Sexual Dimorphism in the Parietal Substrate Associated with Visuospatial Cognition Independent of General Intelligence

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Abstract

■ Sex differences in visuospatial cognition (VSC) with male advantage are frequently reported in the literature. There is evidence for sexual dimorphisms in the human brain, one of which postulates more gray matter (GM) in females and more white matter (WM) in males relative to total intracranial volume. We investigated the neuroanatomy of VSC independent of general intelligence (g) in sex-separated populations, homogenous in age, education, memory performance, a memory- and brain morphology-related gene, and g. VSC and g were assessed with the Wechsler adult intelligence scale. The influence of g on VSC was removed using a hierarchical factor analysis and the Schmid–Leiman solution. Structural high-resolution magnetic resonance images were acquired and analyzed with voxel-based morphometry. As hypothesized, the clusters of positive correlations between local volumes and VSC performance independent of g were found mainly in parietal areas, but also in pre- and postcentral regions, predominantly in the WM in males, whereas in females these correlations were located in parietal and superior temporal areas, predominantly in the GM. Our results suggest that VSC depends more strongly on parietal WM structures in males and on parietal GM structures in females. This sex difference might have to do with the increased axonal and decreased somatodendritic tissue in males relative to females. Whether such sex-specific implementations of the VSC network can be explained genetically as suggested in investigations into the Turner syndrome or as a result of structural neural plasticity upon different experience and usage remains to be shown. ■

INTRODUCTION

Visuospatial cognition (VSC) may be defined as the ability to generate, retain, retrieve, and transform well-structured visuospatial images. Visuospatial abilities occupy a pivotal position in all models of human ability (Jäncke & Jordan, 2007). For example, most models of human abilities state that, together with verbal abilities, VSC captures more variance than any other dimensions in large, representative batteries of ability tests (Thurstone, 1938). Visuospatial abilities have been measured with various tests such as form boards, block manipulation, paper-folding tasks, and mental rotation tests. Many of these tasks are used in contemporary intelligence tests as measures of performance or nonverbal intelligence (i.e., fluid intelligence) such as the block design task from the Wechsler Adult Intelligence Scale—Revised (WAIS-R) (Wechsler, 1981). According to the manual of the WAIS-R, the block design task measures visuospatial and motor skills and therefore indicates the degree of functioning of the parietal and frontal lobes (Jäncke & Jordan, 2007; Warrington, James, & Maciejewski, 1986; Wechsler, 1981). VSC is not a homogenous concept. It comprises at least the three different factors—visuospatial perception, mental rotation, and spatial visualization (Linn & Petersen, 1985). As operationalized in our study, VSC encompasses all three of these factors. According to the current view, a fourth factor representing spatial navigation can be added to this three-factor solution (Jäncke & Jordan, 2007). To date, most functional neuroimaging-based research on these factors has focused on the cognitive domain of mental rotation. Important for mental rotation is the visuospatial ability of imagery through which the appearance of spatially rotated objects can be imagined (Jäncke & Jordan, 2007).

General intelligence, as operationalized by the psychometric factor termed g, is a theoretical construct describing individual differences in cognitive abilities assessed with psychometric tasks. This concept emerges from empirical observations of positively correlated performance in almost all cognitive tasks, no matter which cognitive domain is assessed (Spearman, 1904). Whether general intelligence is better viewed as one single factor or as several factors specific for cognitive subfunctions (Deary & Caryl, 1997) is still disputed. The g-factor comprises all these cognitive abilities in one common factor, although human general intellectual functioning includes more than 60 individual cognitive abilities (Caroll, 1993). The

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block design task is one of the highest g-loading tasks of the WAIS-R battery (Colom, Jung, & Haier, 2006b), hence, this task is strongly confounded by the g-factor. The g-factor and the intelligence quotient (IQ) have been shown to be associated with structural brain differences that are mainly located in frontal and parietal lobes (Jung & Haier, 2007; Colom, Jung, & Haier, 2006a; Colom et al., 2006b; Haier, Jung, Yeo, Head, & Alkire, 2004). Sex differences in the structures associated with the IQ were also reported (Haier, Jung, Yeo, Head, & Alkire, 2005).

The study of VSC or g in isolation from each other is hampered by the following problem. All intelligence measures tap g plus specific cognitive abilities and skills (Jung & Haier, 2007; Colom et al., 2006b; Jensen, 1998). This means that common intelligence measures deliver composite scores derived from both specific cognitive abilities and skills on one hand and g on the other hand. This implies that a particular performance in a cognitive domain results from a combination of g and domain-specific abilities and skills. When either interested in g or in domain-specific abilities and skills, one has to disentangle the contributions of these two cognitive concepts on a particular subject's performance. The investigation of VSC in isolation therefore requires controlling for the g-loadings of the considered visuospatial measures. One way of achieving this is to remove g-specific variance shared by the remaining WAIS subtests (which together represent g) in order to reveal the specific visuospatial component of the considered measure. An appropriate statistical method for estimating the g-loading of any given cognitive measure is the hierarchical factor analysis obliquely rotated with an additional transformation called the Schmid–Leiman solution (SLS; Wolff & Preising, 2005; Jensen, 1998; Schmid & Leiman, 1957).

There is a large body of evidence showing that the parietal lobes are the most important brain structure for spatial (including visuospatial) information processing. A comprehensive empirical review of 275 functional imaging studies in cognition unequivocally demonstrate that parietal cortex in both hemispheres is involved in mental processes such as spatial working memory, spatial perception, spatial imagery, problem solving, attention on orientation, episodic memory encoding of spatial content, and motor skill learning (Cabeza & Nyberg, 2000). More direct support can be derived from functional imaging studies on mental rotation. These studies have reported consistent activations in parietal cortex during mental rotation tasks (Butler et al., 2006; Hugdahl, Thomsen, & Ersland, 2006; Jordan, Wüstenberg, Heinze, Peters, & Jäncke, 2002; Jordan, Heinze, Lutz, Kanowski, & Jäncke, 2001; Thomsen et al., 2000; Unterrainer, Wranek, Staffen, Gruber, & Ladurner, 2000). Further evidence of the involvement of parietal structures in VSC is provided by studies investigating patients with parietal lesions. Such studies confirm the importance of parietal cortex in VSC processing by showing that parietal lesions, such as those observed in patients with spatial neglect, Balint-Holmes syndrome, Gerstmann syndrome, and other spatial disorders, are accompanied by impairments in brain functions associated with spatial information processing (Vallar, 2007; Warrington et al., 1986).

Most studies investigating visuospatial abilities used mental rotation tasks of real 3-D objects such as the figures of Shepard and Metzler (1971). In the case of the block design task from the WAIS-R (Wechsler, 1981) employed in our study, the patterns presented on the cards and, once reconstructed using cubes, the corresponding patterns are actually only in 2-D. Earlier studies revealed that there are no topological activation differences in mental rotation tasks regardless of whether 2-D or 3-D objects are used (Jordan et al., 2001), except that the magnitude of these activations was higher when using real 3-D relative to 2-D objects.

There are further functional imaging studies that support the theory of sex-specific strategies by showing different activation patterns between the sexes when subjects are forced to use visuospatial transformations as required in mental rotation tasks (Hugdahl et al., 2006; Jordan et al., 2002; Unterrainer et al., 2000; Cohen et al., 1996). Whether these activation differences between the sexes as well as the commonly observed higher performance in VSC in males are indeed evoked by a sex-specific neural implementation of the VSC processing network is still unknown. The usually observed advantage in VSC in males compared with females (Voyer, Voyer, & Bryden, 1995), the different activation patterns between the sexes during mental rotation tasks (Hugdahl et al., 2006; Jordan et al., 2002; Unterrainer et al., 2000), and the presence of sexually dimorphic brain structures globally in the whole brain (Allen, Damasio, Grabowski, Bruss, & Zhang, 2003; Gur et al., 1999) as well as locally in the parietal lobes (Im et al., 2006; Allen et al., 2003; Nopoulos, Flaum, O'Leary, & Andreasen, 2000; Verchinski et al., 2000) might indicate that the origin of the VSC performance differences between the sexes observed in the general population (Voyer et al., 1995) is rooted in structural brain differences in the VSC processing network.

The present study aimed to establish the relationship between VSC independently of g on the one hand and local gray matter (GM) and white matter (WM) volume differences on the other hand, while simultaneously controlling for known genetic influences on brain morphology and memory by a single nucleotide polymorphism (SNP) of the gene encoding for the brain-derived neurotrophic factor (BDNF) (Pezawas et al., 2004; Egan et al., 2003). We applied the WAIS-R (Wechsler, 1981) to assess g and used a lower-order factor, mainly comprised by the block design task performance, derived from the same intelligence test battery to assess VSC independent of g. We hypothesized that g-independent VSC correlates positively with GM and WM volume differences in the parietal lobes (Butler et al., 2006; Hugdahl et al., 2006; Jordan et al., 2001, 2002; Thomsen et al., 2000; Unterrainer et al., 2000; Cohen et al., 1996), preferentially in the spatial pro-

cessing dominant right hemisphere (Jäncke & Jordan, 2007; Harris et al., 2000; Warrington et al., 1986) and more pronouncedly in males than in females (Voyer et al., 1995). Stronger correlations for males were expected because, normally, males outperform females in VSC performance in the general population (Voyer et al., 1995).

The sexual dimorphism hypothesis suggested by Gur et al. (1999) postulates that in women, a smaller skull size is compensated during development by a relative increase in the somatodendritic tissue (reflected in the GM) necessary for information processing, rather than being compensated for by connecting axons (reflected in the WM) for transportation of information (Gur et al., 1999). Although this hypothesis was originally postulated globally, that is, for the whole brain, we applied it to the parietal lobe and linked it to VSC. Hence, we expected more structural correlates of VSC in the WM in males due to their relative decrease of somatodendritic tissue in the parietal lobes and due to their relatively larger brains, whereas in females we expected more structural correlates in the GM due to their relative increase of somatodendritic tissue in the parietal lobes and due to their relatively smaller brains.

METHODS

Subjects

The 43 participants were drawn from a larger sample of 354 healthy young subjects (de Quervain et al., 2003). These 43 subjects participated in an fMRI study that investigated brain activity elicited by episodic memory tasks between different allele carriers (Mondadori et al., 2006). Our sample is homogenous with respect to age, education (in years), episodic memory performance, a memory- and brain morphology-related gene (see below), and general intelligence. Taking this age homogeneous sample limits/excludes the impact of maturational processes in younger subjects or early age-related neurodegenerative alterations in older subjects on our measures. The subjects reported no past or current psychiatric, neurological, and neuropsychological problems and denied taking illegal drugs or medication. All subjects gave written informed consent to participate in the study after the nature and possible consequences of the study had been explained. The local ethics committee approved the experiment. The subjects were paid for participating in the study.

Neuropsychology

Domains of intelligence were assessed with the German version of the WAIS-R (Wechsler, 1981) [German version: Hamburg Wechsler Intelligenztest für Erwachsene—Revision 1991 (HAWIE-R)] (Tewes, 1991). We applied all eleven subtests from the WAIS-R and extracted, using hierarchical factor analysis (see below), general intelligence (g, the highest-order factor) in order to control VSC performance (one of the lowest-order factor). VSC independent of g is represented in the lowest-order factor on which the block design task from the WAIS-R loads highest, with some small contributions from other WAIS-R subtests with visuospatial content. The block design task requires putting sets of cubes together to match patterns presented on cards. The faster the cubes are put together the more points are obtained. The maximum of raw scores is 51. We used raw scores because using standardized scores in our study would lead to a minimization of the variance in the block design task performance because WAIS age categories are quite coarse; hence, most subjects would fall into the same category due to the limited age range. In order to rule out any sex differences in memory (especially working memory) capacity that might also influence VSC performance, the Wechsler Memory Scale—Revised (WMS-R) in German (Härting et al., 1999) was also applied to control for potential sex differences in memory performance.

Hierarchical Factor Analysis and the Schmid–Leiman Solution

In order to account for the confounding effect in VSC performance by g, we conducted a hierarchical factor analysis with an additional SLS (Schmid & Leiman, 1957) with syntax written by others (Wolff & Preising, 2005). In short, we first used principal axis factoring with an oblique rotation (PROMAX rotation, kappa = 4) to do a hierarchical factor analysis. In this way, we extracted the pattern matrices that represent only common variance of variables excluding unique variance. Note that principal factor analysis has to be used in this context, whereas the more common principal component analysis is not appropriate here because only the common variance of variables has to be isolated excluding unique contributions of variables. These pattern matrices were then entered into a higher (third)-order hierarchical factor analysis with the SLS. The SLS is a convenient tool with which to determine the independent influence of first- and higher-order factors on a set of primary variables, and thus, eases the interpretation of factors of differing levels (Wolff & Preising, 2005). Finally, the factor score coefficients were computed. This approach to factor analysis of the variables of the WAIS-R produces the highest-order factor as representing g and the next lower-order factors representing verbal and performance (nonverbal) intelligence quotients (IQs), with the lowest-order factors representing specific cognitive abilities and skills. The specific lowest-order factor on which the block design task loads highest was termed VSC independent of g.

MRI Data Acquisition

Magnetic resonance imaging (MRI) scans were acquired on a 3-T Philips Intera whole-body scanner (Philips, Best,

the Netherlands) equipped with a transmit–receive body coil and a commercial eight-element head-coil array. A volumetric 3-D T1-weighted gradient-echo sequence (FFE, fast field echo) scan was obtained with a measured spatial resolution of 1 mm × 1 mm × 1.5 mm (acquisition matrix 224 × 224 pixels) and a reconstructed resolution of 0.9 mm × 0.9 mm × 0.8 mm, echo time (TE) = 2.3 msec, repetition time (TR) = 20 msec, flip angle (FA) $\theta = 20^{\circ}$. Scan time was about 10 min. MRI data acquisition and neuropsychological assessments took place within a 4-week period.

Preprocessing and Postprocessing of MRI Data

Image pre- and postprocessing and statistical analyses were performed with the statistical parametric mapping (SPM, version 5) software package (www.fil.ion.ucl.ac.uk/spm) using MATLAB 7.0.1 R14, SP1 (www.mathworks.com) on a Windows workstation. Based on the volumetric 3-D T1-weighted structural MRI scans, which covered the whole brain, we applied voxel-based morphometry (VBM) (Ashburner & Friston, 2000) implemented in the VBM5 toolbox (http://dbm.neuro.uni-jena.de/vbm.html) for SPM5. With this approach we sought to verify our proposal that local differences in parietal GM and WM volumes correlate with VSC performance independently of g. Because SPM5 enables image registration, tissue classification, and bias field correction within the same generative model (Ashburner & Friston, 2005), the procedure called optimized VBM (Senjem, Gunter, Shiung, Petersen, & Jack, 2005; Good et al., 2001a) is no longer needed when working with SPM5 (Ashburner & Friston, 2005). Additionally, a Hidden Markov Random Field (HMRF) model was used to enhance the segmentation process (Cuadra, Cammoun, Butz, Cuisenaire, & Thiran, 2005; http://dbm.neuro.uni-jena.de/vbm/markov-random-fields/). For spatial normalization and tissue class segmentation, the International Consortium for Brain Mapping (ICBM) 452 standard a priori maps were used. Images were modulated for the affine and nonlinear transformations.

Statistical Analyses

For correlating local GM and WM volumes with the factor score coefficients of the lowest-order factor ''VSC independent of g,'' a factor mainly comprised by the performance in the block design task of the WAIS-R, we used multiple regression analysis based on the general linear model implemented in the SPM5 software package. We used the following measures as nuisance covariates: total GM volume (TGMV) for GM analysis; total WM volume (TWMV) for WM analysis; and education, age, and handedness for both analyses. We also controlled for an SNP because it has been shown that it influences brain morphology (Pezawas et al., 2004). This SNP occurs in the gene that codes for the BDNF (Egan et al., 2003). For the analysis of the pooled sample, we additionally used sex as a nuisance covariate. Given our a priori hypotheses about the expected location of brain structural differences, we set the statistical height threshold to $p = .001$ (uncorrected for multiple comparisons) and the cluster extent threshold was set to $k = 50$ voxels. Additionally, we also report results that were corrected for multiple comparisons as well as cluster sizes that were corrected for nonstationary smoothness. We applied a false discovery rate ($p = .05$) correction combined with a small-volume correction using a sphere of 30 mm diameter.

We used the classical approach of voxel counting and consecutive chi-square (χ^2) testing as well as the lateralization index (LI) tool (Wilke & Lidzba, 2007; Wilke & Schmithorst, 2006) to assess lateralization differences between the sexes in the brain structures that correlate with VSC independent of g. This new approach is based on threshold-dependent laterality curves and on combined bootstrap/histogram analysis. In the classic approach, we summed up all suprathreshold voxels in all clusters located in the parietal lobes. In the LI tool, we assessed the LI voxelwise in both parietal lobes using the nonthresholded correlation maps as input. Here, we report threshold-weighted mean LIs, that is, more significant voxels were weighted stronger. The formula to compute the LI classically is: $LI = [(\Sigma voxel_{left} - \Sigma voxel_{right})/(\Sigma voxel_{left} + \Sigma voxel_{right})]$. A value of 1 indicates an absolute left lateralization and a value of −1 indicates an absolute right lateralization. It is important to note that these two approaches differ in several aspects, hence, their results may be different. To compare tissue type and sex, we computed a tissue type index (TTI) based only on suprathreshold voxels according to the formula: $TTI = [(\Sigma voxel_{GM} - \Sigma voxel_{WM})/(\Sigma voxel_{GM} + \Sigma voxel_{WM})]$. Here, a value of 1 indicates exclusively GM voxels and a value of −1 indicates exclusively WM voxels.

Genotyping

Information on the polymorphic site was derived from the database of single nucleotide polymorphisms (dbSNP) established by the National Center for Biotechnology Information (www.ncbi.nlm.nih.gov/SNP/index.html). Genotyping procedure for the BDNF gene has been described elsewhere (Egan et al., 2003). We decided to control for this SNP because it has been shown to influence not only memory performance but also medial temporal and prefrontal brain morphology (Pezawas et al., 2004). Furthermore, when we regressed the BDNF genotypes against voxelwise local GM and WM volumes, we found a differential effect of this genotype on posterior parietal structures, that is, decreased WM volumes in male BDNF val66met carriers. As suggested by functional neuroimaging studies on mental rotation, which have consistently revealed prefrontal activations in mental rotations tasks (Butler et al., 2006; Hugdahl et al.,

2006; Jordan et al., 2001, 2002; Thomsen et al., 2000; Unterrainer et al., 2000; Cohen et al., 1996), there may also be structural correlates of the VSC network located in prefrontal brain regions.

RESULTS

A summary of the demographic characteristics, cognitive indices, and compartmental brain volumes of the pooled study population and the sex-separated groups is depicted in Table 1. In brief, there were no significant differences between the sexes with respect to age, education, block design task performance, full-scale intelligence quotient (FSIQ), handedness, and BDNF allele frequencies (all $p > .25$). As expected, males and females differed in their compartmental brain volumes. Males had significantly larger total GM and total WM volumes than females (all $p < .0005$). In clear contrast to findings in the pertinent psychological literature (Voyer et al., 1995), neither performance in the block design tasks nor the factor score coefficient of the VSC factor differed significantly between males and females in our study. There were no differences in memory capacity in any of the 12 subtests (the information and orientation test was omitted) of the WMS-R between the sexes.

Positive Correlations in the Pooled Sample

Table 2 presents a summary of all clusters found in the pooled sample. In our pooled sample, we found clusters of positive correlations between local GM volumes and VSC independent of g in the left inferior parietal lobule/precuneus, the left angular gyrus, the left and right superior parietal lobules, and both pre- and postcentral gyri (Figure 1A–C and Table 2). Clusters of positive correlations between local WM volumes and VSC were found in the left and right angular gyrus, left inferior parietal lobule, right superior parietal lobule/precuneus, right postcentral gyrus, right superior temporal gyrus (STG), and the right supplementary motor area (Figure 1A–C and Table 2).

Using the classical approach of voxel counting and chi-square (χ^2) tests, we further tested whether the voxels with positive correlations between local GM or WM volumes and VSC independent of g are stochastically independent from the hemisphere (left or right). The distributions of significant correlations over hemispheres showed a tendency for GM voxels toward the left hemisphere (3499 suprathreshold GM voxels in the left and 1583 in the right hemisphere; lateralization indices $LI_{GM} = 0.38$, left lateralization) and for WM voxels toward the right hemisphere (345 suprathreshold WM voxels in the left and 778 in the right hemisphere; $LI_{WM} = -0.39$; right lateralization), which was statistically significant ($\chi^2 = 3.93$, $df = 1$, $p = .047$). The LIs derived from the lateralization tool and based on the nonthresholded correlation maps across the parietal lobes were $LI_{GM} = -0.35$, right lateralization; $LI_{WM} = 0.06$, no lateralization.

Positive Correlations within the Sex-separated Groups

A summary of all clusters can be found in Table 3 for females and in Table 4 for males. In females, VSC performance correlated positively with local GM volumes in both superior parietal lobules, the right inferior parietal lobule, the left angular gyrus, the right cuneus, lateral occipital cortex, the left superior temporal pole, and the right STG (Figure 2A–C and Table 3). With respect to WM in females, VSC performance correlated positively with local WM volumes in the right precuneus, the left supramarginal gyrus, the right lingual gyrus, the left parahippocampal gyrus, and the left supplementary motor area (Figure 2A–C and Table 3).

In males, VSC performance correlated positively with local GM volumes in the left postcentral gyrus/precuneus, right occipito-parietal cortex, the right paracentral lobule, and the right precentral gyrus/middle frontal gyrus (Figure 3A–C and Table 4). With respect to WM in males, VSC performance correlated positively with local WM volumes in the right superior and inferior parietal lobule, both postcentral gyri, the right precentral gyrus, both angular gyri, and both middle frontal gyri (Figure 3A–C and Table 4).

The distributions of significant correlations over hemispheres in females showed a slight tendency for GM voxels toward the left hemisphere (611 suprathreshold GM voxels in the left and 499 in the right hemisphere; $LI_{GM} = 0.10$, left lateralization), but a moderate tendency for WM voxels toward the right hemisphere (93 suprathreshold WM voxels in the left and 136 in the right hemisphere; $LI_{WM} = -0.19$; right lateralization), which was not statistically significant ($\chi^2 = 0.51$, $df = 1$, $p = .475$). In males, the distributions of significant correlations over hemispheres showed no tendency for GM voxels (320 suprathreshold GM voxels in the left and 315 in the right hemisphere; $LI_{GM} = 0.008$, no lateralization), but a strong tendency for WM voxels toward the right hemisphere (284 suprathreshold WM voxels in the left and 1,531 in the right hemisphere; $LI_{WM} = -0.69$; right lateralization), which was statistically significant ($\chi^2 = 5.37$, $df = 1$, $p = .020$). When lateralization was measured across the whole parietal lobes with the LI tool, LIs were: for GM, $LI_{Female} = -0.20$ and $LI_{Male} = -0.16$; and for WM, $LI_{Female} = -0.12$ and $LI_{Male} = 0.45$.

TTIs, which assess the relation between tissue type and sex, revealed a tendency for GM in the left (TTI = 0.74), in the right (TTI = 0.57), and in the combined hemispheres (TTI = 0.66) in females. In males, there was no tendency for WM in the left hemisphere (TTI = 0.06), but a strong tendency for WM in the right and combined hemispheres (TTI = −0.66 and TTI = −0.48, respectively). Hence, there was a significant difference in the distributions of tissue types between sexes in the left hemisphere ($\chi^2 = 5.95$, $df = 1$, $p = .015$), and highly significant differences in the right and combined

Table 1. Demographic Characteristics, Cognitive Indices, and Compartmental Brain Volumes in the Pooled Sample and the Sex-specific Groups

	Male (n = 18)					*Female (n = 25)*				*Total (N = 43)*			
	Mean	*SD*	*Minimum*	*Maximum*	*Probability: t/χ^2 Test*	*Mean*	*SD*	*Minimum*	*Maximum*	*Mean*	*SD*	*Minimum*	*Maximum*
Age (y)	22.2	2.2	19.0	27.0	$p = .834$	22.4	2.7	19.0	32.0	22.3	2.5	19.0	32.0
Education (y)	13.9	1.8	10.5	17.0	$p = .791$	14.0	1.4	12.0	17.5	14.0	1.6	10.5	17.5
Block design (raw)	42.3	6.2	30.0	50.0	$p = .995$	42.3	6.3	31.0	51.0	42.3	6.2	30.0	51.0
FSIQ	123.3	7.74	105.0	136.0	$p = .820$	124.0	11.4	98.0	137.0	123.7	9.9	98.0	137.0
TGMV (cm^3)	**810.3**	**60.4**	**713.2**	**946.6**	**$p < .0005$**	743.4	**54.5**	**628.7**	**886.7**	771.4	65.5	628.7	946.6
TWMV (cm^3)	**485.1**	**46.2**	**401.8**	**596.8**	**$p < .0005$**	434.7	**31.5**	**359.4**	**493.8**	455.8	45.4	359.4	596.8
TCSFV (cm^3)	368.1	73.3	268.7	491.8	$p = .744$	376.6	89.3	239.5	566.4	373.0	82.2	239.5	566.4
TICV (cm^3)	**1663.1**	**128.3**	**1396.0**	**1906.9**	**$p < .01$**	1554.6	**131.3**	**1319.8**	**1786.5**	1600.3	139.6	1319.8	1906.9
	Frequency					*Frequency*				*Frequency*			
Handedness (r/l/a)	16/2/0				$p = .333$	22/1/2				38/3/2			
	Amino Acids					*Amino Acids*				*Amino Acids*			
BDNF val66met	9 val/val	9 val/met	0 met/met		$p = .267$	17 val/val	7 val/met	1 met/met		26 val/val	16 val/met	1 met/met	

Significant differences between the sexes are highlighted in **bold** (two-tailed *t* test for independent samples and two-tailed χ^2 test). a = ambidexter; BDNF = brain-derived neurotrophic factor; FSIQ = full-scale intelligence quotient; l = left; met = methionine; r = right; raw = raw data; *SD* = standard deviation; TCSFV = total cerebrospinal fluid (CSF) volume; TGMV = total gray matter (GM) volume; TICV = total intracranial volume; TWMV = total white matter (WM) volume; val = valine; y = years.

Table 2. Correlations between Local Gray or White Matter Volumes and Visuospatial Cognition Performance Independent of General Intelligence in the Pooled Sample

Tissue	*Anatomical Location*	*Hem.*	*Brodmann's Area*	*MNI Coordinates*			*Cluster Extent (k = 50 voxels)*	*Nonstationarity Corrected*	*t Value (df = 36), p < .001, Uncorrected*	*SVC* [p (FDR)]*	*Correlation r*	*Effect Size d*
				x	*y*	*z*						
Gray matter	Postcentral gyrus/ inferior parietal lobule	left	2	−30	−36	63	2654	4257	6.00	.001	.68	1.87
	Postcentral gyrus/ precuneus	left	4	−10	−40	62			4.99	.005	.61	1.56
	Angular gyrus	left	39	−52	−62	37	479	1429	4.71	.015	.59	1.47
	Middle temporal gyrus/ angular gyrus	left	39	−54	−65	22	173	418	4.51	.018	.58	1.41
	Postcentral gyrus	right	3	13	−37	62	1239	1636	4.31	.010	.56	1.35
	Superior parietal lobule	right	5	25	−44	64			3.83	.010	.51	1.20
	Superior parietal lobule	left	7	−17	−61	63	193	488	4.19	.029	.55	1.31
	Superior parietal lobule	right	40	39	−41	54	344	530	3.96	.040	.53	1.24
	Superior parietal lobule	right	7	30	−47	56			3.86	.021	.52	1.21
	Precentral gyrus	right	4	16	−23	63	135	231	3.82	.041	.51	1.19
	Middle occipital gyrus	right	19	30	−66	29	194	327	3.79	.057	.51	1.18
	Precentral gyrus	left	4	−32	−19	44	311	469	3.71	.027	.50	1.16
White matter	Lingual gyrus	right	17	8	−80	−4	221	238	4.37	.017	.56	1.36
	Postcentral gyrus	right	3	24	−30	58	209	428	4.31	.050	.56	1.35
	Supplementary motor area	right	6	2	−22	61	192	422	4.30	.046	.56	1.34
	Superior parietal lobule/precuneus	right	7	15	−63	51	314	639	4.25	.025	.55	1.33
	Angular gyrus	left	39	−35	−57	35	206	250	4.06	.066	.54	1.27
	Angular gyrus	right	40	36	−55	35	255	514	4.05	.053	.53	1.27
	Inferior parietal lobule	left	40	−44	−33	41	139	273	3.88	.075	.52	1.21
	Superior temporal gyrus	right	42	54	−37	13	142	169	3.80	.077	.51	1.19

Effect size (d) was computed according to the formula: $d = 2r/(\sqrt{(1 - r^2)})$. *df* = degree of freedom; FDR = false discovery rate; Hem. = hemisphere; MNI = Montreal Neurological Institute; SVC = small-volume correction.

*With a sphere of 30 mm diameter.

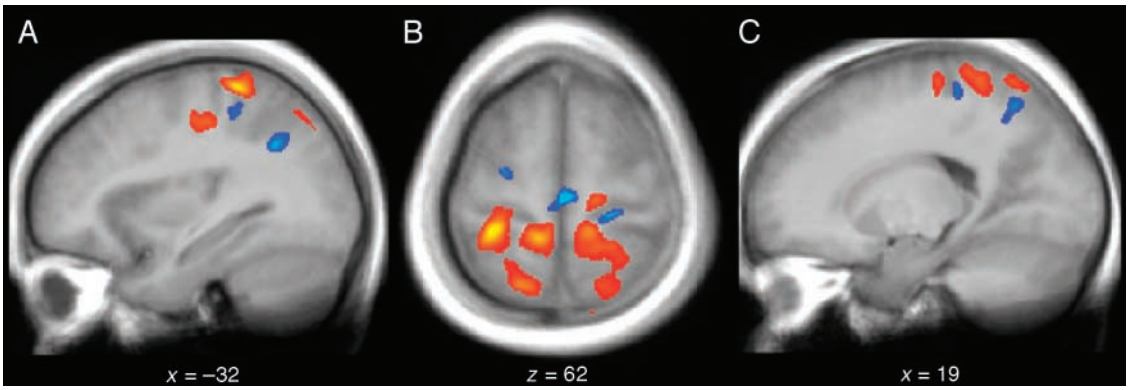

Figure 1. Positive correlations between local GM (red–yellow) or WM (blue–light blue) volumes and visuospatial cognition performance independent of general intelligence in the pooled sample. Structural brain differences were overlaid on the average template of the pooled sample. Coordinates are in Montreal Neurological Institute space. Slices are shown in neurological convention: sagittal plane (A, C) and axial plane (B). Statistical parametric maps for the figures were thresholded with $p < .005$, uncorrected.

hemispheres ($\chi^2 = 14.06$, $df = 1$, $p = .0001$ and $\chi^2 = 12.84$, $df = 1$, $p = .0003$, respectively).

Negative Correlations

Because we expected only positive correlations due to the literature and for theoretical reasons (i.e., negative correlations are rarely reported in the structural neuroimaging literature and are difficult to explain), we did not hypothesize negative correlations a priori. Nevertheless, we also assessed negative correlations between VSC independent of g and local GM and WM volumes and report these correlations for completeness. Generally, clusters of negative correlations were not as frequent as clusters of positive correlations, were smaller in size, were less significant than the clusters of positive correlations, and were not located in our a priori predicted brain regions. In the pooled sample, clusters of negative correlations between VSC and local brain volume were found in the right lingual gyrus, in right lateral occipital cortex, and in both middle frontal gyri (MFG) for GM and in the left anterior STG for WM. In females, clusters of negative correlations were found in the left pars opercularis, in left premotor cortex (PMC), and in the right MFG for GM and in the right STG, in the left supplementary motor area, in the left postcentral gyrus, and in right PMC for WM. In males, clusters of negative correlations between VSC and local brain volume were found bilaterally in the occipital pole, left frontal pole, left MFG, and in both lingual gyri for GM and in left superior and right lateral occipital cortex, and in the right frontal pole for WM.

DISCUSSION

We used VBM to investigate the neuroanatomical substrates of VSC independent of general intelligence (g) in sex-separated populations. As hypothesized, we found clusters of positive correlations between VSC independent of g and local GM and WM volumes, mainly in the parietal lobes, but also in pre- and postcentral regions in the pooled sample. When sexes were analyzed separately, the clusters of correlations between local volumes and VSC were found in males in parietal, precentral, and postcentral areas, predominantly located in the WM, whereas in females, these correlations were found in parietal and superior temporal areas, predominantly located in the GM. The clusters were lateralized in such a way that there was a preponderance of clusters in the left hemisphere in females and in the right hemisphere in males.

The following three questions will be discussed in detail below: (1) Is connectivity among parietal areas more important in the male than in the female brain? (2) Does the preponderance of clusters of correlations between local tissue volumes (mainly GM in females and WM in males) and VSC independent of g in the case of females in the left hemisphere and in the case of males in the right hemisphere point to a sex-specific lateralization of the VSC processing network? (3) Is the involvement of regions associated with motor or somatosensory information processing such as the pre- and postcentral gyri indicative of a differential or additional neural recruitment of a motor or even a somatosensory structure in the VSC processing network in males compared with females?

Sex Differences in Brain Structures Correlated with Visuospatial Cognition Independent of g

Whether connectivity of parietal areas is more important in males than in females can be considered from a theoretical point of view. In a neural network, neural interconnectivity, which is physiologically implemented as

Table 3. Correlations between Local Gray or White Matter Volumes and Visuospatial Cognition Performance Independent of General Intelligence in Females

Tissue	*Anatomical Location*	*Hem.*	*Brodmann's Area*	*MNI Coordinates*			*Cluster Extent (k = 50 voxels)*	*Nonstationarity Corrected*	*t Value (df = 19), p < .001, Uncorrected*	*SVC* [p (FDR)]*	*Correlation r*	*Effect Size d*
				x	*y*	*z*						
Gray matter	Inferior/superior parietal lobule	right	40	53	−40	55	359	390	5.15	.012	.73	2.15
	Superior temporal pole	left	38	−35	25	−29	365	815	5.01	.013	.72	2.09
	Superior temporal gyrus	right	22	72	−37	10	319	353	4.88	.016	.71	2.04
	Superior parietal lobule	left	7	−19	−58	63	155	582	4.53	.069	.69	1.89
	Superior parietal lobule	left	7	−22	−62	56			3.82	.066	.62	1.59
	Superior parietal lobule	left	7	−36	−53	55	90	385	4.53	.075	.69	1.89
	Angular gyrus	left	19	−39	−70	38	366	1649	4.38	.042	.67	1.83
	Lateral occipital cortex	left	39	−49	−67	33			4.35	.029	.67	1.81
	Angular gyrus	left	39	−51	−61	38			4.11	.033	.65	1.71
	Cuneus	right	19	1	−86	28	140	104	4.01	.057	.64	1.67
White matter	Lingual gyrus	right	18	7	−79	−3	167	281	4.95	.021	.72	2.06
	Supplementary motor area	left	6	−4	−15	52	88	315	4.74	.077	.70	1.98
	Precuneus	right	7	16	−60	49	136	461	4.44	.082	.68	1.85
	Parahippocampal gyrus	left	19	−18	−47	0	67	145	4.09	.149	.65	1.71
	Supramarginal gyrus	left	40	−43	−34	41	93	187	4.04	.096	.64	1.68

Effect size (d) was computed according to the formula: $d = 2r/(\sqrt{(1 - r^2)})$. *df* = degree of freedom; FDR = false discovery rate; Hem. = hemisphere; MNI = Montreal Neurological Institute; SVC = small-volume correction.

*With a sphere of 30 mm diameter.

Table 4. Correlations between Local Gray or White Matter Volumes and Visuospatial Cognition Performance Independent of General Intelligence in Males

Tissue	*Anatomical Location*	*Hem.*	*Brodmann's Area*	*MNI Coordinates*			*Cluster Extent (k = 50 voxels)*	*Nonstationarity Corrected*	*t Value (df = 12), p < .001, Uncorrected*	*SVC* [p (FDR)]*	*Correlation r*	*Effect Size d*
				x	*y*	*z*						
Gray matter	Occipito-parietal cortex	right	7	27	−63	30	315	2984	7.44	.007	.88	3.72
	Paracentral lobule	right	5	7	−33	53	571	1360	5.97	.017	.83	2.99
	Postcentral gyrus/ precuneus	left	3	−9	−40	64	320	875	5.33	.04	.80	2.67
	Precentral/middle frontal gyrus	right	9	40	4	32	133	643	4.98	.081	.78	2.49
White matter	Post/precentral gyrus	right	4	27	−28	59	741	4674	11.1	.0002	.94	5.55
	Superior parietal lobule	right	7	19	−59	53	407	1692	7.21	.010	.87	3.61
	Inferior parietal lobule	right	40	41	−51	49	56	961	6.44	.023	.85	3.22
	Postcentral gyrus	right	3	48	−19	53	167	795	5.71	.050	.82	2.86
	Precentral gyrus	right	6	47	−1	37	122	552	5.56	.053	.81	2.78
	Middle frontal gyrus	right	6	36	2	45	101	432	5.43	.058	.81	2.72
	Middle frontal gyrus	left	9	−39	29	27	76	288	4.84	.128	.77	2.42
	Angular gyrus	left	39	−35	−58	33	224	537	4.8	.058	.77	2.40
	Angular gyrus	right	40	34	−51	34	160	224	4.78	.120	.77	2.39
	Postcentral gyrus	left	1	−51	−20	58	60	200	4.62	.058	.76	2.31

Effect size (d) was computed according to the formula: $d = 2r/(\sqrt{(1 - r^2)})$. *df* = degree of freedom; FDR = false discovery rate; Hem. = hemisphere; MNI = Montreal Neurological Institute; SVC = small-volume correction.

*With a sphere of 30 mm diameter.

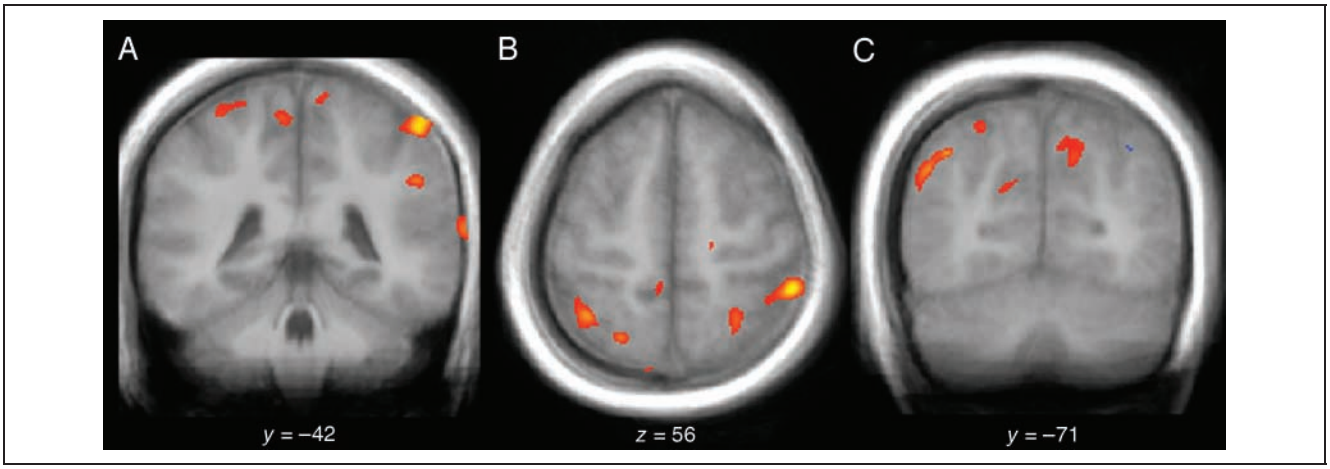

Figure 2. Positive correlations between local GM (red–yellow) or WM (blue–light blue) volumes and visuospatial cognition performance independent of general intelligence in females. Structural brain differences were overlaid on the average template of the females. Coordinates are in Montreal Neurological Institute space. Slices are shown in neurological convention: coronal plane (A, C) and axial plane (B). Statistical parametric maps for the figures were thresholded with $p < .005$, uncorrected.

fiber bundles, and thus, reflected in WM structures between the distant processors, which are physiologically implemented as assemblies of neurons, and thus, reflected in GM structures, might be more important in the male than in the female brain to due the relative decrease in parietal somatodendritic tissue in males compared with females as well as due to the larger male brain. This is the view taken by Gur et al. (1999) in their sexual dimorphism hypothesis that refers to the brain as a whole. The sexual dimorphism hypothesis proposes that the smaller skull size of women is compensated during development by a relative increase in the somatodendritic tissue (reflected in the GM) necessary for information processing, rather than being compensated by connecting axons (reflected in the WM) for transportation of information (Gur et al., 1999). This hypothesis was initially postulated globally and independently of any cognition. When it is applied locally to the parietal lobes, this hypothesis can be linked to VSC performance.

The ''parietal sexual dimorphism hypothesis of VSC (independent of g)'' was strongly corroborated by our data. Clusters of positive correlations between VSC performance and local brain volumes were predominantly located in the WM (reflecting increased connectivity) in males, whereas in females these clusters were predominantly located in the GM (reflecting increased somatodendritic tissue). Other studies lend support to our finding by showing that males and females differ in their global, neural compartmental ratios. Chen, Sachdev, Wen, and Anstey (2007) demonstrated that men have a higher WM to total intracranial volume (ICV) ratio, whereas women have a higher GM to ICV ratio. In another study,

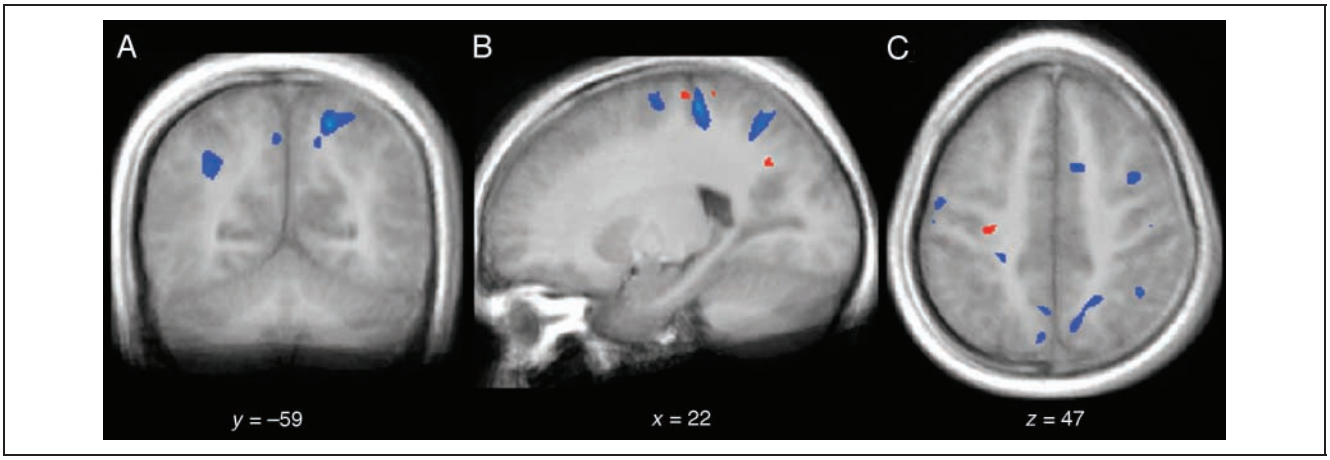

Figure 3. Positive correlations between local GM (red–yellow) or WM (blue–light blue) volumes and visuospatial cognition performance independent of general intelligence in males. Structural brain differences were overlaid on the average template of the males. Coordinates are in Montreal Neurological Institute space. Slices are shown in neurological convention: coronal plane (A), sagittal plane (B), and axial plane (C). Statistical parametric maps for the figures were thresholded with $p < .005$, uncorrected.

larger rescaled GM volumes in females and larger rescaled WM volumes in males were reported, whereas the rescaled total brain and cerebrospinal fluid volumes did not show any significant sex effect (Luders et al., 2005). Kruggel (2006) showed that the relative amount of GM is slightly higher in female brains, which is also reflected in the lower ratio of GM/WM in males. Further evidence of larger relative WM volumes in males and GM volumes in females was reported in other studies (Lemaître et al., 2005; Gur et al., 1999), although there are also conflicting findings, at least as far as GM volumes are concerned (Good et al., 2001b).

At a lobar level, the parietal lobe has been shown as a whole to be highly sexually dimorphic for WM volume (Allen et al., 2003). In that study, the GM/WM ratio effect size for the right parietal lobe was the largest for any of the regions measured, as corroborated by Nopoulos et al. (2000), who showed that the most sexual dimorphic region, that is, with proportionally more GM in females, was the right parietal lobe. Verchinski et al. (2000) found increased GM density in parietal areas in women compared with men. Im et al. (2006) used surface-based morphometry and found that women compared with men also showed increased cortical thickness in the parietal lobes, whereas Luders et al. used the cortical pattern matching method (Thompson, Woods, Mega, & Toga, 2000) and revealed increased gyrification (cortical complexity) in women than in men in parietal and frontal regions (Luders et al., 2004). Developmental studies show that, on one hand, males have a 19.1% reduction in GM volume between 6 and 18 years of age compared with a 4.7% reduction in females, and on the other hand, that males have a 45.1% increase in WM volume and a 58.5% increase in corpus callosum area compared with 17.1% and 27.4% increases in females, respectively (de Bellis et al., 2001).

Most visuospatial tasks are performed under time constraints, meaning that faster processing is beneficial, depending, of course, on the extent of any speed–accuracy tradeoff, because more points are obtained, as reflected in the block design task. Increased WM volume that reflects increased interconnectivity might subserve increased speed of information transfer between the parietal visuospatial processing network nodes, hence, resulting in higher visuospatial task performance in males compared with females as ordinarily observed in the general population. This only happens if increased interconnectivity is implemented by myelin thickening or by increased axonal diameters. Otherwise, if increased connectivity is realized by an increased number of axons or by longer distances of the axons, a decrease in speed of information transfer must be expected. Unfortunately, the cellular basis of the macroscopically observed structural brain differences cannot be investigated by structural neuroimaging. Therefore, we were unable to determine whether increased WM volumes in parietal areas correlated with VSC observed in males are evoked by myelin thickening of the axons or by an increase in the number and distance of the axons. Diffusion tensor MRI might provide information on this issue.

Sex-specific Lateralization of Brain Structures Correlated with Visuospatial Cognition Independent of g

Besides the single dissociation between the sexes found for the GM (more pronounced in females) and WM (more pronounced in males) parietal volumes correlated with VSC independent of g, a double dissociation emerged from the analysis of lateralization of these volumetric brain differences. In females, the GM clusters correlated with VSC were mainly located in the left hemisphere, whereas in males the WM clusters were mainly located in the right hemisphere. The general view is that there is a right-hemispheric dominance for visuospatial processing and a left-sided dominance for language, whereas the relative extent of lateralized domain dominance is greater for language functions. Therefore, our findings might help to explain the generally observed higher level of visuospatial processing performance in males (Voyer et al., 1995) by showing that in females, the parietal areas in the spatial processing nondominant left hemisphere seem to be more involved in visuospatial processing compared with males whose visuospatial processing relies more on a parietal network in the right hemisphere. We are not aware of any functional imaging study that supports this pattern of lateralization. The question of lateralization is further complicated by the fact that there are laterality shifts in spatial processing depending on the menstrual cycle (Rode, Wagner, & Güntürkün, 1995). Furthermore, one EEG study revealed that a simple two-dimensional mental rotation task was associated with more left-parietal than right-parietal activation in men and more right-parietal than left-parietal activation in women (Roberts & Bell, 2003), the opposite lateralization pattern of the one observed in our study. The complex three-dimensional mental rotation task in the same study was associated with greater right-parietal than left-parietal activation in both sexes (Roberts & Bell, 2003). It is important to note that the relationship between EEG power and GM and WM volumes is still uncharacterized and that the performance in the complex three-dimensional mental rotation task was not matched between the sexes. Whether the right hemisphere is the dominant side for visuospatial processing at all is still a matter of controversy. Functional imaging studies consistently revealed almost bilateral parietal activations during mental rotation tasks (Jäncke & Jordan, 2007; Butler et al., 2006; Hugdahl et al., 2006; Jordan et al., 2001, 2002; Harris et al., 2000; Thomsen et al., 2000; Unterrainer et al., 2000; Cohen et al., 1996).

The two different approaches to compute lateralization indices applied in our study revealed discrepant re-

sults. This discrepancy is mainly derived from the inclusion of voxels correlated at the subthreshold level in the computation of the LIs with the LI tool. Because we were only interested in suprathreshold correlations, we based on the LIs that were derived from the classical approach of voxel counting. This classical approach revealed a weak left lateralization of GM voxels in females (LI = 0.10) and no lateralization of GM voxels in males (LI = 0.008), whereas there was a weak-to-moderate right lateralization of WM voxels in females (LI = −0.19) and a strong right lateralization of WM voxels in males (LI = −0.69). Therefore, VSC processing seems to be more dependent on WM parietal structures in the right than the in the left hemisphere, at least in males for whom the difference between the number of significantly correlated voxels in the left and right hemispheres was statistically significant ($p = .020$).

Sex Differences in the Visuospatial Cognition Processing Strategy

A number of brain structures correlated with VSC independent of g. Leaving aside the clusters located in the parietal lobes, the clusters found in the pre- and postcentral gyri in males might reflect a motor (or even a somatosensory) processing component in VSC in general, similar to what was specifically proposed for mental rotation tasks by other researchers. Kosslyn, Thompson, Wraga, and Albert (2001) and Kosslyn, DiGirolamo, Thompson, and Albert (1998) suggest that such a motor, or egocentric strategy, results when people mentally rotate a visual mental image in the same way they rotate an actual object physically. They found activations in the primary motor area when subjects mentally rotated a hand compared with rotating other objects mentally (Kosslyn et al., 1998, 2001). Besides the already mentioned WM and GM clusters that positively correlated with VSC independent of g located in the pre- and postcentral gyri of males, further clusters supporting a motor component in visuospatial processing in males were found in the GM of the right paracentral lobule and in the WM of the right and left middle frontal gyrus (see Table 4). In females, there was only one such motor-related cluster located in the left supplementary motor area (see Table 3).

Other functional imaging studies support the theory of sex-specific strategies by showing different activation patterns when subjects are forced to use visuospatial transformations as required in mental rotation tasks (Hugdahl et al., 2006; Jordan et al., 2002; Unterrainer et al., 2000). Other authors suggested that males use a ''gestalt'' strategy and females use a ''serial'' reasoning strategy when approaching mental rotation tasks (Thomsen et al., 2000), reminiscent of the earlier speculations about ''holistic'' and ''analytic'' processing strategies in the psychological literature. This means that males generally tend to use more effective visuospatial holistic strategies in which the object is mapped in the mind and then rotated as a whole, and that females tend to prefer less efficient analytic strategies that result in a more piecemeal (analytic) mental rotation process. Butler et al. (2006) referred to more effortful and conscious ''top–down'' (analytic) processing in females and to more effective and unconscious ''bottom–up'' (holistic) processing in males. In contrast to the motor, or egocentric strategy, proposed by Kosslyn et al. (1998, 2001), which is supported by our findings, the ''holistic'' (bottom–up) and ''analytic'' (top–down) strategy distinction (Butler et al., 2006) would imply that structural correlates of VSC should be expected in prefrontal cortex in females due to their analytic strategy in visuospatial information processing. This expectation is not supported by our structural data, although functional studies in mental rotation tasks revealed strong evidence of activation differences in prefrontal brain areas between sexes (Hugdahl et al., 2006; Thomsen et al., 2000), hence, supporting the ''holistic'' (bottom–up) strategy in males and the ''analytic'' (top–down) strategy in females. In order to investigate different cognitive processing strategies in mental rotation and VSC, functional imaging techniques are more suitable than structural methods.

Possible Mechanisms Mediating a Sex-specific Implementation of the VSC Processing Network

To explain the parietal sexual dimorphism of VSC independent of g, biological (genetic, hormonal, evolutionary) and environmental (spatial activities, socialization) factors are often discussed (Casey, Nuttall, & Pezaris, 1999; Kimura, 1999; Casey, 1996). Genetic and hormonal factors may exert considerable effects on the VSC processing network. For example, females with Turner syndrome (X-chromosome deficiency) are impaired in visuospatial information processing and have structural anomalies in the parietal lobes (Brown et al., 2004; Molko et al., 2003, 2004), therefore, X-chromosome-linked influences on parietal structures have to be assumed, and might help to further elucidate the observed sex-specific pattern of structures correlated with VSC (i.e., GM in females vs. WM in males). Besides genetic factors, sexual hormones exert a considerable effect on cognitive performance, at least in females (Bayer, Kessler, Güntürkün, & Hausmann, 2008; Sherwin, 2003; Rode et al., 1995), and might modulate GM and WM volumes even in the parietal lobes (Goldstein et al., 2001).

However, to explain the structural brain differences between sexes from an environmental point of view, we would like to highlight the influence of regular training and frequent usage, as shown in other contexts by Draganski et al. (2004, 2006). These two seminal studies indicate that learning- and training-induced cortical plasticity is also reflected at the structural level. With respect to the time scale, such structural changes are

already detectable 7 days after training commencement (Driemeyer, Boyke, Gaser, Büchel, & May, 2008) and also in older subjects (Boyke, Driemeyer, Gaser, Büchel, & May, 2008). The impact of these environmental factors during longer time periods was also shown in other populations, for example, in taxi drivers of London (Maguire et al., 2000), in professional musicians (Gaser & Schlaug, 2003; Münte, Altenmüller, & Jäncke, 2002), and in mathematicians (Aydin et al., 2007). The direction of cause and effect is not yet fully understood in these populations, although the positive correlations between GM density and expertise point to a preference of environmental over genetic explanations.

The structural brain differences found in our study might reflect the simple fact that boys move more frequently (and faster) than girls (Campbell & Eaton, 1999); hence, boys encounter more differentiated environments (and faster alterations) that place greater demands on visuospatial information processing. These sex-specific differences in locomotion probably affect visuospatial processing abilities, that is, boys may acquire different strategies and/or more experience in visuospatial information processing, which in turn modulates parietal lobe structures. Further studies revealed that sex-stereotyped space-related activities predict visuospatial performance and that females improve in (visuo-)spatial information processing performance when engaged in male-associated space-related activities (e.g., video games and sports) (Ginn & Pickens, 2005; Devlin, 2004; Signorella, Jamison, & Hansen Krupa, 1989).

The cellular basis of these structural alterations is still not fully understood and cannot be investigated using structural neuroimaging methods. Such events may include synaptogenesis, dendritic expansion, myelin thickening, increased neuronal sizes, or the genesis of glial or even neuronal cells. We prefer to relate our finding of macroscopic brain differences to changes in myelo- and cytoarchitectonics because it has been shown that the T1-weighted intensity profiles in structural MRI are best explained by a weighted sum of myelo- and cytoarchitectonic profiles (Eickhoff et al., 2005). Imaging results have to be compared with histological data for the identification of the structural basis at the microscopic level.

Our Finding in the Context of a Parieto-frontal Integration Theory of Intelligence

According to Jung and Haier (2007), there is converging evidence derived from functional and structural neuroimaging studies for a parieto-frontal integration theory of intelligence. We also evaluated the neuroanatomy of VSC performance uncorrected for g. This analysis revealed only a quantitative difference in the correlates of VSC uncorrected for g compared with the analysis for which VSC was corrected for g. Particularly, there were less and smaller parietal clusters when general intelligence variance was not removed. Actually, we expected any involvement of prefrontal brain regions when VSC is not controlled for g because it has been shown that from all WAIS-R subtests the block design task loads highest on the g-factor on the one hand (Colom et al., 2006a), and prefrontal brain regions were proposed to be involved in the network of intelligence on the other hand (Jung & Haier, 2007). We found correlates of VSC (corrected as well as uncorrected for g) mainly in the parietal lobes, whereas Colom et al. (2006a) found correlates of the block design task performance (uncorrected for g) across all lobes with a preponderance in the parietal and frontal lobes, but also in subcortical and limbic structures. In view of the high g-loading of the block design task, it is really surprising that the results differ only slightly between the analysis for which g was controlled for compared with the analysis where intelligence variance was not removed. The high correlation between the block design task and g means that much variance was partialized out when VSC was controlled for g, so the results should look different. However, the sample sizes are almost equal between our study ($N = 43$) and the study of Colom and colleagues ($N = 48$), whereas the age ranges are quite different between the studies (19–32 years in ours and 18–84 years in the Colom study) and might, in part, be responsible for the discrepant results. Beside the age factor, there are methodological differences between these two studies (SPM2 vs. SPM5; density vs. volume; no HMRF-weighting vs. HMRF-weighting; MR images from one scanner vs. images from two different scanners). Further differences between the results of the two studies could be explained by differences in memory performance and the more homogenous nature of our sample with respect to other demographical measures such as education. In a combined magnetic resonance spectroscopy and morphometry study, block design task performance and global GM volume were stronger correlated in females ($r = .45$) than in males ($r = .29$), whereas block design task performance and global WM volume were correlated positively in males ($r = .25$) and weakly negatively in females ($r = -.08$) (Jung et al., 2005), results that are consistent with the sexual dimorphism hypothesis. The *N*-acetylaspartate concentration in a left occipito-parietal WM region was strongly correlated with block design task performance in females ($r = .68$), whereas these measures were not correlated in males ($r = .05$) (Jung et al., 2005). Although these correlations differ between the sexes, it is still unknown for what *N*-acetylaspartate is a marker for; hence, we did not try to interpret these correlations.

The current study contributes to a growing body of evidence demonstrating that even if sex is not associated with differences in VSC performance (in our study independent of g), the neural substrate of VSC is different. In future studies, it would be interesting to dissect the interplay between the genetic/hormonal (nature)

and exposure/usage (nurture) basis on the parietal lobe structures correlated with VSC performance independent of g.

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Competing interests statement: The authors declare that they have no competing financial interests.

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