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The neuroanatomy of general intelligence: sex matters

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We examined the relationship between structural brain variation and general intelligence using voxel-based morphometric analysis of MRI data in men and women with equivalent IQ scores. Compared to men, women show more white matter and fewer gray matter areas related to intelligence. In men IQ/gray matter correlations are strongest in frontal and parietal lobes (BA 8, 9, 39, 40), whereas the strongest correlations in women are in the frontal lobe (BA10) along with Broca's area. Men and women apparently achieve similar IQ results with different brain regions, suggesting that there is no singular underlying neuroanatomical structure to general intelligence and that different types of brain designs may manifest equivalent intellectual performance.

Keywords: Neuroanatomy; General intelligence; Sex

Introduction

Recent evidence from structural brain imaging of normal adults indicates that individual differences in general intelligence as assessed with the Wechsler Adult Intelligence Scale (WAIS), one measure of the intelligence quotient (IQ), are strongly related to differences in gray matter (GM) and white matter (WM) volumes in a number of specific areas distributed mostly in frontal, temporal, and parietal regions (Haier et al., 2004). Moreover, the relative contribution of GM and WM volumes in these areas to explaining variance in intelligence scores shifts with age. For instance, older adults show more GM–IQ relationships in the frontal and parietal areas, whereas younger adults show more relationships in temporal and limbic areas.

Comparisons of general intelligence assessed with standard measures like the WAIS show essentially no differences between men and women (Jensen, 1998), but it remains to be determined whether the neuroanatomical basis for general intelligence is the same in men and women. A myriad of sex differences in brain structure have been reported (de Courten-Myers, 1999; Luders et al., 2004). Here, we examine whether there are male and female differences in the correlations between IQ and GM or WM volumes based on optimized voxel-based morphometry (VBM) of structural MRI data. Earlier studies of brain structure and intelligence were based on region-of-interest (ROI) methods, which have a number of limitations for examining the entire brain (Andreasen et al., 1993; Flashman et al., 1997). Functional brain imaging studies have reported a number of sex differences (Cahill et al., 2001; Gur et al., 2000; Haier and Benbow, 1995; Mansour et al., 1996; Neubauer et al., 2002; Shaywitz et al., 1995, 2001), but task-specific demands on cognitive resources with functional studies must always be considered as the task itself could affect interpretation of functional imaging results. Structural imaging correlated with off-line analyses of various cognitive performance measures and traits, on the other hand, can identify those differences in neuroanatomy which may underlie the cognitive measure of interest, irrespective of any task design constraints.

Materials and methods

Subjects

Two independent samples of normal volunteers were studied. The first sample of 23 volunteers (14 women and 9 men; mean age = 27, SD = 5.9, range = 18–37) were recruited from the University of New Mexico (UNM). The second sample of 25 volunteers (13 men and 12 women, mean age = 59, SD = 16; range 37–84) were recruited from the University of California, Irvine (UCI) as middle-aged and older normal controls for an imaging study of dementia in Down syndrome and Alzheimer's disease (Haier et al., 2003a). These are the same subjects used in our previous report (Haier et al., 2004), except that one additional female subject was added to the UCI sample. All of the 48 subjects were in good physical and mental health; none had a history of head injury and none showed any clinical signs of dementia.

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Intelligence testing

To assess general intelligence, subjects were tested with the WAIS. The WAIS battery (Wechsler, 1981) consists of 11 diverse subtests which tap a variety of verbal and non-verbal mental abilities which contribute to general intelligence. The WAIS full scale IQ score (FSIQ) is based on performance of all 11 subtests (according to age based norms). Factor analytic studies (Jensen, 1998) show that each subtest loads on the *g* factor and the FSIQ score loads the highest (about 0.90 or 81% of the variance in *g*). For this reason, FSIQ is considered one of the best indexes of individual differences in general intelligence, as first described by Spearman (1904). Mean FSIQ for all 23 males was 118.8 (SD = 15.1; range 95–155) and 113.5 (SD = 13.4; range 90–134) for all 25 females. This was not significantly different between groups ($t = 1.29$, $P = 0.20$; two-tailed). In sample 1 (UNM), mean FSIQ for the males was 122.8 (SD = 16; range 109–155) and 111.1 (SD = 12.4; range 90–133) for females. In sample 2 (UCI), mean FSIQ for the males was 116.3 (SD = 14.5; range 95–142) and 116.5 (SD = 14.6; range 90–134) for females.

Six of the WAIS subtests can be summarized as a single score on verbal IQ (VIQ) and five subtests can be summarized as performance IQ (PIQ). These are highly inter-correlated ($r = 0.83$ in the male sample; $r = 0.68$ in the female sample) and with FSIQ (0.97 and 0.94, respectively, in the males; 0.96 and 0.86 in the females). Although FSIQ is the single best summary score for general intelligence, VIQ and PIQ scores may yield additional information when correlated to VBM results.

Structural MRI imaging parameters

Sample 1 MRIs were obtained with a 1.5-T scanner, head coil, and software (Signa 5.4; General Electric Medical Systems, Waukesha, WI). A T1 sagittal localizer sequence (TE = 6.9 ms, TR = 200 ms, FOV = 24 × 24 cm^2, five slices, thickness = 5 mm, spacing = 2.5 mm, matrix = 256 × 128) was acquired, followed by a T1 weighted axial series (fast RF spoiled gradient-recalled, TE = 6.9 ms, TR = 17.7 ms, flip angle = 25°, matrix = 256 × 192, 120 slices, thickness = 1.5 mm) to give full brain coverage. Sample 2 MRIs were obtained with a 1.5-T clinical Phillips Eclipse scanner (Philips Medical Systems, N.A., Bothell, WA). We used T1-weighted, volumetric SPGR MRI scans (FOV = 24 cm, flip angle = 40, TR = 24, TE = 5). The images consisted of 120 contiguous 1.2-mm-thick axial slices, each with an in-plane image matrix of 256 × 256 image elements, to achieve full brain coverage. All images in both samples were visually inspected to ensure image quality.

Voxel-based morphometry (VBM)

We applied VBM to identify brain areas where GM and WM volumes were correlated to IQ separately for males and females. We used Statistical Parametric Mapping software (SPM2; The Wellcome Department of Imaging Neuroscience, University College London) to create one study-specific template for the combined sample of UNM and UCI males and a separate template for the combined female samples. The optimized VBM protocol was applied to males and females separately using the methods of Ashburner and Friston (2000) and Good et al. (2001). To preserve the amount of tissue in any given anatomical region after spatial normalization, the optimal GM and WM partitions were multiplied by the Jacobian determinants of their respective spatial transformation matrix. The reason for performing this modulation step is so that the final VBM statistics will reflect local deviations in the absolute amount (volume) of tissue in different regions of the brain (Ashburner and Friston, 2000). Since this was done separately for the men and women, brain size differences between the groups should not be confounded. The modulated GM and WM partitions were then smoothed with a 12-mm FWHM isotropic Gaussian kernel to account for slight misalignments of homologous anatomical structures and to ensure statistical validity under parametric assumptions.

Statistical conjunction approach

We specifically tested whether regional GM or WM volumes were correlated with FSIQ scores treating any effects of age and intra-sex brain size (total brain GM or WM, respectively) as nuisance variables in the SPM2 design matrix. We used the conjunction approach (Price and Friston, 1997) to show where GM and WM correlations with FSIQ overlapped for the UNM and the UCI samples (i.e., voxels with correlations in common for both samples) separately for the males and females. We repeated these analyses separately for VIQ and PIQ. The conjunction approach minimizes potential problems associated with combining data from different scanners and has the additional advantage of maximizing statistical power because all subjects are used in the analysis. Findings are considered significant at $P < 0.05$ corrected for multiple comparisons; findings at $P < 0.001$ uncorrected also are shown for hypothesis generation regarding FSIQ. R^2 estimates were determined using the formula: $R^2 = t^2 / (df + t^2)$, where $df = 17$ for the males and 19 for the females (from the SPM2 conjunction design matrix). Locations of significant clusters (centroids) are converted from Montreal Neurological Institute (MNI) to Talairach atlas (Talairach and Tournoux, 1988) coordinates and reported as closest Brodmann area (BA) where possible. Only clusters of at least 10 voxels are reported.

Results

In our sample of men, the conjunction analysis showed GM volume was correlated to FSIQ most strongly ($P < 0.05$ corrected for multiple comparisons) in bilateral frontal lobes (BA 8, 9) and in left parietal lobe; Wernicke's area (BA 39 and 40). In the women, the strongest GM-FSIQ correlation was in the right frontal lobe (BA10) and the largest cluster was in Broca's area (left BA 44, 45). These significant areas are shown in Fig. 1; the exact anatomical locations and cluster sizes are listed in Table 1, along with the estimated variance accounted for in FSIQ by each GM cluster (41–54% for the most significant clusters).

WM volume correlations with FSIQ were not as strong ($P < 0.001$, uncorrected), but they were more extensive in the women, as illustrated in Fig. 1 and detailed in Table 2. All correlations in Tables 1 and 2 are positive; there were no appreciable negative correlations. As shown in Table 3, most of the GM findings for men were evenly distributed in frontal and parietal lobes (45% each), whereas the GM findings were predominately in the frontal lobe (84%) for women. WM findings were predominately in temporal lobes for the men (82%) and in frontal lobes for the women (86%).

GM voxels correlated to FSIQ represented 9.6% of all GM voxels (693,360) in the male brain. GM voxels correlated to FSIQ

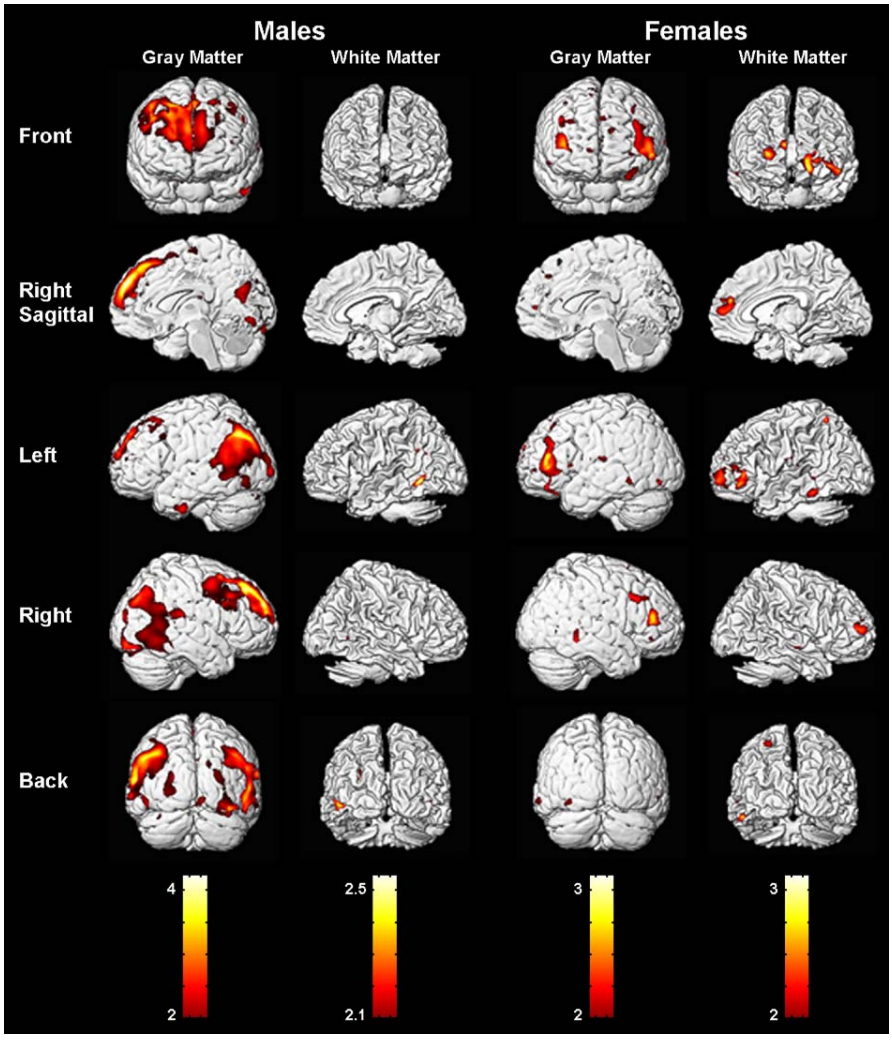

Fig. 1. Correlations ($P < 0.001$) in men ($N = 23$) and women ($N = 25$) between gray matter and white matter volumes and IQ conjuncted across the UNM and the UCI samples. Anatomical locations, atlas coordinates and cluster sizes are listed in Tables 1 and 2. Color scale bars at bottom refer to t test values for each analysis.

represented only 1.7% of all GM voxels (612,007) in the female brain. WM voxels correlated to FSIQ represented only 0.1% of all WM voxels (492,814) in the male brain. WM voxels correlated to FSIQ represented 1.3% of all WM voxels (416,630) in the female brain.

VIQ correlations with GM and WM were computed using PIQ as an additional nuisance variable along with age and total GM (or WM); the PIQ correlations used VIQ as an additional nuisance variable. Only two results were significant when corrected for multiple comparisons. In the men, PIQ correlated with GM ($P = 0.057$) in BA7 (right parietal lobe; $x = 10$, $y = -57$, $z = 59$). In the women, VIQ correlated with GM ($P = 0.018$) in the thalamus/pulvinar area ($x = 4$, $y = -29$, $z = 15$).

Discussion

These results expand upon our previous report (Haier et al., 2004), which combined men and women into a single analysis to maximize statistical power. In that analysis, GM and WM volumes were correlated to FSIQ with sex treated as a nuisance variable; the results showed correlations in several regions distributed throughout the brain. Here, we have systematically sought to explore sex differences in the structural brain organization underlying general intelligence. Of the major areas identified in our earlier analysis combining men and women, the sex-specific analyses show that some of the previous significant areas are found more in men and others are found more in the women; the relative roles of GM and WM also differ between the men and women.

These present results highlight an important dissociation of brain morphology related to intellectual functioning in normal adult brains, as the pattern of voxel types and voxel locations linked with intellectual functioning differed substantially between the sexes. With respect to voxel types, men had roughly 6.5 times the number of GM voxels identified as related to intellectual functioning as did women, and women had roughly nine times more WM voxels than did men. With respect to regional effects, in women, 84% of the identified GM voxels correlated to IQ were in the frontal region, as compared to 45% in men. Even greater sex differences were observed in WM, where for women 86% of the identified voxels were frontal, as compared to 0% in men. More left hemisphere voxels (GM plus WM) were identified in both men

Table 1
Areas of Correlation ($P < 0.001$) between gray matter and IQ in males (top) and females (bottom) conjuncted for UNM and UCI samples (see Fig. 1)

Nearest gray matter	Cluster size	*x*	*y*	*z*	*t*	r^2
Males						
Right superior frontal gyrus, BA 8*	28,757	31	43	40	4.51	0.54
Right superior frontal gyrus, BA 9*		8	55	26	4.29	0.52
Left superior frontal gyrus, BA 9*		−5	53	28	4.09	0.50
Left parietal lobe, angular gyrus, BA 39*	16,938	−51	−59	34	4.09	0.50
Left temporal, supramarginal gyrus, BA 40*		−61	−50	25	3.84	0.46
Left superior temporal gyrus, BA 39*		−56	−57	28	3.81	0.46
Right parietal lobe, precuneus, BA 39	11,394	44	−72	36	3.37	0.40
Right inferior parietal lobule, BA39		45	−64	41	3.23	0.38
Right superior temporal gyrus, BA 42		69	−30	21	3.20	0.38
Left inferior temporal gyrus, BA 20	886	−55	−8	−32	3.33	0.39
Left inferior temporal gyrus, BA 20		−49	−1	−32	2.30	0.24
Right parietal lobe, precuneus, BA 31	1724	19	−67	26	3.33	0.39
Right parietal lobe, precuneus, BA 18		18	−68	18	2.19	0.22
Right middle occipital gyrus, BA 18	3030	43	−79	−10	3.16	0.37
Right inferior occipital gyrus, BA 18		35	−87	−6	3.01	0.35
Right middle occipital gyrus, BA 19		27	−84	20	2.45	0.26
Left superior frontal gyrus, BA 8	439	−41	21	51	2.65	0.29
Left middle frontal gyrus, BA 8		−40	27	42	2.28	0.23
Left middle frontal gyrus, BA 8		−34	31	45	2.11	0.21
Left inferior temporal gyrus, BA 37	472	−48	−71	−2	2.48	0.27
Left middle occipital gyrus, BA 18	1050	−21	−97	7	2.43	0.26
Left middle occipital gyrus, BA 18		−23	−90	19	2.37	0.25
Left middle occipital gyrus, BA 18		−28	−93	8	2.24	0.23
Right occipital lobe, lingual gyrus, BA 18	552	10	−74	−2	2.42	0.26
Right occipital lobe, lingual gyrus, BA 18		6	−78	−7	2.16	0.22
Left middle frontal gyrus, BA 9	116	−50	16	36	2.40	0.25
Left superior frontal gyrus, BA 9	211	−24	51	32	2.38	0.25
Left superior frontal gyrus, BA 8		−25	44	39	2.24	0.23
Left sub-lobar extra-nuclear, claustrum	61	−23	28	4	2.38	0.25
Left sub-lobar extra-nuclear, claustrum		−22	22	11	2.22	0.22
Left superior frontal gyrus, BA 8	450	−21	26	52	2.34	0.24
Left superior frontal gyrus, BA 8		−16	33	52	2.11	0.21
Left middle frontal gyrus, BA 6		−26	20	51	2.09	0.20
Right medial frontal gyrus, BA 6	151	1	−9	62	2.27	0.23
Left inferior occipital gyrus, BA 18	42	−34	−85	−17	2.23	0.23
Right sub-lobar thalamus	24	22	−22	18	2.19	0.22
Left middle frontal gyrus, BA 10	12	−39	54	10	2.18	0.22
Left superior temporal gyrus, BA 22	15	−57	−17	1	2.16	0.22
Left temporal lobe, fusiform gyrus, BA19	28	−46	−78	−14	2.14	0.21
Left sub-lobar, thalamus, pulvinar	29	−26	−28	12	2.12	0.21
Right occipital lobe, cuneus, BA 19	16	6	−78	37	2.09	0.20
Right inferior frontal gyrus, BA 47	41	13	10	−23	2.09	0.20
Left occipital lobe, lingual gyrus, BA 18	18	−11	−76	2	2.06	0.20
Females						
Right middle frontal gyrus, BA 10*	2025	40	40	13	3.61	0.41
Right middle frontal gyrus, BA 10		35	37	7	3.21	0.35
Left inferior frontal gyrus, BA 45	4663	−49	36	7	2.78	0.29
Left inferior frontal gyrus, BA 46		−46	41	2	2.66	0.27
Left inferior frontal gyrus, BA 47		−52	28	0	2.61	0.26
Left limbic lobe, cingulate gyrus, BA 31	446	−15	−40	30	2.66	0.27
Right middle frontal gyrus, BA 9	907	40	18	33	2.64	0.27
Right middle frontal gyrus, BA 9		35	29	32	2.30	0.22
Left parietal lobe, postcentral gyrus, BA 40	141	−67	−18	15	2.61	0.26
Left inferior frontal gyrus, BA 11	632	−29	28	−22	2.59	0.26
Left inferior frontal gyrus, BA 11		−34	36	−9	2.36	0.23
Left middle frontal gyrus, BA 11		−31	36	−17	2.33	0.22
Left superior frontal gyrus, BA 10	103	−12	65	23	2.59	0.26
Left limbic lobe, anterior cingulate, BA 32	344	−15	27	24	2.51	0.25
Left middle frontal gyrus, BA 8	109	−32	35	45	2.43	0.24
Right middle temporal gyrus, BA 21	404	56	−40	−5	2.38	0.23
Right middle temporal gyrus, BA 22		57	−40	2	2.19	0.20

(continued on next page)

Table 1 (*continued*)

Nearest gray matter	Cluster size	*x*	*y*	*z*	*t*	r^2
Females						
Left inferior occipital gyrus, BA 19	143	−32	−77	−4	2.38	0.23
Right superior frontal gyrus, BA 8	45	39	26	51	2.36	0.23
Right medial frontal gyrus, BA 10	104	14	51	4	2.29	0.22
Left inferior temporal gyrus, BA 20	45	−67	−11	−23	2.24	0.21
Left medial frontal gyrus, BA 6	151	0	39	35	2.21	0.20
Right superior frontal gyrus, BA 6	20	11	31	58	2.19	0.20
Left middle temporal gyrus, BA 21	132	−63	−45	−4	2.18	0.20
Right inferior frontal gyrus, BA 47	53	55	38	−7	2.16	0.20
Left frontal lobe, precentral gyrus, BA 44	73	−49	15	7	2.16	0.20
Left medial frontal gyrus, BA 8	39	−8	33	37	2.15	0.20
Left medial frontal gyrus, BA 10	19	0	64	12	2.15	0.20
Left middle frontal gyrus, BA 10	48	−31	52	0	2.13	0.19
Right superior frontal gyrus, BA 6	27	14	19	65	2.11	0.19
Right superior frontal gyrus, BA 6		5	17	63	2.11	0.19
Left sub-lobar insula, BA 13	10	−33	−31	20	2.02	0.18

x, *y*, *z* coordinates converted from original MNI to Talairach.
* $P < 0.05$ corrected.

and women (64.6% and 65.3%, respectively), consistent with previous reports of left lateralization of both anatomic and higher brain functions (Geschwind, 1972).

It is well established that men have a larger cerebrum than women by about 8–10% (Filipek et al., 1994; Nopoulos et al., 2000; Passe et al., 1997a,b; Rabinowicz et al., 1999; Witelson et al., 1995). Thus, for the current study, we created separate templates for males and females to facilitate comparisons between the sexes, as opposed to "stretching" one gender's brain to fit the size of another. Many studies have now confirmed a consistent sex difference in human brains: the GM/WM ratio is slightly higher in women than men (Allen et al., 2003; Goldstein et al., 2001; Gur et al., 1999; Passe et al., 1997a,b; Peters et al., 1998; Schlaepfer et al., 1995). In our sample, using the voxel classifications obtained with VBM, women showed a slightly higher GM/WM matter ratio (1.47) than did men (1.41), consistent with these previous reports. More specific regional analyses of GM volume differences (Goldstein et al., 2001) have shown that women have greater GM volume than men in regions including the precentral gyrus (BA 6, 4), fronto-orbital cortex (BA 47), superior frontal (BA 6, 8, 9), and lingual gyri (BA 17, 18), while men had larger volumes in frontomedial cortex (BA 11, 12), hypothalamus, amygdala, and angular gyrus (BA 39).

Table 2
Areas of Correlation ($P < 0.001$) between white matter and IQ in males (top) and females (bottom) conjuncted for UNM and UCI samples (see Fig. 1)

Nearest gray matter	Cluster size	*x*	*y*	*z*	*t*	r^2
Males						
Left middle temporal gyrus, BA 37	498	−50	−56	4	2.69	0.30
Left inferior temporal gyrus, BA 37		−45	−52	−1	2.59	0.28
Left parietal, sub-gyral WM matter	90	−28	−51	31	2.21	0.22
Right middle temporal gyrus, BA 37	19	49	−55	5	2.18	0.22
Left parietal lobe, sub-gyral, BA 37	25	−24	−59	28	2.12	0.21
Females						
Left middle temporal gyrus, BA 20	380	−51	−37	−12	3.46	0.39
Left medial frontal gyrus, BA 10	1487	−16	54	2	3.36	0.37
Left medial frontal gyrus, BA 10		−8	64	0	2.15	0.20
Left medial frontal gyrus, BA 10		−17	47	−8	2.11	0.19
Left inferior frontal gyrus, BA 47	1652	−47	37	−9	3.34	0.37
Left inferior frontal gyrus, BA 47		−36	31	1	2.97	0.32
Left middle frontal gyrus, BA 47		−43	33	−4	2.89	0.31
Right medial frontal gyrus, BA 9	722	4	45	16	3.32	0.37
Right medial frontal gyrus, BA 9		2	53	19	2.88	0.30
Right middle temporal gyrus, BA 21	106	56	−13	−7	2.74	0.28
Right superior frontal gyrus, BA 10	997	27	54	7	2.73	0.28
Right medial frontal gyrus, BA 10		23	47	11	2.45	0.24
Left superior parietal lobule, BA 7	205	−24	−50	60	2.66	0.27
Left transverse temporal gyrus, BA 41	15	−42	−23	14	2.33	0.22
Left middle temporal gyrus, BA 22	26	−55	−40	3	2.24	0.21
Left sub-lobar, insula, BA 13	20	−44	−11	20	2.06	0.18
Left sub-lobar, insula, BA 13	11	−44	−17	21	2.05	0.18

x, *y*, *z* coordinates converted from original MNI to Talairach.

Table 3
Number and size of voxel clusters with a significant correlation ($P < 0.001$) between gray and white matter volume and IQ for each brain lobe in the male ($N = 23$) and female ($N = 25$) samples[a]

	Frontal	Parietal	Temporal	Limbic	Occipital	Sub-lobar	Totals
Gray matter							
Male no. of clusters	8	3	4	0	6	3	24
Male total voxels	30,177	30,056	1401	0	4708	114	66,456
% of total voxels	45	45	2	–	7	<1	
Female no. of clusters	16	1	3	2	1	1	24
Female total voxels	9018	141	581	790	143	10	10,683
% of total voxels	84	1	5	7	1	<1	
White matter							
Male no. of clusters	0	1	2	0	0	1	4
Male total voxels	0	90	517	0	0	25	632
% of total voxels	–	14	82	–	–	4	
Female no. of clusters	4	1	4	0	0	2	11
Female total voxels	4858	205	527	0	0	31	5621
% of total voxels	86	4	9	–	–	<1	

[a] These data are summarized from Tables 1 and 2; sub-clusters are not included.

For GM voxel locations correlated with FSIQ in our study, men exhibited an anterior–posterior combination of bilateral frontal (BA 8, 9) and left parietal (BA 39, 40; Wernicke's area) areas, and women exhibited predominantly frontal lobe regions (BA 10) and, to a lesser extent, Broca's area (BA 44, 45). The role of GM volume in language areas appears to be noteworthy with Broca's area being correlated with FSIQ in women and Wernicke's area in men. Moreover, functional imaging studies with both men and women combined have implicated broad areas of activation during problem solving tasks involving memory and attention, including BA 6, 8, 9, 10, 45, 46, 47 in frontal regions, and BA 7, 39, and 40 in parietal regions (Cabeza and Nyberg, 2000). Thus, our data are consistent with attempts to relate individual differences in general intelligence to fundamental cognitive functions, and support the distributed nature of the neural basis of intelligence throughout the brain (Deary et al., 2004; Gray et al., 2003; Haier et al., 1992, 1988, 2003b; Isaacs et al., 2004) in contrast to the view that the frontal lobes alone are the basis for general intelligence (Duncan et al., 2000).

Women showed fewer GM and more WM voxels related to FSIQ than did men. These results should be interpreted in the context of the sex difference in GM to WM ratio; hence, for each sex, variation in intellectual ability is limited more by the size of voxel clusters in that tissue compartment which is relatively diminished relative to the general human brain design. It is also important to note that functional variation in women's brains emerge from a relatively smaller and more anterior set of clusters. Considered in the context of reduced overall GM and WM volumes in women, and the fact that the sexes do not differ in FSIQ, the current results suggest that different types of brain designs may manifest equivalent intellectual performance.

Other researchers have found that WM sex differences appear to support greater associations with cognition in women than in men. For example, Gur et al. (1999) regressed intelligence on total brain WM and observed that the slope was steeper in women, suggesting that individual variation in WM volume was relatively more important for women than men; this was not the case for total GM. Larger anterior callosal size was significantly correlated with all measures of cognition in women, while no significant correlations were found between regional callosal size and cognitive performance in men (Davatzikos and Resnick, 1998). Finally, research utilizing Proton Magnetic Resonance Spectroscopy (^{1}H-MRS) has established that concentration of N-acetyl-aspartate (NAA) was significantly correlated with a measure of vocabulary (high *g*-loading) in women, but not in men within left frontal WM (Pfleiderer et al., 2004). NAA has been shown in several studies to correlate positively with cognitive ability (Driscoll et al., 2003; Jung et al., 1999a,b; Valenzuela et al., 2000; Yeo et al., 2000). Taken together, these results are consistent with our data indicating relatively more covariation of WM volume and general ability in women.

Interestingly, while early researchers found relatively larger frontal cortices in humans compared to other primates (Brodmann, 1912), more contemporary research finds little evidence of proportional differences between primates when great apes are included in the sample (Semendeferi et al., 2002), except for BA 10 which is relatively larger in humans (Semendeferi et al., 2001). Consistent with the current results, both human and animal lesion studies have found that frontal lesions are relatively more detrimental to cognitive performance in women than men. Kimura (1993) noted that for both Block Design and Vocabulary, two WAIS subtests correlating highly with FSIQ, anterior and posterior cerebral lesions had adverse effects for men, but only anterior lesions had a significant adverse effect for women. Similar results emerged with respect to analysis of sex differences in the representation of left hemisphere language skills. Men were rendered aphasic by either anterior or posterior lesions, while anterior lesions were much more apt to produce aphasia than posterior lesions in women. The clusters identified through VBM for each sex in the current analysis thus map onto the left hemisphere regions linked with language for each sex, highlighting the overlap of linguistic and intellectual functions in the human brain.

VBM and ROI methods have their respective strengths and weaknesses (Ashburner and Friston, 2001; Bookstein, 2001; Davatzikos, 2004; Friston and Ashburner, 2004). Some extra caution is required when VBM analysis is applied to relatively small sample sizes like the ones in this study. For this reason, we have limited our discussion mostly to the brain areas identified at $P < 0.05$, corrected for multiple comparisons, although this by no means ensures that there are no false-positive results or that all

relevant brain areas have been identified. Also, the mean FSIQ in our samples was about one standard deviation above the population mean. Whether our findings also hold across the full range of FSIQ and a normal distribution must be determined with larger and more representative samples scanned in a standard protocol on the same machine.

The current results contribute to a growing body of evidence demonstrating that, although the sexes do not differ in general intellectual ability, the neural substrates of general intelligence are different. Whether similar neuroanatomical differences are associated with specific mental abilities (assessed for example by WAIS subtests) remains to be determined; our VIQ and PIQ findings need replication with larger samples. Although GM and WM volumes are highly hereditable in many areas (Posthuma et al., 2002; Thompson et al., 2001), there is evidence that GM volume in humans can increase with motor learning (Draganski et al., 2004) or the acquisition of a second language (Mechelli et al., 2004) and the nature of genetic determinism in general is now controversial (Silverman, 2004). Future research will require regionally specific analyses of tissue quality (e.g., neurometabolites assessed with MRS, WM matter organization assessed with DTI), coupled with the sorts of morphometric analyses employed here, as well as functional studies of brain activation during a variety of *g* loaded tasks in large samples. Investigation of sex differences may provide a window into the structural and functional brain design principles underlying human intelligence.

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