of the comparison between genders for global morphological measures. Boys had larger total

Table 2 Global morphological measures

Measure	Males (n = 37) Mean (s.d.)	Females (n = 37) Mean (s.d.)	<i>P</i> ^a
Intracranial volume (cm ³)	1462 (113)	1351 (78)	<0.001
Cerebral volume ^b (cm ³)	1214 (106)	1120 (79)	<0.001
Frontal volume ^c (cm ³)	472 (49)	433 (37)	<0.001
Corrected frontal volume ^d	38.86 (1.01)	38.64 (1.26)	0.413

^aIndependent samples *t*-test.

^bGray and white matter, cerebellum and brain stem excluded.

^cGray and white matter.

^dPercent of total cerebral volume (frontal volume divided by cerebral volume \times 100). Bold values are statistically significant at $P \leq 0.05$.

intracranial volume ($P < 0.001$) and cerebral volume ($P < 0.001$) than girls. As we were interested in frontal subregion morphology, frontal lobe measures were also compared. Total frontal volume was larger in boys compared to girls ($P < 0.001$). However, when corrected for total cerebral volume, an index of brain size, there was no difference in frontal volume between sexes ($P = 0.413$).

Ventral frontal cortical subregion volumes

Mean ventral frontal cortex subregion volumes by sex are shown in Table 3. There was no significant main effect of the within subjects factor hemisphere [$F(2, 68) = 0.004$, $P = 0.996$] or the interaction of sex and hemisphere [$F(2, 68) = 0.718$, $P = 0.491$] on volumes. However, there was a significant main effect of sex [$F(2, 68) = 4.48$, $P = 0.015$] and the sex by age interaction [$F(2, 68) = 3.60$, $P = 0.033$] on VFC subregion volumes. Contrasts revealed that the SG was larger in boys than in girls [$F(1, 69) = 8.83$,

$P = 0.004$]. The OFC, however, was not significantly different in volume between sexes [$F(1, 69) = 0.166$, $P = 0.69$]. Similarly, contrasts also showed that there was a significant effect of the interaction between age and sex for the SG [$F(1, 69) = 7.17$, $P = 0.009$], but not the OFC [$F(1, 69) = 0.072$, $P = 0.79$].

To further evaluate the sex by age interaction in the SG, in a post hoc analysis correlations were performed between age and corrected total SG volume for each sex. A significant negative correlation was present in the boys ($r = -0.592$, $P < 0.001$) but not in the girls ($r = -0.117$, $P = 0.490$). These correlations were statistically significantly different between sexes (Fisher's r - to Z -test, effect size -0.40 , $P = 0.02$) indicating that rates of gray matter change with age differ between boys and girls in the SG. A scatterplot of total SG volume by age and grouped by sex is shown (Figure 2A). Linear regression lines with corresponding R^2 values are also included to illustrate the significant decrease in SG gray matter volume in boys, compared to the relatively stable gray matter volume in girls from age 7 to 18 years. For comparison, a similar plot is shown for the OFC (Figure 2B).

Table 3 Gender differences in ventral frontal cortex volumes

Region	Males ($n = 37$)		Females ($n = 37$)	
	Volume (cm^3) Mean (s.e.)	Corrected ^a Mean (s.e.)	Volume (cm^3) Mean (s.e.)	Corrected ^a Mean (s.e.)
Ventral frontal cortex	51.05 (0.88)	49.77 (0.73)	47.56 (0.75)	48.83 (0.73)
Orbitofrontal cortex	44.37 (0.81)	43.36 (0.72)	41.73 (0.72)	42.73 (0.72)
Right	22.58 (0.47)	22.00 (0.43)	21.46 (0.43)	22.03 (0.43)
Left	21.80 (0.41)	21.36 (0.37)	20.27 (0.35)	20.71 (0.36)
Straight gyrus	6.68 (0.22)	6.41 (0.16)	5.83 (0.14)	6.09 (0.16)
Right	3.68 (0.13)	3.53 (0.11)	3.23 (0.11)	3.37 (0.11)
Left	3.00 (0.12)	2.88 (0.09)	2.60 (0.09)	2.72 (0.09)

^aFrontal gray matter subregion volumes controlling for age and total frontal volume with GLM multivariate estimated marginal means (age = 12.5, total frontal volume = 452.8.).

Interpersonal perception task

To test social perception abilities, 33 boys and 31 girls completed the IPT. There was no significant difference in mean scores between sexes ($P = 0.629$, Table 4), possibly because our sample size was not large enough to detect a significant gender difference. In a sample of 400 individuals, taking an expanded version of the IPT with 30 questions, a difference of only 1.1 points was detected (Costanzo and Archer, 1989).

The relationships between corrected VFC subregion volumes and IPT score were also explored using partial correlations controlling for age (Table 5). In girls, significant correlations were found between IPT score and right SG

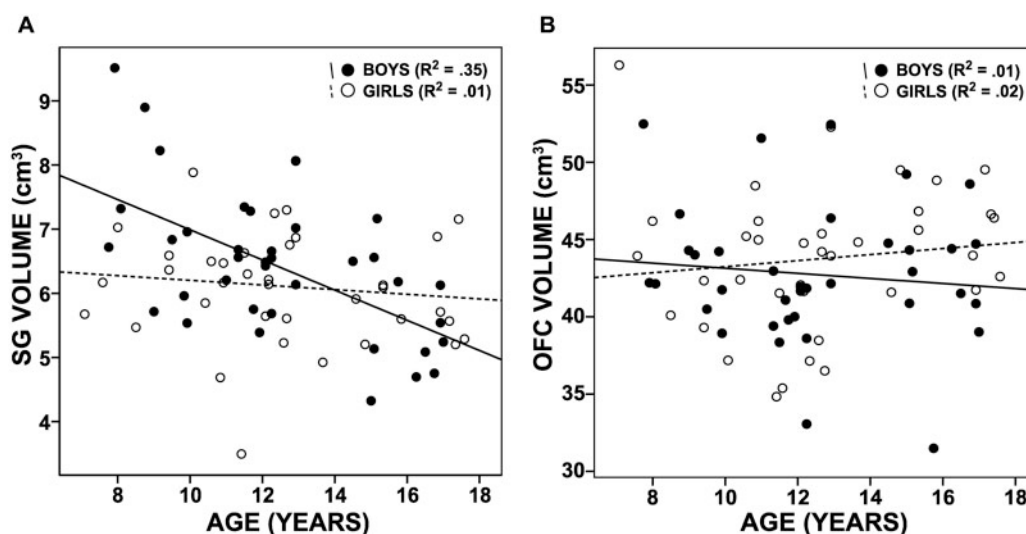


Fig. 2 Age-related differences between sexes in the straight gyrus. (A) Scatterplot of total straight gyrus volume vs age with linear regression fit lines for boys (solid line) and girls (dashed line). (B) The orbitofrontal cortex shown for comparison.

Table 4 Gender differences in IPT and CI scores

	Males Mean (s.d.)	Females Mean (s.d.)	<i>P</i> ^a
IPT ^b	8.61 (1.87)	8.84 (1.97)	0.629
CI ^c	-0.72 (4.69)	5.92 (5.39)	<0.001

^aIndependent samples *t*-test.

^bIPT is expressed as number correct out of 15.

^cCI is total self-rating with feminine items scored +1 to +4 and masculine items scored -1 to -4, with possible scores ranging from -30 (most masculine) to +30 (most feminine).

Bold values are statistically significant at $P \leq 0.05$.

Table 5 Correlation between IPT scores and ventral frontal cortex measures

Region	Partial correlation coefficient ^a (<i>P</i>)		
	Males (<i>n</i> = 33)	Females (<i>n</i> = 31)	Total (<i>n</i> = 64)
Volume ^b Orbitofrontal cortex	0.219 (0.23)	-0.273 (0.14)	0.021 (0.87)
Right	0.222 (0.22)	-0.247 (0.19)	0.041 (0.75)
Left	0.173 (0.34)	-0.243 (0.20)	-0.004 (0.98)
Straight gyrus	-0.117 (0.53)	-0.226 (0.23)	-0.103 (0.42)
Right	-0.210 (0.25)	-0.483 (0.01)	-0.304 (0.02)
Left	0.032 (0.86)	0.183 (0.33)	0.149 (0.24)

^aControlling for age.

^bSubregion volumes corrected for total frontal volume.

Bold values are statistically significant at $P \leq 0.05$.

($r = -0.483$, $P = 0.01$), but not left SG volume ($r = 0.183$, $P = 0.33$). This difference between right SG and left SG correlations in girls was statistically significantly different (Fisher's *r*- to *Z*-test, effect size -0.50 , $P = 0.008$). Thus, in girls, smaller right SG volumes correlated with better performance on the IPT. In boys, a correlation in the same direction, but not achieving statistical significance, was present with the right SG (right $r = -0.210$, $P = 0.25$; left $r = 0.032$, $P = 0.86$). The right SG correlation, significant in girls, was not significantly different from the trend in boys (Fisher's *r*- to *Z*-test, effect size 0.22 , $P = 0.23$). When boys and girls were analyzed as a group, a similar significant negative correlation between IPT score and right SG volume was present ($r = -0.304$, $P = 0.02$). In contrast, no significant correlations were found between OFC volumes and IPT scores in boys, girls or the group.

Children's inventory

To evaluate identification with feminine and masculine stereotypes, children were administered the CI. There was no significant correlation between CI score and IPT score in boys ($r = -0.317$, $P = 0.08$), girls ($r = 0.103$, $P = 0.59$) or the group ($r = -0.036$, $P = 0.78$). As expected, girls scored significantly higher (more feminine) than boys ($P < 0.001$, Table 4). As with IPT scores, evaluation of relationships between CI scores and corrected VFC subregion volumes was performed with partial correlations controlling for age (Table 6). In girls, significant correlations were found

Table 6 Correlation between CI scores and ventral frontal cortex measures

Region	Partial correlation coefficient ^a (<i>P</i>)		
	Males (<i>n</i> = 36)	Females (<i>n</i> = 37)	Total (<i>n</i> = 73)
Volume ^b Orbitofrontal cortex	-0.173 (0.32)	-0.031 (0.86)	-0.021 (0.86)
Right	-0.080 (0.65)	-0.028 (0.87)	0.033 (0.78)
Left	-0.243 (0.16)	-0.030 (0.86)	-0.077 (0.52)
Straight gyrus	0.197 (0.26)	-0.362 (0.03)	-0.178 (0.14)
Right	0.074 (0.67)	-0.402 (0.02)	-0.232 (0.05)
Left	0.258 (0.13)	-0.084 (0.62)	-0.034 (0.78)

^aControlling for age.

^bSubregion volumes corrected for total frontal volume.

Bold values are statistically significant at $P \leq 0.05$.

between CI score and right SG ($r = -0.402$, $P = 0.02$) and total SG ($r = -0.362$, $P = 0.03$) volumes, but not left SG volume ($r = -0.084$, $P = 0.62$). There was a significant difference between the right and left SG correlations (Fisher's *r*- to *Z*-test, effect size -0.50 , $P = 0.008$). Thus, in girls, high (feminine) CI scores were correlated with smaller right SG volumes. No significant correlations with the SG were present in boys (right $r = 0.074$, $P = 0.67$; left $r = 0.258$, $P = 0.13$; total $r = 0.197$, $P = 0.26$). The significant correlation between CI score and right SG volume in girls was statistically significantly different from the lack of correlation in boys (Fisher's *r*- to *Z*-test, effect size 0.350 , $P = 0.05$). When boys and girls were analyzed as a group a moderate correlation was found between right SG volume and CI score ($r = -0.232$, $P = 0.05$), due to the strong correlation between CI score and right SG volume in girls compared with the absence of correlation in boys. For OFC volumes, no significant correlations were found with CI score in boys, girls or the group.

DISCUSSION

In a previous study of adults aged 18–50, we found that females had significantly larger corrected SG volumes compared to age and IQ matched males (Wood *et al.*, in press). In contrast, in the current study of children, the SG was slightly *smaller* in females. Likely this difference is secondary to developmental changes which continue through childhood, adolescence and into early adulthood. During this time, myelination results in overall increases in white matter and pruning results in overall decreases in gray matter volumes, with changes differing by brain region and by gender (Caviness *et al.*, 1996; Giedd *et al.*, 1996, 1999; De Bellis *et al.*, 2001; O'Donnell *et al.*, 2005; Blakemore and Choudhury, 2006). For the frontal lobe, gray matter volume peaks at age 11 for girls and age 12 for boys, indicating that in this large region, girls are overall slightly ahead developmentally (Giedd *et al.*, 1999). Data from the current study support this, showing that across the age range 7–17 volume of the SG changed little in girls, but decreased significantly in boys. Therefore, smaller SG gray matter

volumes in girls with a mean age of 12.5 suggest that for this region females may be ahead on the developmental trajectory, with earlier gray matter pruning. By adult years, boys catch up and complete developmental gray matter changes and SG size ends smaller than females (Wood *et al.*, in press). A study of ventral frontal cortex morphology spanning childhood to middle age is in progress and will further refine understanding of sexual dimorphism in ventral frontal cortical development.

The differences in sexual dimorphism patterns of corrected SG volume between children and adults are parallel to the observed correlations between IPT score and corrected straight gyrus volume. In adults positive correlations between corrected SG size and IPT score were found (Wood *et al.*, in press). Thus, larger SG size was related to better social perception. In contrast in children, IPT score was *negatively* correlated with corrected SG volume; therefore, smaller SG volumes correlated with better performance on the IPT. As discussed above, the smaller SG volume suggests maturity, thus greater proficiency in social cognitive tasks. In support of this notion, theory of mind, emotion recognition, and social perspective, elements of social cognition, have been shown to improve with age in children and adolescents (Walker, 2005; Blakemore and Choudhury, 2006). The relatively weak association between IPT score and SG volume in boys, compared to the strong correlation in girls, may be related to several factors. One possibility is that the IPT is a relatively insensitive tool for detecting the subtle differences in social perception related to dimorphic cortical subregion structure. Alternatively, boys may also rely on other brain regions for assessing social information.

Our data also indicate that SG morphology is related to femininity. In adults, we found that larger SG size correlated with self-ratings of feminine traits in both men and women (Wood *et al.*, in press). In children, however, *smaller* proportional SG volumes correlated with higher degrees of identification with feminine traits in girls, but not boys. Again, as with the IPT, these data argue that smaller, more mature SG volumes in girls are correlated with greater identification with stereotypically feminine characteristics. Contrary to findings in girls, however, no significant relationship between VFC morphology and CI score was found in boys, despite correlations in an adult sample. One explanation is that the relationship with the SG is specific to femininity and, in this age group, boys are reluctant to acknowledge feminine characteristics. Alternatively, boys may not develop these characteristics until much later in adolescence. Indeed, studies using a variety of measures, including the CI, demonstrate that ratings of masculinity and femininity may vary with time despite a solid gender identity (Spence *et al.*, 1975; Boldizar, 1991; Liben and Bigler, 2002). Consistent with correlations of IPT and CI scores with corrected right SG volumes, several studies support the role of a right hemisphere network in social cognition (Tranel *et al.*, 2002; Wicker *et al.*, 2003).

Despite numerous studies indicating that the orbital frontal cortex is important in many aspects of social cognition (Malloy *et al.*, 1993; Blair *et al.*, 1999; Bechara *et al.*, 2000; Brunet *et al.*, 2000; Adolphs, 2001, 2003; Moll *et al.*, 2002), we did not identify any significant relationships between OFC morphology and gender, CI score or IPT score. One explanation is that the OFC, as defined by our methods (Crespo-Facorro *et al.*, 1999), encompasses a large, heterogeneous region comprised of nearly 20 cytoarchitecturally distinct areas (Carmichael and Price, 1994; Ongur and Price, 2000; Ongur *et al.*, 2003). In contrast, the straight gyrus (gyrus rectus), is a small and more distinct region.

The SG constitutes the medial edge of Brodmann area 11, medial to the olfactory sulcus (Figure 1). Analyses of connectivity using tracer injections in human and monkey brain slices show two distinct networks within the orbital and medial prefrontal cortex: the lateral sensory network and the medial visceromotor network (Morecraft *et al.*, 1992; Carmichael and Price, 1994; Ongur and Price, 2000; Ongur *et al.*, 2003). The region of the SG is somewhat unique, theoretically providing a pathway for communication between the orbital and medial prefrontal networks (Carmichael and Price, 1995b; Ongur and Price, 2000; Ongur *et al.*, 2003).

The area of the SG receives afferents from the caudal and lateral orbitofrontal sensory network, hippocampus and limbic structures (Morecraft *et al.*, 1992; Carmichael and Price, 1995a; Ongur and Price, 2000). SG projections extend with the medial prefrontal visceromotor network to the medial and caudal dorsomedial thalamic nucleus, hypothalamus, periaqueductal gray and brainstem. Reciprocal connections also provide feedback to the SG (Ongur and Price, 2000). Taken together, these data suggest the SG may integrate somatic and visceral sensory, affective and memory information with autonomic and motor output. Reciprocal connections may provide monitoring of internal somatic states ('gut feelings' or 'somatic markers') to constantly modulate cognitive, emotional and behavioral responses (Nauta, 1971; Damasio, 1994; Adolphs, 2001). Consistent with a modulatory role, cognitive response inhibition was impaired in individuals with localized post-surgical lesions of the straight gyrus (Szatkowska *et al.*, 2007). Unfortunately, social perception was not studied in these patients. Future studies using diffusion tensor imaging may clarify the complex connections between medial and orbital prefrontal cortices.

The extensive connectivity data are consistent with a role of the SG in social cognition. Numerous functional neuroimaging studies of elements of social perception show activation of the regions neuroanatomically connected to the ventral frontal cortex as described above (Adolphs, 2001, 2003; Ochsner *et al.*, 2004; Amodio and Frith, 2006). In a PET study investigating attribution and perception of emotion by showing subjects pictures of the eye regions of actors expressing emotional *vs* neutral affect, the right

straight gyrus, referred to as the medial orbitofrontal cortex (Talairach coordinates 1, 34, -18), was activated (Wicker *et al.*, 2003). Patients with lesions of the right ventromedial prefrontal cortex, which includes the medial OFC and the straight gyrus, had significant impairments of interpersonal behavior and emotional processing; however, patients with similar lesions on the left were stably employed and displayed normal social behavior (Tranel *et al.*, 2002). Furthermore, compared to psychiatrically healthy individuals, male patients with schizophrenia had significantly less surface area of the right straight gyrus (Crespo-Facorro *et al.*, 2000). Social withdrawal, emotional and affective flattening and interpersonal oddity result in significant social dysfunction, which is a central feature of the disease. In a second study, VFC size was negatively correlated with both pre-morbid and postonset social functioning and total SG volume was greater in the subset of patients with the highest social functioning, though not to a degree achieving statistical significance (Chemerinski *et al.*, 2002). Taken together, these studies support a role of the right straight gyrus in social perception. This is further supported by our findings of correlation between right, but not left or total, SG morphology and IPT score in children.

The origins of the relationship between sexual dimorphism of SG morphology and social cognition have not yet been elucidated. However, it is likely that early *in utero* hormonal exposure interacting with expression of specific genes facilitates the development of elaborate social cognition and behavior systems (Adolphs, 2001). Several sex chromosome localized genes are expressed to significantly different degrees in the prefrontal cortices of males and females (Vawter *et al.*, 2004). In addition, brain regions with the highest expression of sex steroid receptors during fetal development also have the greatest degree of sexual dimorphism (Goldstein *et al.*, 2001). Further studies investigating the interplay between sexually dimorphic gene expression and morphology of brain regions involved in social perception may lend insights into gender differences in several psychiatric illnesses in which social dysfunction is prominent.

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