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Morphology of the Ventral Frontal Cortex: Relationship to Femininity and Social Cognition

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Females have been shown in a number of studies to be more adept in social perception compared with males. In addition, studies have reported that brain regions important in interpretation of nonverbal social cues, such as the ventral frontal cortex (VFC), are morphologically different between genders. To investigate the relationship between the structure of the VFC and social cognition, gray matter volume and surface area of the VFC were measured on magnetic resonance imaging (MRI) scans from 30 men and 30 women matched for age and IQ. The VFC was subdivided into the orbitofrontal cortex (OFC) and the straight gyrus (SG). The SG, but not the OFC, was proportionately larger in women. A subset of subjects was administered the Interpersonal Perception Task (IPT), a test of social perceptiveness, and the Personal Attributes Questionnaire (PAQ), a scale of femininity and masculinity. Identification with more feminine traits on the PAQ correlated with greater SG gray matter volume and surface area. In addition, higher degrees of femininity correlated with better performance on the IPT. Taken together, these data suggest a complex relationship between femininity, social cognition, and the structure of the SG.

Keywords: brain, gender differences, neuroimaging, sex characteristics, social cognition, straight gyrus

Introduction

Over the last several decades, studies investigating gender differences in cognition and behavior have demonstrated small, consistent trends in divergent characteristics between the sexes. Considerable data show that in general men tend to perform better in mathematical reasoning and visuospatial tasks, whereas women tend to score higher on tasks involving mathematical calculations, verbal fluency, and perceptual speed (Hyde et al. 1990; Springer and Deutsch 1993; Christiansen 2001; Hyde and Linn 1988). In addition, prominent differences are present in social behavior and cognition. Men tend to form larger social groups and be less accepting of nongroup members, whereas women tend to prefer dyadic interactions and are more compromising (Geary 2002). Men make more frequent displays of physical aggression than women, though women are more likely to participate in relational aggression such as gossiping and backstabbing (Christiansen 2001; Geary 2002). Women generally perform slightly better in tasks of social cognition (Hall 1984; Costanzo and Archer 1989). In a study of over 4000 subjects including school-aged children and adults in several different countries, females consistently were more adept at interpreting nonverbal cues of emotion, such as vocal intonation, facial expressions, and body language (Hall 1984).

Differences found in social cognition in school-aged children are consistent with other studies that have shown significant differences in social behavior emerging as early as 1 year of age. For example, girls tend to be more fearful and exhibit more empathy and emotional support helping behavior than boys, whereas boys demonstrate more impulsivity and physical play (Sanchez-Martin et al. 2000; Geary 2002; Cote et al. 2003; Fabes et al. 2003). Some 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 (Geary 2002), implying 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).

Given the sex differences in social cognitive skills and data suggesting a biological and genetic component, differences in brain structure in regions mediating these faculties might be expected. Gender differences in brain structure have been documented, including larger cerebrum volume after correction for body size in men, greater gray to white matter ratios in women, and differences in frontal and temporal subregion volumes (Nopoulos et al. 2000; Goldstein et al. 2001; Gur et al. 2002). Studies of patients with brain lesions as well as neuroimaging experiments have revealed several regions important in social cognition, including the superior temporal sulcus, fusiform gyrus, amygdala, and prefrontal regions (Adolphs 2001, 2003). In particular, the ventral frontal cortex (VFC), consisting of the orbitofrontal cortex (OFC) and straight gyrus (SG), is essential for normal social behavior in humans (Fig. 1). The VFC contributes to social cognition in tasks involving facial recognition, attribution of intentions (Brunet et al. 2000), and perception of anger in others (Blair et al. 1999; Wicker et al. 2003). The ability to experience moral emotions, which appear to be linked to altruism, also involves the VFC (Moll et al. 2002). Damage to the ventral prefrontal cortex leaves intellectual functioning intact, but patients show a lack of concern for others, stereotyped social manners, disinhibition, and impairment of reasoning about the mental states of others (Malloy et al. 1993; Bechara et al. 2000; Adolphs 2001, 2003). In patients with schizophrenia, ventral frontal cortical gray matter volume is negatively correlated with social dysfunction but not with several other symptoms, duration of illness, or medication exposure, supporting the idea that the VFC in part mediates social function (Chemerinski et al. 2002).

In women, larger VFC volumes relative to total cerebral or intracranial volume have been observed in 2 studies (Goldstein et al. 2001; Gur et al. 2002). Given that several lines of data implicate the VFC in social cognition and behavior, this suggests that the larger VFC in women may be associated with better skills of social perception. To further investigate the gender divergence in brain morphology and social cognition, we compared VFC morphological measures between sexes and correlated this with tests of social perception and masculinity/femininity, predicting that in women the VFC is larger, that they perform better on tests of social cognition, and that VFC size correlates with test performance.

Table 1
Demographic data

	Males (n = 30)		Females (n = 30)		P^a
	Mean (SD)	Range	Mean (SD)	Range	
Age (years)	28.83 (8.72)	19–50	29.00 (8.05)	18–50	0.93
Full-scale IQ	113.17 (9.22)	95–128	113.62 (7.37)	100–127	0.84
Education (years)	14.7 (2.07)	9–20	14.93 (1.39)	12–18	0.63
Parental social class	2.73 (0.58)	1–4	2.96 (0.51)	2–4	0.12
Height (cm)	179.27 (6.84)	168–194	165.96 (7.52)	152–178	<0.001

[a]Independent samples t-test.

Materials and Methods

Subjects

The study population consisted of 60 healthy, right-handed, Caucasian volunteers recruited from the community by newspaper advertisements. Thirty males were matched by age (±2 years) to 30 females (Table 1). An experienced research assistant performed a structured clinical interview to assess subjects' medical and psychiatric histories using an abbreviated form of the Comprehensive Assessment of History and Symptoms (CASH; Andreasen, Flaum, et al. 1992). Subjects were excluded if significant (requiring medical intervention) medical, neurological, or psychiatric illness, including alcohol and other substance abuse, was present. A handedness scale developed by Benton (1967) was used to quantitatively determine handedness. IQ measures were obtained using the Wechsler Adult Intelligence Scale-Revised, which was given as part of a cognitive testing battery. Parental social class was determined using a modified Hollingshead scale of 1–5, with the lower the number, the higher the socioecomonic status. Subjects' demographics are shown in Table 1. Written informed consent was obtained 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) T_1-weighted images using a spoiled grass sequence 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 degrees, 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 T_2 sequences were acquired with the following parameters: TE 36 ms for PD and 96 ms for T_2, 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 3 modalities.

Image Processing

Image data were processed using the locally developed software BRAINS2 (Brain Research: Analysis of Images, Networks, and Systems) as previously described (Andreasen, Cohen, et al. 1992; Andreasen et al. 1993, 1994; Cohen et al. 1992). Briefly, the T_1 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 T_2 and proton density images were aligned to the spatially normalized T_1 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 and cerebellum and subcortical regions. This method permits morphological measurements to be made in nonnormalized or "raw" space.

To classify tissue volumes into gray matter, white matter, and cerebrospinal fluid, a discriminant analysis method of tissue segmentation based on automated training class selection was used with data from the T_1, T_2, and proton density sequences (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). Using the method described by Wyvill et al. (1986), an initial polygonalization of the cortical surface was performed. The image was reduced from 300 000 to 500 000 down to 100 000 triangles per hemisphere using a retiling algorithm (Turk 1992). This triangulated surface was used in calculations of regional cortical volumes and surface areas as well as total cerebral volume.

Gray Matter Volume and Cortical Surface Measurements

Regions of interest (ROIs) were hand-traced 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 ROIs were defined on each 2D slice. The thickness measurement for the selected surface region was used to calculate the gray matter volume of that cortical plane.

ROI Definition

The procedures and anatomic boundaries utilized in the definition of the OFC and SG 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 VFC 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 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 and then the inferior margin of the circular sulcus of the insula. 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 anteriorly. One author (J.L.W.) hand traced each ROI in left and right hemispheres of the MRI from each subject. Analysis time per subject was ~50–60 min.

Reliability

After practicing OFC and SG tracing on an independent set of scans, the rater (J.L.W.) traced these ROIs on a set of 10 test scans for a reliability study. Interrater reliability was calculated for J.L.W.'s 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

A subset of subjects were administered the Interpersonal Perception Task (IPT) and the Personal Attributes Questionnaire (PAQ). This group

consisted of 6 men and 7 women. Age, full-scale IQ, education, and parental social class were similar to the complete set of subjects (as shown in Table 1) without significant differences between males and females. The IPT was designed to measure social perception (Costanzo and Archer 1989). It consists of a videotape of 30 short independent scenes showing from 1 to 4 individuals interacting and speaking. After each vignette, one question is asked about relationships between individuals, truthfulness of an individual, victory of one individual in a sports match, or status of individuals in relative to one another. These correspond to kinship, intimacy, deception, competition, and status scales. Scores for the IPT are the total number of questions answered correctly. The PAQ is a 24-item questionnaire asking subjects to rate themselves on a scale from 0 to 4 for certain personality characteristics demonstrated to be stereotypically male or female (Spence et al. 1975). Items are then scored such that 0 corresponds to very feminine and 4 to very masculine. For each individual, the mean score from the 24 items was calculated to yield an overall rating of masculinity–femininity.

Statistical Analyses

All analyses were performed using SPSS 11.5 for Windows. To correct for the difference in body and cerebrum size between sexes, SG and OFC volumes and surface areas were expressed as a proportion of frontal lobe gray matter volume or frontal lobe cortical surface area, respectively. This is consistent with other imaging studies that have used proportional volumes to compare men and women (Goldstein et al. 2001). For example, OFC gray matter volume was divided by the total frontal gray matter volume, and OFC surface area was divided by the frontal lobe surface area. Independent samples' *t*-tests were used to compare demographic, MRI, and social cognitive task data between sexes. All tests assumed equal variance and were 2 tailed with $\alpha = 0.05$. To evaluate relationships between morphology, IPT, and PAQ scores, the bivariate correlation procedure was used to compute Pearson's correlation coefficients and significance levels. To reduce the likelihood of a type I error with multiple correlations, this analysis was limited to the regions that showed significant structural differences between the sexes. All tests assumed equal variance and were 2 tailed with $\alpha = 0.05$.

Results

Demographics

Mean age, full-scale IQ, years of education, parental socioeconomic status, and height for males and females are shown in Table 1. There were no significant differences in any of these measures except for height, in which men were significantly taller than women ($P < 0.001$).

Cerebral Measures

Studies have demonstrated that in general males have larger brains than females, even after controlling for height, suggesting that a correction is necessary when comparing brains between sexes (Nopoulos et al. 2000; Gur et al. 2002). Consistent with this intracranial volume ($P < 0.001$), total cerebral volume ($P < 0.001$) and total cerebral surface area ($P < 0.001$) were significantly greater in men than in women (Table 2). As we were interested in frontal gray matter subregions, morphological indices were also compared for the frontal lobes. Males had larger frontal gray matter volume ($P < 0.001$) and total frontal lobe surface area ($P < 0.001$). When frontal indices were corrected for global cerebral gray matter volume or surface area, no differences between sexes were detected for frontal gray volume ($P = 0.630$) or frontal surface area ($P = 0.720$). Therefore, to correct for differences in frontal lobe size in subsequent analyses, frontal subregion gray matter volumes were expressed as a proportion of total frontal gray matter volume. Similarly, frontal subregion surface areas were expressed as a proportion of total frontal surface area.

Table 2
Gender differences in global and total frontal brain measures

	Region	Males ($n = 30$)	Females ($n = 30$)	P[a]
		Mean (SD)	Mean (SD)	
Raw volume (cm^3)	Total intracranial	1513 (122)	1346 (107)	<0.001
	Total cerebral[b]	1306 (111)	1159 (94)	<0.001
	Cerebral gray matter	723 (61)	648 (47)	<0.001
	Frontal gray matter	278 (27)	247 (21)	<0.001
Corrected[c]	Frontal gray matter	38.41 (1.73)	38.20 (1.53)	0.720
Raw surface area (mm^2)	Total cerebral	182687 (13598)	167102 (13024)	<0.001
	Frontal	72556 (6116)	66069 (5456)	<0.001
Corrected[d]	Frontal	39.73 (1.89)	39.56 (1.73)	0.630

[a]Independent samples *t*-test.
[b]Gray matter, white matter, and cerebrospinal fluid with cerebellum and brain stem excluded.
[c]Percentage of total cerebral gray matter volume (frontal gray volume divided by cerebral gray matter volume × 100).
[d]Percentage of total cerebral surface area (frontal surface area divided by the total cerebral surface area × 100).

Ventral Frontal Cortical Gray Matter Volumes

Uncorrected means of the volumes of the VFC ($P < 0.001$) and OFC ($P < 0.001$) were significantly larger in men compared with women; however, there was no difference between groups in the volume of the SG ($P = 0.532$) (Table 3). After correction for frontal lobe gray matter volume, there were no significant differences between males and females in the volume of the VFC or the subregion OFC. However, the mean SG volume was significantly greater in females compared with males ($P = 0.055$). Frontal subregions were also divided into right and left sides to evaluate for unilateral sex-dependent volume differences that were masked in analysis of total volumes. In females, the corrected gray matter volume of the right SG was significantly larger than in males ($P = 0.026$). The corrected volume of the left SG was also greater in females, though not to a degree reaching significance. This suggests that gender-dependent morphology is not a unilateral phenomenon but is more robust on the right. No corrected gray matter volume differences were found between men and women for the left or right OFC.

Ventral Frontal Cortical Surface Areas

Cortical gray matter volumes are a product of both depth and surface area; thus, identical volumes may have significantly different surface dimensions, which in turn may reflect developmental differences and variations in functional parcellation. Similar to differences in brain volumes, uncorrected VFC ($P = 0.013$) and OFC ($P = 0.008$) surface areas were significantly greater in men than women (Table 4). Mean uncorrected SG surface area was roughly equal ($P = 0.80$) in subjects of both genders. After correction for total frontal lobe surface area, there were no significant sex differences in VFC and OFC surface areas; however, the mean corrected SG surface area was significantly greater in women ($P = 0.020$). As with volumes, frontal subregions were also divided into right and left sides. In females, the corrected right SG surface area was significantly larger than in males ($P = 0.007$). As observed with volumes, the corrected surface area of the left SG was greater in females, though not significantly so.

Interpersonal Perception Task

A subset of the study population consisting of 7 females and 6 males completed the IPT, and no significant differences in

Table 3
Gender differences in frontal subregion gray matter volumes

	Region	Males (n = 30)	Females (n = 30)	P[a]
		Mean (SD)	Mean (SD)	
Raw (cm^3)	VFC	45.61 (5.64)	40.62 (4.46)	<0.001
	OFC	40.18 (5.50)	35.34 (4.17)	<0.001
	Right	20.31 (2.68)	17.93 (2.59)	<0.001
	Left	19.87 (3.00)	17.40 (2.05)	<0.001
	SG	5.43 (0.77)	5.28 (1.07)	0.532
	Right	2.95 (0.43)	2.94 (0.66)	0.934
	Left	2.48 (0.49)	2.34 (0.54)	0.300
Corrected[b]	VFC	16.42 (1.31)	16.39 (0.95)	0.900
	OFC	14.46 (1.35)	14.26 (1.06)	0.521
	Right	7.31 (0.70)	7.23 (0.72)	0.637
	Left	7.15 (0.75)	7.03 (0.63)	0.525
	SG	1.96 (0.27)	2.13 (0.37)	0.055
	Right	1.07 (0.16)	1.18 (0.23)	0.026
	Left	0.90 (0.17)	0.94 (0.20)	0.315

[a]Independent samples t-test.
[b]Percentage of total frontal gray matter volume (subregion volumes divided by the total frontal gray matter volume × 100).

Table 4
Gender differences in frontal subregion surface areas

	Region	Males (n = 30)	Females (n = 30)	P[a]
		Mean (SD)	Mean (SD)	
Raw (mm^2)	VFC	12303 (1348)	11434 (1277)	0.013
	OFC	10771 (1343)	9885 (1170)	0.008
	Right	5354 (690)	4923 (700)	0.019
	Left	5416 (703)	4961 (587)	0.009
	SG	1532 (215)	1549 (307)	0.803
	Right	840 (112)	870 (187)	0.452
	Left	692 (137)	679 (152)	0.729
Corrected[b]	VFC	16.94 (1.46)	17.27 (1.09)	0.338
	OFC	14.83 (1.53)	14.94 (1.13)	0.757
	Right	7.37 (0.82)	7.44 (0.74)	0.737
	Left	7.45 (0.80)	7.49 (0.66)	0.833
	SG	2.12 (0.28)	2.33 (0.40)	0.020
	Right	1.17 (0.16)	1.32 (0.24)	0.007
	Left	0.95 (0.18)	1.02 (0.21)	0.190

[a]Independent samples t-test.
[b]Percentage of total frontal surface area (subregion surface areas divided by the total frontal surface area × 100).

performance were detected (P = 0.327, Table 6). This is to be expected with such a small sample. Correlation between IPT score and morphology was also assessed (Table 5). No significant correlations were observed with any of the morphological indices examined when males and females were analyzed separately or as a group, again likely due to the small sample. However, on examination of the patterns of correlation for the SG, all are positive in direction and, with the exception of one, large in size (average Pearson correlation in men is 0.374 and in women is 0.557). The direction of the correlations is as expected with larger SG volumes and surface areas correlating with better IPT performance. Because morphological indices are expressed as a ratio of frontal lobe cortex, any global relationships between social cognition and total frontal lobe measurements would be controlled for in our analysis. This supports the notion that our findings are specific to the SG and are not a result of a more generalized phenomenon.

Personal Attributes Questionnaire

Several aspects of social cognition are stereotypically feminine in nature, for example, insight into others' feelings, helpfulness,

Table 5
Correlation between IPT scores and SG measures

	Region	Pearson correlation coefficient (P)		Total (n = 13)
		Males (n = 6)	Females (n = 7)	
Volume[a]	SG	0.147 (0.781)	0.650 (0.114)	0.206 (0.499)
	Right	0.002 (0.997)	0.554 (0.197)	0.080 (0.795)
	Left	0.508 (0.303)	0.633 (0.127)	0.276 (0.361)
Surface area[b]	SG	0.590 (0.217)	0.530 (0.280)	0.374 (0.231)
	Right	0.505 (0.307)	0.419 (0.409)	0.208 (0.517)
	Left	0.494 (0.320)	0.555 (0.253)	0.431 (0.161)

[a]Subregion gray matter volumes divided by the total frontal gray matter volume.
[b]Subregion surface areas divided by the total frontal surface area.

and empathy (Spence et al. 1975). To compare degrees of masculinity and femininity in our study population, the same subset of subjects was administered the PAQ. As expected, male subjects scored higher (more masculine) than females (P = 0.048, Table 6). Interestingly, PAQ scores were strongly negatively correlated with IPT scores in men (r = –0.953, P = 0.003,). Thus, lower (more feminine) PAQ scores were correlated with better performance on the IPT. A similar trend was observed in women (r = –0.602, P = 0.152).

Pairwise correlation coefficients were calculated between PAQ scores and SG morphological measures as shown in Table 7. When analyzed as a group containing both sexes, a statistically significant negative correlation was found between the PAQ score and the proportional left SG volume (P= 0.028, r= –0.604), with trends present in both men and women. Thus, a lower PAQ score, which corresponds to higher identification with feminine characteristics, was correlated with a larger left SG volume. In addition to the significant correlation, it is important to note that all but one correlation are in the negative direction, supporting the hypothesis that lower, more feminine PAQ scores are associated with greater SG size. As with the IPT, expression of morphological measures as a ratio of frontal lobe cortex suggests that our findings are specific to the SG.

Regarding specificity of femininity/masculinity, one would expect that gender-based differences would likely be associated with inherently feminine or masculine characteristics. However, rating of identification with masculine and feminine characteristics (PAQ score) is a quantitative and refined method for assessing a spectrum, in contrast to the dichotomy of "male versus female." Our data showed correlations between morphology, social perceptiveness, and the degree (quantity) of femininity, not only in females but also in males. If morphology (or social cognition) was simply a function of gender, one would not expect a correlation between SG size (or social cognition) and quantification of femininity/masculinity in each gender individually. Taken together, these data suggest that associations with femininity are specific and not simply a result of gender alone.

Discussion

Small differences in cortical volume between sexes have been demonstrated for several regions of the brain. This study found significant differences between males and females in proportional gray matter volume and cortical surface area in a subregion of the VFC, specifically the SG. The SG (or gyrus rectus) constitutes the medial edge of Brodmann area 11 and the VFC. Two previous studies have shown significant gender differences in ventral prefrontal morphology, including greater VFC volumes

Table 6
Gender differences in IPT and PAQ scores

	Males (n = 6)	Females (n = 7)	P
	Mean (SD)	Mean (SD)	
IPT[a]	16.83 (3.19)	15.43 (1.62)	0.327
PAQ[b]	2.13 (0.27)	1.74 (0.34)	0.048

[a]IPT is expressed as number correct out of 30.
[b]PAQ is mean self-rating with 0 corresponding to high identification with very feminine items and 4 to very masculine items.

Table 7
Correlation between PAQ scores and morphological measures

	Region	Males (n = 6)	Females (n = 7)	Total (n = 13)
		Pearson correlation (P)	Pearson correlation (P)	
Volume[a]	SG	−0.133 (0.801)	−0.510 (0.242)	−0.502 (0.080)
	Right	0.075 (0.888)	−0.297 (0.518)	−0.264 (0.384)
	Left	−0.705 (0.117)	−0.586 (0.167)	−0.606 (0.028)
Surface area[b]	SG	−0.670 (0.145)	−0.141 (0.791)	−0.384 (0.218)
	Right	−0.389 (0.447)	−0.169 (0.749)	−0.433 (0.160)
	Left	−0.684 (0.134)	−0.110 (0.836)	−0.277 (0.384)

[a]Subregion gray matter volumes divided by the total frontal gray matter volume.
[b]Subregion surface areas divided by the total frontal surface area.

in women (Goldstein et al. 2001; Gur et al. 2002). In both studies, however, the SG (medial Brodmann area 11) was included with other subregions and not measured as a separate region. Our study further refines gender differences in VFC morphology.

Morphological differences were most pronounced in surface areas. The cortical surface area has expanded immensely throughout evolution without an associated increase in cortical thickness (Rakic 1988). Rakic has described the mechanism by which the cortex becomes functionally parcellated. During fetal development, groups of progenitor cells in the ventricular zone give rise to ontogenic columns. Each column receives afferents from the thalamus and other brain regions, developing into a basic processing unit, with both genetic and epigenetic phenomena influencing functional parcellation. Increased surface area is a result of increased ontogenic columns. Thus, an increased surface area would provide more basic units to process external stimuli relayed by the thalamus. In terms of social cognition, a relative increase in surface area may include units to facilitate interpretation of more subtle social cues. In our study, correlations were strongest with volumes, not surface areas. Surface area is a more specific measurement of cortical structure in contrast to volume, which measures both surface area and depth. Thus, our findings suggest that both surface area and cortical thickness are involved; however, interpretation of this observation is limited by the small sample size.

In addition to the findings of proportionally larger SG size in females, this study supports a direct relationship between SG morphology and social perception, with large positive Pearson correlations between corrected SG size with IPT score. This is consistent with previous studies showing impairment of social perception, as measured by the IPT (Mah et al. 2004) or the Tests of Social Intelligence (Mah et al. 2005), in subjects with lesions to the ventromedial prefrontal cortex. Moreover, our data indicate that this relationship appears to be modified by the characteristics of masculinity and femininity. Individuals who identified with more feminine characteristics performed better at interpreting social cues in the videotaped vignettes. This relationship was particularly strong for men. This is interesting in light of previous studies, which have demonstrated that women generally perform better in social perception. These data suggest that femininity and social cognition may be linked.

Laterality is important in effects of emotion on memory, and through this mechanism, likely also social perception. A recent study of patients with unilateral temporal lobectomy found right-sided, but not left-sided, lesions impaired recollection of negative, high-intensity emotions. These data are consistent with a right hemisphere network for recognition of emotions in others, an essential element of social cognition (Buchanan et al. 2006). Several studies support the role of the right ventromedial prefrontal cortex in social cognition. In a PET study investigating perception of emotion by showing subjects pictures of the eye regions of actors expressing friendly or hostile emotions, the right SG, referred to as the medial OFC, was activated (Wicker et al. 2003). Patients with lesions of the right ventromedial prefrontal cortex, which includes the medial OFC and the SG, 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 with psychiatrically healthy individuals, male patients with schizophrenia had significantly less surface area of the right SG (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 premorbid 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 SG in social perception. Our findings in part support these studies. The right SG was the subregion with the largest size difference between genders; however, the left SG was also larger, though to a lesser extent, in women compared with men. In addition, negative correlations with PAQ score and positive correlations with IPT were present for both sides. Further studies will be needed with larger samples to elucidate what role laterality plays and to refine the exact role of each side.

Theories as to the origin of gender differences in social cognition have focused on biological and hormonal influences as well as cultural and environmental factors. More recent studies in the neural basis of social cognition have begun to integrate biological and psychological theories in light of evolution (Adolphs 2001; Geary 2002). Primates have developed highly complex social systems in which mutual support furthers survival of the species; however, this also requires a brain capable of understanding and directing social interactions. Therefore, social cognition, the ability to attribute intentions and emotions to others, and brain size have coevolved. Neocortical volume corrected for body size is directly proportional to a species' developmental period and social complexity (Adolphs 2003; Geary 2002; Mah et al. 2005). In humans, the long internal gestation period and high degree of care an infant requires postnatally are a significant investment for the female; thus, it is important for her to be sensitive to her children's needs. Consistent with this, females have become more adept at sociocognitive skills required for rearing young, such as

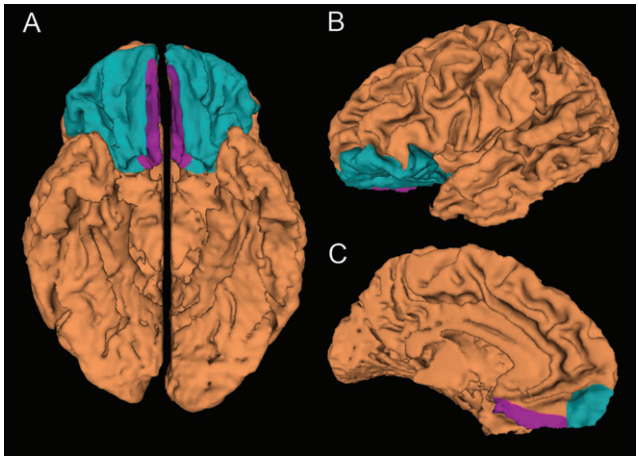

Figure 1. The OFC and SG. (*A*) Ventral, (*B*) lateral, and (*C*) medial views of the OFC (blue) and SG (purple).

interpreting body language, facial expressions, and babies' early preverbal sounds. Taken together, this suggests that these skills coevolved with increased VFC size as more ontogenic columns were added for interpretation of social cues.

In regard to a potential genetic etiology for social cognition, recent studies have shown 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 genes located on the sex chromosomes are expressed to significantly different degrees in the prefrontal cortices of males and females (Vawter et al. 2004). Brain regions with the greatest degree of sexual dimorphism are those with the highest expression of sex steroid receptors during fetal development (Goldstein et al. 2001). In further support of a strong genetic component in the development of social cognition, the heritability of some social behaviors in children and adolescents has been estimated at 0.68, with higher heritabilities at younger ages (Scourfield et al. 1999). 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.

Notes

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