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Handedness and cerebral anatomical asymmetries in young adult males

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Using voxel-based morphometry, we measured the cerebral anatomical asymmetries in a sample of 56 young right-handed males and then compared voxelwise asymmetry indices of these subjects to those of 56 young left-handed males. In the right-handed, the clusters of grey matter asymmetry corresponding to the leftward occipital petalia and planum temporale asymmetries were retrieved. Strong rightward temporo-parietal asymmetries were also observed, but the rightward grey matter asymmetry in the frontal lobe was less massive than previously described. Group comparisons of left- and right-handed subjects' asymmetry maps, performed at a statistical threshold not corrected for multiple comparisons, revealed significant effects of handedness on this pattern of anatomical asymmetry in frontal regions, notably in the lower central and precentral sulci, and also in the planum temporale, with right-handed subjects being more leftward asymmetric. Concerning white matter, although almost no focal differences between left- and right-handed subjects were detected, volumetric analyses at the hemispheric level revealed a leftward asymmetry, which happened to be significantly less marked in the left-handed. This latter result, together with the pattern of leftward white matter asymmetries, suggested that anatomical correlates of the left hemispheric specialization for language would exist in white matter. In the population we studied, differences in anatomical asymmetry between left- and right-handed subjects provided structural arguments for a greater functional ambilaterality in left-handed subjects.

Keywords: Brain asymmetry; Handedness; Hemispheric specialization; MRI; VBM

Introduction

Neuropsychological studies on aphasia, unilateral neglect, or callosotomized patients have shown that the two cerebral hemispheres, despite their sharing of a same overall structure, specialize for differing functions. In the right-handed, the left hemisphere hosts language and praxis functions (for a review, see Josse and Tzourio-Mazoyer, 2004; Meador et al., 1999), whereas the right one is more implied in visuospatial and attentional functions (Heilman et al., 1985; Mesulam, 1999). Functional differences between the motor systems of the left and right hemispheres also underlie the behavioral phenomenon of hand dominance, defined as the preferred used of one hand, which is the right in 90% of the cases, for daily life mono-manual activities. Recent research suggests that macroscopic anatomical changes occur with behavioral improvements in the visuospatial (Maguire et al., 2000), visuomotor (Draganski et al., 2004), language (Mechelli et al., 2004), or auditory (Schneider et al., 2002) domains, even in adults, suggesting a general structure function relationship (Mechelli et al., 2004). It may then be that some structural hemispheric asymmetries in grey matter (GM) macrostructure reflect the hemispheric asymmetries of language and other functions and the hand preference behavior.

Large-scale anatomical asymmetries exist in the human brain, such as the left occipital and right frontal protrusions or the upper lift of the right sylvian fissure. Focal asymmetries, more easily interpretable as regards their relationships with brain function, were also evidenced in dedicated ROI studies. Notably, the leftward asymmetry of the planum temporale (PT), an auditory cortex region at the back of the superior temporal surface which is involved in phonetic processing (Jancke et al., 2002), is considered as an anatomical marker of left hemispheric functional specialization for language (Shapleske et al., 1999; Geschwind and Levitsky, 1968). Anatomical asymmetry also concerns the central sulcus (CS), where it furthermore seems to interact with handedness: the upper

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region of the CS, which hosts the M1 hand area, is deeper on the left in the right-handed, while it tends to be rightward asymmetric in the left-handed (Amunts et al., 1996, 2000). An increased contralateral M1 hand area surface is thus associated with the greater abilities of the preferred hand. Further, a study showed that the way hand skill related to CS anatomy could differ between the two handedness groups (Herve et al., 2005).

Interestingly, effects of handedness on brain structure extend beyond the primary motor area of the hand: anatomical asymmetry of language regions also appears to vary according to handedness. This is in line with the well-known fact that left handedness is related to a different cerebral functional organization, for language in particular, as the proportion of atypical (i.e., non-leftward) hemispheric specialization for language raises up to 30% in the left-handed, while it is less than 10% in right-handed subjects (Woods et al., 1988). The precise reasons of this observed relationship remain undetermined. The effect of handedness on the anatomical asymmetry of language regions was mainly evidenced in the PT area, where a less marked leftward surface asymmetry was found in the non-right-handed, supporting the hypothesis that the anatomy of this area is indeed a marker of hemispheric specialization (Steinmetz et al., 1991). This finding was reproduced and also extended to the pars triangularis and opercularis in Broca's area (Foundas et al., 1995, 1998a).

Besides, white matter (WM) asymmetries may also constitute an important part of the anatomical underpinnings of hemispheric specialization. Notably, a study demonstrated with diffusion tensor imaging (DTI) the existence of handedness-related differences in the WM asymmetry of the precentral gyrus (Buchel et al., 2004). From a theoretical point of view, the setting up of a large-scale distributed network such as that of language implies for the various involved cortical functional fields to find each other on the basis of the existing WM pathways. Hemispheric differences in the strength of anatomical connections between language regions, as well as their adaptation to the particular requirements of speech processing, constitute a potential bias for the hemispheric clustering of networks (Parker et al., 2005). This is supported by DTI studies that have described a leftward asymmetry of the arcuate bundle or insular WM (Cao et al., 2003; Buchel et al., 2004).

From a methodological point of view, the study of cerebral asymmetry has largely benefited from the advent of powerful methods for analyzing structural magnetic resonance images. These techniques can rapidly bring accurate descriptions of the whole cerebral anatomical asymmetry pattern in large populations. The most commonly used is voxel-based morphometry (VBM) (Wright et al., 1995; Ashburner and Friston, 2000), which is a fully automated technique, based on voxelwise statistical analyses of GM or WM densities after segmentation of spatially normalized MRI scans. To date, only three studies have detailed comparisons of the relative focal GM and WM densities of the two hemispheres with VBM (Good et al., 2001a; Watkins et al., 2001; Luders et al., 2004). Though using different implementations of this method, all three have retrieved known asymmetries (petalia and PT), while uncovering others in regions not yet investigated. However, no significant effect of handedness could be evidenced in the two studies that tackled the subject. Good et al., working on 465 subjects from the general population, observed sex but not handedness effect on brain morphology, even when looking at small volumes of interest or with reduced statistical thresholds (Good et al., 2001a). Watkins et al., on a smaller sample of comparable composition, did not detect significant effects of sex or handedness, but when processing either men or right-handed subjects separately, found variations in t statistics, suggesting that an impact of these two factors could be evidenced on a greater sample or a sample more fairly distributed for handedness and matched for sex and age (Watkins et al., 2001).

Such effects are not expected to be easily evidenced, since the classical dual handedness group classification may well be quite inaccurate to represent this factor, which can be continuous or contain several distinct groups instead of two. Also, handedness effects on cerebral asymmetry, at least in the CS, are less likely to be found in females (Amunts et al., 2000). Given the necessity of large samples for VBM studies, it may thus be interesting to focus first on the male population, all the more as large differences in GM/WM ratio and average brain volume exist between the two sexes, constituting an important source of anatomical variability (Gur et al., 1999; Good et al., 2001a; Luders et al., 2002). Aside of the important question of handedness effects on cerebral anatomical asymmetry, other authors (Ochiai et al., 2004) also pointed that apparently conflicting results exist between VBM studies of asymmetry and ROI guided studies in some regions, such as the leftward asymmetries of the upper CS (Amunts et al., 1996) and the inferior frontal gyrus (Foundas et al., 1998a), and it may thus be necessary to improve our understanding of VBM as applied to hemispheric asymmetries. In this context, our study was firstly aimed at establishing via VBM the anatomical asymmetry pattern in young male right-handed subjects, often used in neuroimaging studies and, secondly, to compare it with the one found in an analogous group of left-handed subjects, in order to evidence effects of handedness on cerebral WM and GM asymmetries in regions not yet investigated by ROI studies.

Materials and methods

Subjects

56 young right-handed males (age 22.8 ± 2.8 years ranging from 18 to 34) underwent an MRI anatomical examination at the occasion of their participation to various functional imaging studies performed at our laboratory. They neither had a history of neurological or psychiatric troubles nor were concerned by the classical exclusion criteria for MRI examination and did not display anatomical abnormalities on their T1 MRI. We added to these subjects another set of 56 young left-handed males (age 21.6 ± 2.4 years, ranging from 18 to 31), 1 year younger than the right-handed group on average (two sample t test, $P < 0.05$). They were specifically recruited for this study and came mostly from the same student population. The informed and written consent of each subject was obtained before inclusion in this protocol, which received the approval of the local ethics committee. The criterion for right handedness was an Edinburgh Handedness Inventory larger than 30 (broom item excluded). Thus, only consistent right-handed subjects were included in the "right-handed" group, while all "non-right-handed" subjects were placed in the left-handed group. The laterality quotients were, for the left-handed sample, comprised between −100 and +22.2 on the Edinburgh scale, while those of the right-handed ranged between +42.8 and +100 (Fig. 1 presents the characteristic J-shaped distribution of the Edinburgh scores on the 112 subjects).

MRI examination

A T1-weighted MRI scans of each subject's head was acquired using a 1.5 T Signa Horizon LX scanner (General Electric, BUC, France). All acquired volumes contain 124 axial slices of 256 × 256 pixels, with a voxel size of 0.94 × 0.94 × 1.5 mm^3. A three-dimensional IR-SPGR sequence (TR = 10.3 ms, TE = 2.1 ms, FA = 10°, TI = 600 ms, one excitation) was used for data acquisition. Before processing, volumes were interpolated to an isotropic voxel size of 0.94 × 0.94 × 0.94 mm^3. Finally, each image was centered on the anterior commissure.

Voxel-based morphometry

Overview

Data were processed according to the optimized VBM protocol (Good et al., 2001b) using the SPM99 software package. We ran analyses on both GM and WM spatial distributions. Basically, VBM is composed of four steps: spatial normalization of the MRI scans in a stereotaxic reference space, followed by segmentation into GM, WM cerebro-spinal fluid and non-brain tissue partitions, smoothing of tissular maps, and finally, statistical parametric mapping (Ashburner and Friston, 2000). The Bayesian segmentation procedure of SPM uses stereotaxic a priori tissular probability maps for each of the four compartments it considers (GM, WM, cerebrospinal fluid, and extra-cerebral tissue), on which the final outcome of the segmentation is partly dependant. This is why the "optimized protocol", in which the native space GM map of each subject is spatially normalized on a GM template, finally improves the segmentation of the images: the tissular densities stand in better alignment with the probability maps, making the segmentation more accurate. The normalization of the brains would also be ameliorated, as the cortical ribbon, which delimitates the borders of the brain, is used for the spatial normalization. Besides, not only symmetric templates but also symmetric spatial probability maps should be used when considering asymmetries, so as not to bias the results towards either side (Luders et al., 2004).

Initial segmentation step

This step involves, firstly, a 12-parameter affine spatial normalization of the native T1 image on a T1 template, secondly, a Bayesian segmentation of the normalized T1 image in the corresponding stereotaxic space, and thirdly, the sending of the segmented images back in their native space. We used symmetrical versions of the SPM99 default T1 normalization template and corresponding segmentation priors, obtained by averaging these images with their mirrored images along the *x* axis. The obtained grey matter images were cleaned of non-brain tissue, using the SPM "brain mask" function.

Optimized normalization and segmentation

The obtained grey matter images were then normalized on the same symmetric grey matter template that was previously used for the first segmentation. Here, we applied a non-linear spatial normalization, allowing a better fit of the overall shape of the brain with the template. As for parameters, we used "8 × 8 × 8" non-linear basis functions, this parameter indexing the spatial resolution of the warps. The "heavy" level of regularization (a function penalizing the strength of the warps) was chosen, in order to avoid sharp focal deformations, which, in some cases, make no biological sense. The obtained normalization matrices were then applied to the native T1 volumes, which were resliced in the stereotaxic space with a voxel size of 1.5 × 1.5 × 1.5 mm^3.

The optimally normalized T1 images were then segmented using the same symmetric prior probability images as those of the first step. As for the previous step, the resulting GM and WM images were cleaned of non-brain tissue.

Once the T1 scans optimally normalized and segmented, the deformations induced by the non-linear spatial normalization were corrected ("modulation" step) by multiplying the GM images by the Jacobian determinants of the corresponding spatial normalization matrices, which exactly correct the local volumetric contraction or dilatation the images undergo during warping.

Statistical analyses

Volumetric data

Volumetric data were obtained for the left and right hemispheres by summing the intensities of every voxels on the left and right halves (voxels with *x* coordinate inferior to 0 and *x* coordinate superior to 0 respectively) of the modulated GM and WM images. Volumetric data (GM and WM volumes, their sum and ratio) were analyzed using repeated measures ANOVA, with side as within-subject factor and handedness as between-subject factor.

VBM: asymmetries in a group of 56 right-handed subjects

Prior to this analysis, the modulated images GM and WM were smoothed with a 12-mm FWHM Gaussian kernel. Mirror images of the obtained 56 GM and 56 WM smoothed probability maps were computed. For evaluating the focal inter-hemispheric differences in GM or WM volume subsisting after symmetrical normalization and segmentation, normal and flipped GM or WM images were entered as pairs in the paired two sample one-tailed *t* test design of SPM99, yielding statistical maps of regions where the mean difference in GM or WM volume in the two hemispheres differed from zero.

In a usual SPM analysis, two unilateral contrasts are computed separately on the whole brain, respectively showing the differences favoring each of the two conditions. When dealing with differences between the left and right sides of the brain, a single contrast gathers, on the left side of the brain, the positive differences between the left and right hemisphere (leftward asymmetry), and, on the right side of the brain, the positive differences between the right and left hemisphere (rightward asymmetry). Although this is convenient, this also results in doubling the number of tests inside a same contrast and thus over-correction for multiple comparisons. This is why, for these GM and WM asymmetry analyses, two contrasts were computed (left minus right, right minus left), on the sole left hemisphere. A large number of highly significant peaks were found. Thus, for practical reasons, only those surviving a threshold of $P < 0.05$ corrected for multiple comparisons were detailed in the tables. A more permissive statistical threshold of $P < 0.001$ uncorrected for multiple comparisons was however used for displaying these maps, as this offered a better illustration of the results.

VBM: comparison of the asymmetries in right- and left-handed groups

For this analysis, voxelwise anatomical asymmetry indices (AAI) maps were computed, for GM and WM, by subtracting the

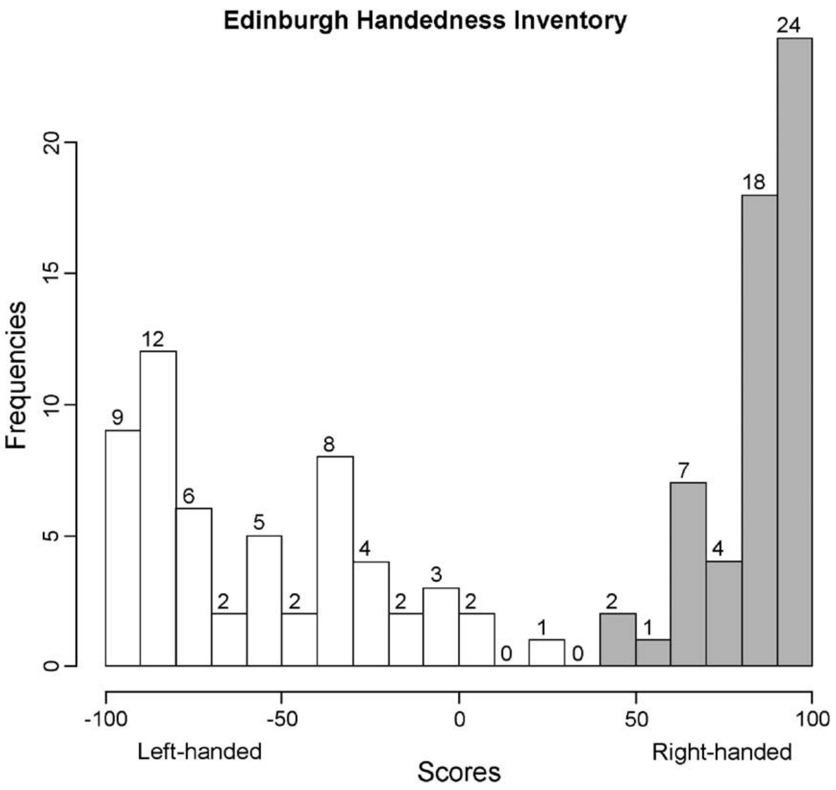

Fig. 1. Distribution of the Edinburgh Handedness Inventory scores in the total sample of 112 male subjects. The left-handed group (score < 30) corresponds to the white bars, and the right-handed group to the grey bars.

reversed to the normal images. Group comparisons of these AAI maps of the right- and left-handed groups were then conducted (two sample t tests). The out coming statistical parametric maps provided the regions where the right-handed subjects had more positive AAI than the left-handed, i.e., greater leftward (or smaller rightward) and greater rightward (or smaller leftward) asymmetry in the right-handed for left and right hemisphere clusters, respectively. Although inter-hemispheric asymmetries as probed with VBM are highly significant and massive effects (Good et al., 2001a; Watkins et al., 2001), it is not the case of inter-group differences in inter-hemispheric asymmetries. Hence, the statistical threshold chosen for the group comparisons corresponded to a P value of 0.001 uncorrected for multiple comparisons. No correlation with the EHI scores was performed, as the bimodal distribution of this variable (Fig. 1) makes it particularly unsuited for such purposes: it would eventually amount to the group comparisons we performed.

Results

Hemispheric volumes

Results of the volumetric analyses are reported in Table 1 and Fig. 2. Significant side by handedness interactions was evidenced for WM volume ($P < 0.01$), hemisphere volume ($P < 0.05$), GM/WM ratio ($P < 0.05$), but not for GM volume. Leftward WM and hemisphere volume asymmetries were present in both handedness groups but were more marked in the right-handed, whereas a rightward GM asymmetry was found that did not differ according to handedness. The GM/WM ratio was hence greater on the right side in both groups but less importantly in the left-handed. As a consequence, highly significant main effects of side were found for GM, WM, and GM/WM ratio ($P < 10^{-4}$). No significant main effect of handedness was found on these variables.

Table 1
Mean values (SD) of grey matter and white matter volumes (cc), sum of grey and white matter and grey/white matter ratios, per group and hemisphere, and mean hemispheric difference for these variables

	Left hemisphere		Right hemisphere		L – R difference		Hand	Hemi	Interaction
	Right-handers	Left-handers	Right-handers	Left-handers	Right-handers	Left-handers			
GM volume	409.5 (28.1)	417.1 (33.5)	413.7 (28.1)	422.1 (33.9)	−4.13 (4.08)	−4.94 (3.74)	NS	***	NS
WM volume	229.1 (20.3)	232.1 (21.9)	219.5 (19.5)	224.2 (20.1)	9.54 (2.32)	7.94 (2.29)	NS	***	**
GM+WM	638.6 (45.3)	649.3 (53.1)	633.2 (44.2)	646.3 (52.5)	5.41 (5.21)	3.01 (4.57)	NS	***	*
GM/WM	1.79 (0.11)	1.80 (0.19)	1.89 (0.12)	1.89 (0.10)	−0.10 (0.02)	−0.09 (0.02)	NS	***	*

Main effects of handedness and hemisphere, and interaction (repeated measures ANOVA) are reported (*$P<0.05$, **$P<0.001$, ***$P<0.0001$).

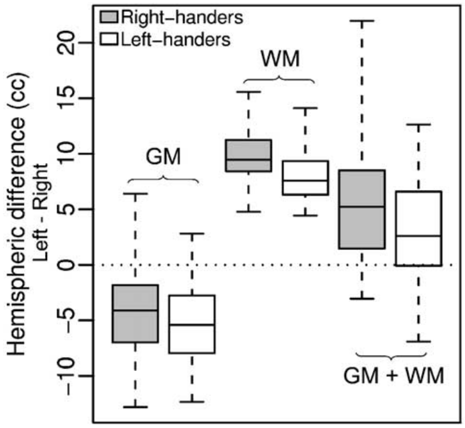

Fig. 2. Box-whisker plots figuring the distributions of hemispheric differences (left minus right) in grey matter (GM), white matter (WM), and total brain tissue computed as the sum of grey and white matter, in right- and left-handers. See Table 1 for descriptive and inferential statistics.

VBM: anatomical asymmetries in a sample of 56 right-handed male subjects

Statistical peaks of GM asymmetries are presented in Tables 2 and 3, and GM asymmetry maps are showed in Fig. 3 (whole brain). Peak statistics for WM asymmetries is given in Table 4, while a map of leftward WM asymmetry is shown in Fig. 4.

Grey matter

Frontal lobe. In the frontal region, leftward GM asymmetries were seen in the medial wall of the sylvian fissure (middle and upper anterior insular cortex) and focally in the inferior part of the central and precentral sulci. Leftward asymmetry also appeared in a region corresponding to the superior rostral sulcus, under the anterior origin of the cingulate sulcus.

Several foci of rightward asymmetry were detected, namely, in the anterior and inferior regions, such as the inferior frontal gyrus (mainly the pars orbitaris), orbital part of the superior frontal gyrus, and anterior part of the gyrus rectus. Concerning medial parts of the frontal lobe, a focus of rightward GM asymmetry was detected in the anterior cingulate gyrus, extending in more posterior parts (Fig. 3).

Temporal lobe. In the temporal lobe, the upper surface of the superior temporal gyrus (STG), inside the sylvian fissure, displayed a greater GM volume in the left hemisphere, with a strong peak in its medial and posterior part, corresponding to the PT. Heschl's gyrus was encompassed in this patch of leftward asymmetry. Leftward GM asymmetry also occurred focally in the hippocampus and in the inferior temporal and lingual gyri.

Rightward asymmetry was found in the depths of the superior temporal sulcus (STS), on its whole length, with a peak under Heschl's gyrus (Fig. 3). The most posterior part of the inferior temporal sulcus also was rightward asymmetric. The likely relationship between the well-known positional asymmetries of this region and the observed VBM results was studied by means of isocontours

Table 2
Rightward grey matter volume asymmetry peaks in the sample of 56 right-handed subjects (MNI coordinates in the left hemisphere, threshold corresponding to a P value of 0.05 corrected for multiple comparisons)

Region	Peak location	*x*	*y*	*z*	*t* values ($t > 5.06$)	Cluster size
Frontal	IFG orbitaris	−42	44	−8	9.51	706
	Gyrus rectus	−4	58	−20	6.44	173
	Anterior cingulate gyrus	−10	40	6	9.54	4428
	IFG orbitaris	−27	32	−16	9.23	–
	Anterior cingulate gyrus	−8	3	27	5.55	–
Sub-cortical	Caudate head (Ant)	−15	27	3	12.69	–
	Thalamus (Ant)	−8	−9	12	10.80	–
Hand area	Central sulcus	−40	−26	52	11.65	13,551
	Precentral gyrus	−32	−18	62	8.92	–
Parietal	Supra-angular gyrus	−54	−45	38	13.20	–
	Supra-marginal gyrus	−45	−10	27	9.57	–
	Central sulcus (Inf)	−54	−28	28	9.46	–
	Superior parietal gyrus	−28	−56	57	6.32	–
Temporal	Superior temporal sulcus	−45	−24	−8	17.64	–
	Superior temporal sulcus	−51	−40	9	13.33	–
	Middle temporal gyrus	−48	−58	2	9.37	–
	Temporal pole	−44	−4	−27	7.22	–
	Inferior temporal gyrus	−56	−48	−14	6.73	–
	Middle temporal gyrus	−42	−8	−39	5.32	–
Occipital	Intra-occipital sulcus	−33	−81	21	8.55	–
	Middle occipital gyrus	−36	−76	33	7.24	–
	Intra-occipital sulcus	−33	−80	9	7.14	–
Medial Occipital	Calcarine fissure	−15	−54	8	10.27	3745
	Parieto-occipital fissure	−4	−70	34.5	7.03	–
Cerebellum	VIIb	−39	−57	−44	15.11	6530
	IX	−2	−46	−50	9.56	–
	VIII	−15	−66	−50	6.69	–
	Vermis	−2	−56	−9	6.22	–

IFG—inferior frontal gyrus. Hyphens in the cluster size column indicate peaks belonging to the same cluster as the preceding.

Table 3
Leftward grey matter volume asymmetry peaks in the sample of 56 right-handed subjects (MNI coordinates, statistical threshold corresponding to a P value of 0.05 corrected for multiple comparisons

Region	Peak location	*x*	*y*	*z*	*t* values (>5.06)	Cluster size
Frontal	Superior rostral sulcus	−6	32	−15	10.80	834
	Precentral sulcus	−52	10	30	6.77	98
	Post-central sulcus (inf)	−68	−21	28	5.61	51
Parietal	Precuneus	−14	−48	36	5.46	42
Temporal	Planum temporale	−39	−32	12	13.05	2699
Insula	Middle Insula	−39	−4	3	9.40	–
	Superior anterior insula	−30	26	3	6.45	107
Occipital	Middle occipital gyrus	−52	−81	15	9.02	2131
	Inferior temporal sulcus	−62	−69	2	8.59	–
	Middle occipital gyrus	−46	−87	18	8.01	–
	Transverse occipital sulcus	−34	−94	20	5.55	–
Sub-cortical	Caudate head (post)	−10	8	4	10.38	229
	Thalamus (post)	−9	−28	−3	9.13	521

Hyphens in the cluster size column indicate that the peak belongs to the same cluster as above).

of the mean GM image of the left and right hemispheres (Fig. 5). The sylvian fissure ended earlier in the right than in the left hemisphere, and the upper posterior branch of the STS was shifted forward in the right hemisphere as well (for a review, see Toga and Thompson, 2003). This inter-hemispheric difference in sulcal pattern explains the peak of GM asymmetry observed in the right angular gyrus, since the termination of the right STS was opposed to gyral WM on the left. Additionally, a longer left PT and a deeper right STS were also obvious on the mean GM image, partly explaining our VBM results for these regions (Fig. 5).

Parietal lobe. In the parietal lobe, a cluster of rightward asymmetry was found in the inferior precuneus.

Rightward asymmetries were found at the parieto-temporal junction, in the supra-marginal and angular gyri, in the parietal operculum above the PT, and also in the central regions of sensorimotor cortices, around the upper part of the CS. In the medial part of the parietal lobe, the parieto-occipital sulcus also displayed a larger GM amount in the right hemisphere.

Occipital lobe. In the occipital lobe, we observed a leftward asymmetry spreading over the postero-lateral surface of the brain, corresponding to the occipital petalia.

Rightward asymmetries appeared nonetheless in more internal parts, particularly in the intra-occipital sulcus, middle occipital gyrus, and occipital pole. The calcarine fissure and parieto-occipital sulcus also exhibited a rightward asymmetry.

Deep brain structures and cerebellum. Sub-cortical structures also displayed asymmetries: leftward asymmetry of smaller amplitude was seen in the very posterior parts of these structures. Conversely, the anterior parts of the caudate nucleus and thalamus were rightward asymmetric.

Rightward asymmetry was found in most of the cerebellum, in the central parts of the VI, inferior and superior semi-lunar, VII, VIII, and IX lobules.

White matter

WM asymmetries were mainly detected opposite to GM asymmetries (see Tables 2 and 4, Tables 3 and 5, and Figs. 3 and 4), and mostly located in the more lateral parts of the brain (Fig. 4).

Perisylvian region. Leftward WM asymmetry was detected in the inferior frontal region and in the parietal operculum as well (Table 4). In the temporal lobe, a leftward asymmetry was seen near the depths of the temporal sulci, in accordance with opposite GM results. The sylvian fissure was thus surrounded by leftward WM asymmetry (Fig. 4, top left). Notably, peaks of WM asymmetry were seen in regions corresponding stereotaxically (Talairach and Tournoux, 1988) to the arcuate (Fig. 4, left and middle) and uncinate bundles (Fig. 4, right).

A rightward WM asymmetry was found in the PT region, opposite to the GM asymmetry (Table 5).

Internal capsule. A peak of leftward asymmetry was found between the striatum and thalamus, at the putative locus of the corticospinal projection fibers of the hand (Fig. 4). Accordingly, a leftward asymmetry was also observed along the post-central and precentral gyri.

Other regions. In the medial wall, leftward asymmetry was seen in the genu of the anterior corpus callosum, near the region of rightward GM asymmetry. Rightward WM asymmetry was seen by the gyrus rectus and anterior cingulum. Increased WM in the left hemisphere was also seen immediately anterior to the parieto-occipital fissure.

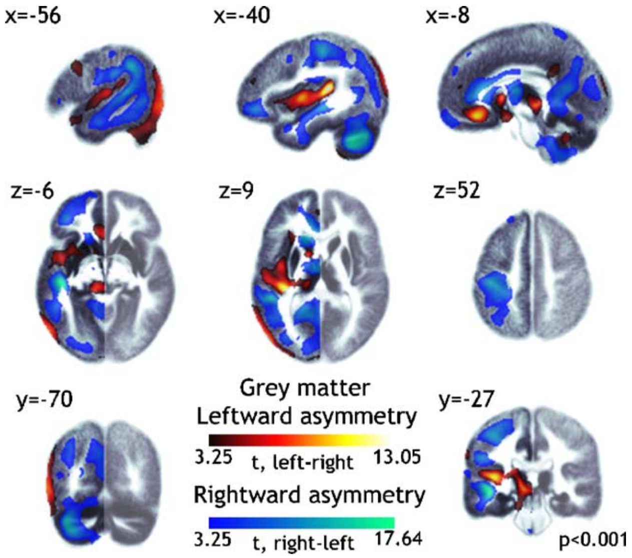

Fig. 3. Leftward (from red to yellow) and rightward (from blue to green) asymmetries in the sample of 56 right-handed subjects, overlaid on their mean left hemisphere grey matter image in the MNI space (statistical threshold corresponding to $P < 0.001$ uncorrected). To signal that all results were reported in left hemisphere coordinates, the right hemisphere was shaded.

Table 4
Leftward white matter volume asymmetry peaks in the sample of 56 right-handed subjects (MNI coordinates, statistical threshold corresponding to a P value of 0.05 corrected for multiple comparisons)

Region	Peak location	x	y	z	t values (>4.88)	Cluster size
Frontal	IFG orbitaris	−44	42	−8	10.14	1734
	Uncinate fasciculus	−21	15	−15	9.02	–
	Uncinate fasciculus	−30	28	−15	8.10	–
Central	Post-central gyrus	−48	−24	56	12.97	17,808
	Post-central gyrus	−33	−32	68	11.01	–
	Post-central gyrus	−60	−14	32	10.31	–
Internal capsule	Corticospinal tract	−16	−9	0	9.93	–
Temporo-parietal	Superior longitudinal fasciculus	−48	−32	0	16.37	–
	Inferior longitudinal fasciculus	−40	10	−28	13.16	–
	Parietal operculum	−57	−28	28	11.58	–
	Supramarginal gyrus	−56	−46	39	10.77	–
	Inferior longitudinal fasciculus	−51	−62	2	8.90	–
Frontal	IFG opercular	−50	6	12	6.36	–
Medial	Corpus callosum (genu)	−3	30	10	10.51	–
Parietal	Precuneus	−18	−54	9	8.37	733
Occipital	Middle occipital gyrus	−34	−84	22	8.09	987
	Middle occipital gyrus	−42	−82	10	7.27	–
Cerebellum	Pedunculus	−38	−58	−38	13.22	1953

IFG—inferior frontal gyrus. Hyphens in the cluster size column indicate peaks belonging to the same cluster as the preceding.

In the occipital region, leftward matter asymmetry was found near the intra-occipital sulcus.

VBM: comparison of anatomical asymmetries in left- and right-handed subjects

The statistical comparison of the GM asymmetry patterns of the two groups evidenced subtle deviations from the previously described pattern in the left-handed group. The t map revealed greater AAI in right-handed subjects in several regions, almost exclusively on the left side of the brain, indicating more leftward asymmetry in right-handed subjects (Table 6 and Fig. 6). Mean AAI of each group at these locations are reported in Fig. 7. Differences in WM asymmetries between the two groups were scarcely found at this threshold (Table 6).

Grey matter

At the relatively liberal threshold of $P < 0.001$ uncorrected for multiple comparisons, significant clusters were found, primarily in the frontal lobe, in the precentral sulcus and CS, and also in the superior and inferior frontal sulci. In the parietal lobe, a significant left hemisphere cluster was found near the intra-parietal sulcus. In the temporal lobe, differences between the right- and left-handed groups were detected in the para-hippocampal region and in the PT. At this latter site, right-handed subjects had a significant leftward asymmetry, whereas no asymmetry was found in the left-handed (Fig. 7). Lastly, larger AAI in the right-handed were detected in the inferior and lateral part of the left occipital lobe and adjacent cerebellum.

The sole cluster where right-handed subjects had greater AAI than left-handed subjects on the right side of the brain was found in the cerebellum, more precisely in the interior and lateral part of the superior semi-lunar lobule.

White matter

Two small clusters of differing WM asymmetry between left- and right-handed were observed at $P < 0.001$ in the cerebellum and middle frontal gyrus. They were the counterparts of differences seen on the precedent comparison of GM asymmetries. This indicates that the aforementioned hemispheric effect of handedness on WM asymmetry was diffuse, in other words, not due to strong focal divergences between the two groups, but to a small difference concerning a large number of voxels.

Discussion

At the hemispheric level and in the particular population we considered (young male subjects), rightward asymmetry was seen for GM, while a relatively stronger opposite asymmetry was

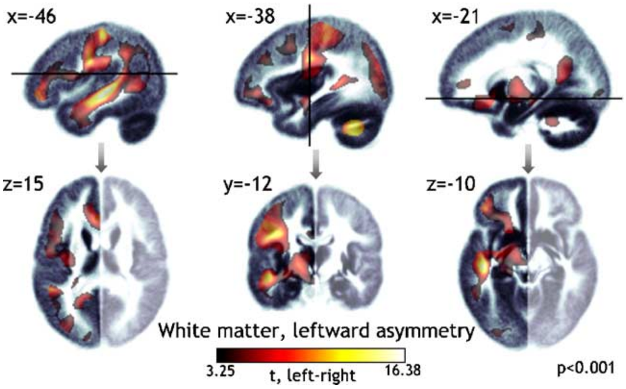

Fig. 4. Statistical map of leftward white matter asymmetry in the sample of right-handed subjects ($P < 0.001$ uncorrected), overlaid on the mean grey matter image of the left hemisphere (MNI space). The black lines in the first row figures are the cut planes of the corresponding slices of the second row, as indicated by the arrows. Left column: pervasive perisylvian white matter asymmetry in the lateral part of the brain, notably in regions statistically corresponding to the superior and inferior longitudinal bundles. Middle column: strong asymmetry in the precentral and mostly the post-central gyri and internal capsule. Right column: clusters observed in the inferior frontal region may relate to the uncinate bundle.

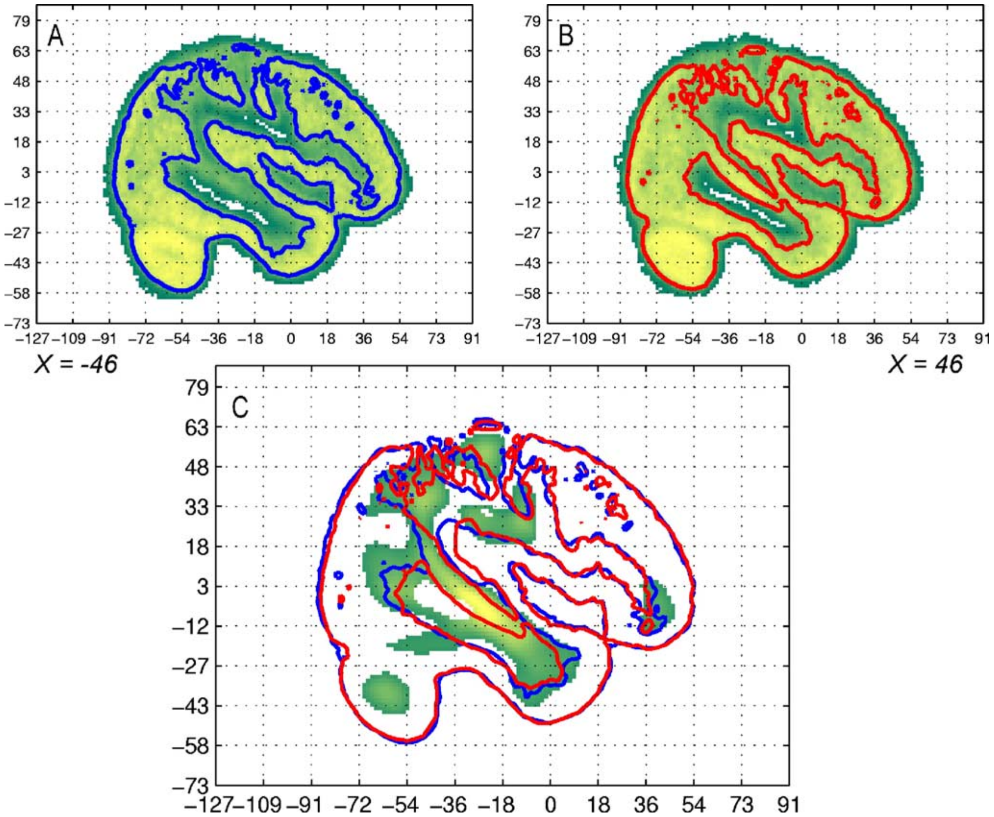

Fig. 5. Isocontours of lateral sagittal cuts of the mean grey matter image (in green shades) of the 56 right-handed subjects, at a grey matter probability level of 0.55. (A) Left hemisphere, at $x = -46$ mm, MNI space. (B) Right hemisphere, at $x = 46$ mm. (C) The two isocontours (left in blue, right in red) are displayed over the statistical map of rightward asymmetries (in green, SPM t map thresholded at $t = 3.25$). The superior temporal sulcus was obviously deeper on the right, as its grey matter trace was already present on the right but not on the left cut. It was also found at a higher position, and its terminal ascending branch was shifted anteriorly relatively to its left counterpart, in line with a strong rightward grey matter asymmetry. Accordingly, the PT was shorter and higher in the right hemisphere. Lastly, a discrepancy existed between the left and right contours of the occipital surface that was not found in the frontal part of the brain.

observed for WM, eventually biasing overall hemispheric volumes in favor of the left side. Although the magnitude of the asymmetries was relatively small (particularly for the whole hemisphere), these asymmetries were very reproducible across subjects and thus reached statistical significance (Fig. 2). Although diverging patterns have been reported, notably of a higher GM/WM ratio in the left hemisphere (Gur et al., 1999; Allen et al., 2003), recent studies found larger WM volumes in the lateral parts of the left hemisphere, as well as extensive rightward asymmetries in GM (Good et al., 2001a; Pujol et al., 2002). Considering the distribution of the tissular volume asymmetries (notably, all subjects displayed a leftward WM asymmetry, as seen on Fig. 2), it seems plausible that these stable and global anatomical asymmetries reflect genetically specified divergent developmental patterns of the two hemispheres. They also are an average of what is observed at a finer scale with VBM, where strong asymmetries were evidenced for both tissues.

Considering the regional (VBM) results, the asymmetry pattern we obtained in young male right-handed subjects is coherent with the asymmetries classically described in the literature, with leftward occipital and planum temporale asymmetries and rightward parietal and frontal asymmetries. It was notably close to the

Table 5
Rightward white matter volume asymmetry peaks in the sample of 56 right-handed subjects (MNI coordinates, statistical threshold corresponding to a P value of 0.05 corrected for multiple comparisons)

Region	Peak location	x	y	z	t values (>4.88)	Cluster size
Medial wall	Anterior cingulum	−6	33	−15	11.31	699
Insula	Upper anterior insula	−27	26	4	6.90	339
Internal capsule	Anterior limb	−8	9	2	8.27	279
Temporal	Superior temporal gyrus	−42	−32	14	13.87	1136
Parietal	Precuneus	−8	−50	60	5.44	63
Corpus callosum	Bulb	−14	−44	26	6.24	329
	Body	−21	−22	33	5.58	43
Occipital	Lingual gyrus	−18	−64	3	7.63	149
	Superior occipital gyrus	−18	−80	22	6.12	76
Cerebellum	Pedunculus	−8	−56	−40	5.87	80

Table 6
Significant grey and white matter volume asymmetry differences between right-handers (n = 56) and left-handers (n = 56)

Peak location	*x*	*y*	*z*	*t* values (>3.17)	Cluster size (>40)
Grey matter					
Precentral sulcus	−51	12	32	4.85	207
Central sulcus	−56	−18	45	4.68	480
Inferior occipital region	−44	−76	−24	4.49	985
Inferior parietal gyrus	−46	−57	50	4.26	251
Planum temporale	−57	−18	12	4.24	163
Superior frontal sulcus	−28	39	39	4.08	92
Inferior frontal sulcus	−39	45	15	3.98	106
Hippocampal region	−15	−21	−24	3.63	176
Cerebellum	38	−58	−39	3.60	99
White matter					
Cerebellum	−39	−60	−36	3.98	144
Middle frontal gyrus	38	45	14	3.55	40

Left hemisphere peaks indicate more leftward asymmetry in right-handers, while right hemisphere peaks indicate more rightward asymmetry in right-handed subjects as compared to left-handed subjects (MNI coordinates, statistical threshold corresponding to a P value of 0.001 uncorrected, clusters over 40 voxels).

one described with texture analysis after linear transformation to the Talairach space (Kovalev et al., 2003), with particularly salient asymmetries in the temporal sulci and parietal and occipital lobes. We further showed (Fig. 5) that these results, in the present study, were not unrelated to the forward and upper shift of the right temporal sulci, as described by others (Blanton et al., 2001; Sowell et al., 2002b). Along with the central region asymmetries, this parallels the fact that both language and motor systems are strongly lateralized in humans. The tackling of several methodological points should help the understanding and interpretation of the present VBM results.

VBM of cerebral asymmetry: methodological issues

Positional asymmetries

Indeed, local GM volume changes tracked by VBM are dependent on the residual anatomical variability after spatial normalization. This residual variability concerns the size and shape (morphology) of neuroanatomical structures but also their position in the stereotaxic space. When interpreting such results, it is often assumed that structures are, on average, in alignment between subjects and group of subjects, so that differences observed at a particular coordinates range can be mainly attributed to inter-group size or shape differences of a same structure. We observed that although a symmetrical normalization template and a non-linear spatial normalization were used, significant sulcal position differences still existed in the parieto-temporal region, with a forward and upper shift of right hemisphere structures (Fig. 5), that is well described in the literature (Toga and Thompson, 2003). In this region, the same structures were aligned on both sides across subjects but to slightly differing coordinate ranges across hemispheres. As this analysis compares GM volumes at identical coordinates of the two hemispheres, and although spatial smoothing helps reducing spatial homology differences of small amplitude, positional asymmetries will appear as GM volume asymmetries. This represents a limit of the VBM analysis since it prevents a systematic interpretation of statistical maps in straightforward terms of larger left or right GM volume or concentration.

More to the point, the occipital petalia observed here is interpretable as a positional asymmetry between the hemispheres, with the occipital lobe simply being more salient on the left side. It is noteworthy that other studies already reported a more significant occipital petalia as compared to the frontal (Weinberger et al., 1982; Ashburner et al., 1998; Raz et al., 2004), and that only the occipital petalia is accompanied by a clear deviation of the sagittal midline (to the right), indicating a stronger inter-hemispheric shape difference in the posterior region. Furthermore, immediately beneath the corresponding cluster, strong rightward GM asymmetry was found (notably along the intra-occipital sulcus, Fig. 3 at $x = -38$), contrary to what would otherwise be expected. Overall, this supports the hypothesis that the petalias are associated with displacements of the cerebral boundaries (Lancaster et al., 2003) without congruent GM volume changes (Sowell et al., 2002a). It was recently proposed that shallower sulci in the hemisphere with the petalia would cause more cortex to be exposed on the lateral surfaces of the posterior region, which would then induce the left/right dimorphism in the occipital and frontal regions (Allen et al., 2003; Mangin et al., 2004).

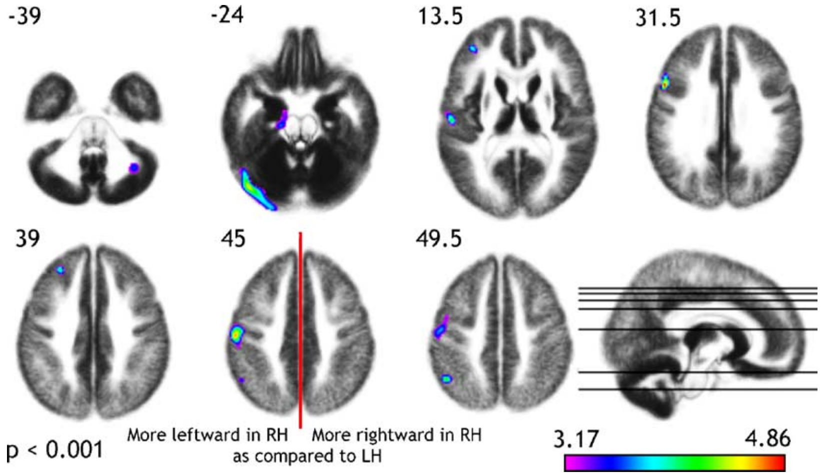

Fig. 6. Grey matter asymmetry differences between right- and left-handers (n = 56), on axial cuts of the mean grey matter image. The heights of the cuts in the z axis are given in millimeters, MNI space. The statistical threshold corresponds to a P value of 0.001 uncorrected. Clusters found in the left hemisphere correspond to more leftward asymmetry in right-handers as compared to left-handers.

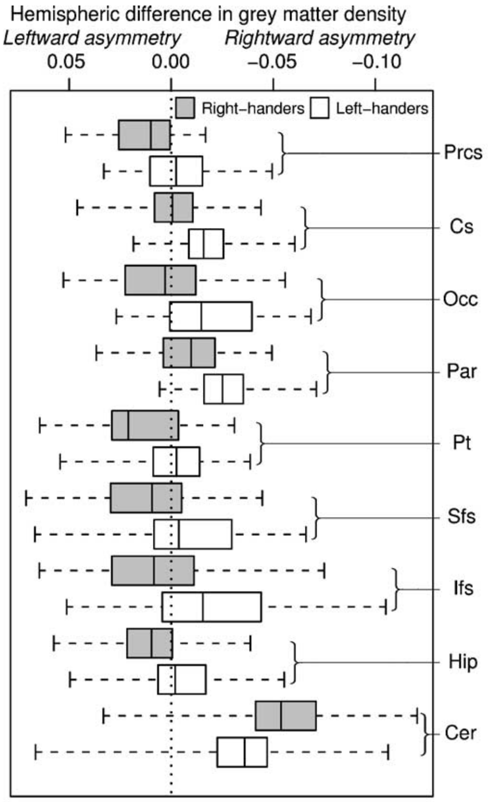

Fig. 7. Box-whisker plots of the clusters of significantly different grey matter volume asymmetry (anatomical asymmetry indices) between right-handed and left-handed groups. Positive values indicate leftward asymmetry, negative values indicate rightward asymmetry. More leftward asymmetry in right-handers (8 first clusters) can possibly originate from opposite asymmetries in the two groups, less marked leftward asymmetry in left-handers as compared to right-handers, or from a less marked rightward asymmetry in right-handers as compared to left-handers. The last cluster displayed more rightward asymmetry in right-handers as compared to left-handers (cerebellum). Prcs: precentral sulcus, Cs: central sulcus, Occ: occipital region, Par: inferior parietal lobule, Pt: PT, Sfs: superior frontal sulcus, Ifs: inferior frontal sulcus, Hip: hippocampal region, Cer: cerebellum.

Interpretation of VBM asymmetries

Another concern is the fact that GM asymmetries favoring one hemisphere are most often balanced by opposite WM asymmetries (see Fig. 3). In an ideal case of perfect inter-hemispheric alignment, two types of interpretations of a same result can be made, depending on whether one sees it from a GM or WM viewpoint. Considering WM, the tension based theory of morphogenesis (Van Essen, 1997) postulates that adjacent regions with high anatomical connectivity form gyral crests (outward folds) in order to diminish axonal tension, while adjacent regions less densely connected are found inside sulci (inward folds). Within this frame, the amount of WM fibers connecting the two sides of an inward fold may however be constraining its growth and hence influence sulcal depth (Davatzikos and Bryan, 2002). Concerning GM, an increased amount of cortex can obviously be obtained via an increase in cortical surface, as exemplified by the leftward PT surface asymmetry. Not considering the effects of modulation, the VBM signal is, whatever its actual anatomical origin (shape or position differences), based on focal displacements of the tissue interfaces (see Fig. 5). The origin of a particular GM/WM boundary change is eventually often difficult to attribute to one or the other tissue, and GM and WM asymmetries should therefore be as much as possible considered altogether.

We will discuss the results concerning the motor and language systems, on the basis of current knowledge on cerebral anatomy and function, and then the possible interpretations of asymmetries favoring the right hemisphere.

Primary sensorimotor area of the hand, corticospinal tracts, and handedness

The CS can be sub-divided in several parts, with notably an omega- or epsilon-shaped genu which constitutes a folding correlate of the primary hand motor region, and is a locus of increased depth. Due to its relationship with handedness, the anatomical asymmetry of the cortical sensorimotor projection of the hand was the object of several studies. This sulcus was found leftward asymmetric in its upper part by Amunts, using manual tracings, and an interaction with handedness was noticeable (Amunts et al., 1996, 2000; Foundas et al., 1998b). More recently, Davatzikos et al. obtained opposite results (Davatzikos and Bryan, 2002), with rightward asymmetry in both men and women, and stressed the importance of position and curvature differences of this sulcus across the two hemispheres. As explained by these authors, higher connectivity between the two banks on the left side may explain this result. On the WM asymmetry map of the group of right-handed subjects, we indeed observed a WM leftward asymmetry around the CS, which extended downwards (Fig. 4), and was strongly evocative of a leftward asymmetry of the precentral and post-central tracts (Kretschmann and Weinrich, 1998). Some previous DTI and post-mortem studies already reported leftward asymmetries for the precentral pyramidal tract (Rademacher et al., 2001a; Guye et al., 2003), but absence of asymmetry was found by other investigators in each modality (White et al., 1997; Ciccarelli et al., 2003). A higher M1 connectivity in the left hemisphere was also reported (Guye et al., 2003). Further analysis of the present data via probabilistic mapping of the CS supported the hypothesis that the rightward asymmetry of the CS as observed with VBM is in fact influenced by the surrounding relative gyral WM amounts (Herve et al., 2005). Gyral WM amounts tended to be less leftward asymmetric in left-handed as compared to right-handed subjects (Fig. 4), supporting the idea that WM amounts in this region are relevant to handedness. Besides, a recent study on WM asymmetry as assessed with fractional anisotropy reported opposite asymmetries between left- and right-handed subjects in the WM of the precentral gyrus, with leftward asymmetry in the right-handed (Buchel et al., 2004).

Right- and left-handed showed diverging GM asymmetries immediately behind the CS, slightly under the hand area (Rumeau et al., 1994; Yousry et al., 1997). Amunts had not evidenced any difference in CS depth between the two groups at this height. This region did also not correspond to the M1 tongue area (Fox et al., 2001). At this location, leftward anatomical asymmetry was significant in the right-handed (Fig. 3). Interestingly, Mangin et al., studying the cortical folding patterns of the 14 left-handed subjects of the Watkins study sample, observed sulcal asymmetry differences in the inferior precentral and central region, which may relate to an inflation of the left “motor” precentral gyrus in right-handers (Mangin et al., 2004). It is very possible that the difference between left- and right-handed subjects arises from sulcal course differences, which appear to take place at least in the more dorsal part of the CS (Herve et al., 2005).

Perisylvian asymmetries, language, and handedness

Leftward GM asymmetries were mostly found in regions of auditory cortex: The most salient was found in the region corresponding to the PT in terms of probabilistic anatomy (Westbury et al., 1999), paralleling the fact that the PT is larger and longer in the antero-posterior axis on the left (Geschwind and Levitsky, 1968; Shapleske et al., 1999). This asymmetry extended into Heschl's gyrus and in the posterior insula, whose callosal crossing fibers are intermixed with those of primary auditory cortex, and which is also involved in auditory processing (for a review, see Bamiou et al., 2003). A leftward anatomical asymmetry was also found in Heschl's gyrus in previous SPM VBM studies (Good et al., 2001a; Luders et al., 2004). Yet, this finding may have to be taken with caution as probabilistic mapping works on this structure either reported no asymmetry in grey matter but leftward white matter asymmetry (Penhune et al., 1996), or no overall asymmetry (Rademacher et al., 2001b), and further evidenced a strong asymmetry in the position of Heschl's gyrus, what may be problematic in the present context.

Further inferences can be made considering the GM differences between left- and right-handed subjects. In particular, a cluster was found in the PT (Fig. 6). The mean asymmetry indices for this cluster revealed a leftward asymmetry in right-handers versus no asymmetry in left-handers (Fig. 7), in agreement with ROI studies (Steinmetz et al., 1991; Shapleske et al., 1999). A recent work has shown that VBM GM asymmetry indices near the PT region were indeed very highly correlated with manual tracings of this structure (Luders et al., 2004). It is hence possible that, aside of handedness per se effects in the central region, some of the relative GM deficits of the left hemisphere as compared to the right, in the left-handed as compared to the right-handed, are associated with the less frequent left hemispheric specialization for speech in left-handed subjects (Satz, 1979; Hécaen et al., 1981). A general relationship between leftward GM and functional asymmetry could thus exist in auditory regions of the temporal and posterior insular cortex, possibly due to a specific tuning for the processing of speech sounds. It is known that hemisphere specific increases in PT surface can be associated with particular auditory abilities: for instance, studies on absolute pitch musicians have demonstrated an increased left PT surface in this group (Keenan et al., 2001).

Considering regions more involved in speech production, an absence of larger GM amount in Broca's area as compared to its right homotope is noteworthy (Watkins et al., 2001). There is no consensus in the ROI literature regarding the asymmetry of the inferior frontal gyrus. A significant left over right asymmetry was reported for both the pars triangularis and opercularis (Foundas et al., 1998a). The ascending and horizontal rami of the pars triangularis were also described as being more developed in the left hemisphere, what was interpreted as a consequence of a larger cortical surface (Ide et al., 1999). A post-mortem study had found a slight rightward asymmetry of the external surface of the frontal operculum (region encompassing the pars opercularis and a posterior part of the pars triangularis) while somehow observing more densely packed gyri in this area on the left (Wada et al., 1975). More recently, a probabilistic mapping study on a large sample reported no asymmetry of the pars opercularis (Tomaiuolo et al., 1999). At the cytoarchitectonic level, a systematic left over right asymmetry of Brodmann's area 44 was demonstrated in a group of five male subjects and interpreted as a correlate of the left hemispheric specialization for speech (Amunts et al., 1999). Area 44 spans over the free cortical surface of the pars opercularis, but its actual borders are difficult to define with sulcal landmarks, and thus, the relationship between micro and macroscopical anatomy in this region is very elusive (Amunts et al., 1999). Overall, it appears possible that, as repeatedly suggested by VBM studies, there is an absence of leftward macroscopic cortical asymmetry of the inferior frontal gyrus.

However, in the right-handed group (Fig. 3), the left "upper anterior corner" of the insula, involved in language production, was leftward asymmetric. This was previously noticed (Good et al., 2001a). Here, this asymmetry extended to the central sulcus of the insula that serves articulation during language tasks (Wise et al., 1999; Dronkers, 1996).

In the comparison of left- and right-handed subjects, two small regions bordering the inferior frontal gyrus (inferior frontal sulcus and precentral sulcus) displayed leftward asymmetry in the right-handed, and no asymmetry or rightward asymmetry in the left-handed group (Figs. 6 and 7). In parallel with the difference between left- and right-handed subjects observed in the PT, a posterior speech perception area, these clusters may relate to functional asymmetries of the anterior language region.

Along with Broca's area, the superior temporal sulcus is another key language region (Scott et al., 2000) that displays rightward GM asymmetry (Table 2, Fig. 3). This VBM result is very reproducible (Luders et al., 2004; Good et al., 2001a and particularly Watkins et al., 2001) and is observed in the depth of the sulcus. Actually, it reveals a rightward depth asymmetry of the STS: the right STS extends farther internally (Barrick et al., 2005) and is then opposed to the WM of the left hemisphere. A recent study comprehensively detailed the morphology of the STS and had reported a greater depth and more anterior position of this sulcus in the right hemisphere (Ochiai et al., 2004). Anatomy of the STS was also shown to be relevant to cerebral functioning and behavior (social interactions), as it is bilaterally altered in children with autistic disorder (Boddaert et al., 2004). The STS is a high order area, involved bilaterally in many tasks, and one should thus not necessarily expect a leftward anatomical asymmetry of the STS because of its relation to language. As regards semantic and syntactic networks, anatomical correlates may rather lie in WM asymmetries.

Indeed, DTI fractional anisotropy studies have notably revealed an asymmetry of the arcuate (or superior longitudinal) bundle (Buchel et al., 2004; Parker et al., 2005) that is likely related to hemispheric specialization for speech since this tract connects the anterior and posterior language poles. It is, at this point, noteworthy that the inferior and superior longitudinal (arcuate) bundle clusters highlighted in the voxel-based study by Buchel et al. fit with the ones observed here (Buchel et al., 2004). Leftward asymmetry was also reported for the uncinate bundle in control subjects (Kubicki et al., 2002 but Highley et al., 2002). A recent study reported that right-handed subjects had leftward asymmetric arcuate bundles (as assessed by combined fMRI and tractography), while this bundle tended to be rightward asymmetric in left-handed subjects (Martuzzi et al., 2004). Here, asymmetry was seen in regions statistically corresponding to parts of both the arcuate and uncinate fiber tracts (Fig. 4). The fact that no significant focal effects of handedness could be detected in these regions in the present study may indeed be due to the imprecise measurement of WM by VBM relatively to other methods.

At a higher scale, the volumetric analyses revealed a systematically larger WM volume in the left hemisphere in both groups, balanced by an opposite asymmetry of GM. Similar results were already reported in the lateral brain (Pujol et al., 2002) or parietal lobe (Golestani et al., 2002). As all these authors pointed, WM asymmetries are theoretically important for the understanding of hemispheric specialization, which can be viewed as a predominance of intra-hemispheric over inter-hemispheric connections in distributed functional networks, notably that of language. A larger WM volume in the left hemisphere could provide a structural basis for greater intra-hemispheric connectivity, favoring the clustering of some of these networks inside the left hemisphere. However, at the hemispheric level, no subject displayed the reverse WM asymmetry (Fig. 2). Thus, rather than a strict anatomical determinant of hemispheric specialization for speech, degree of WM asymmetry would constitute a possible predictor of hemispheric specialization for speech, among others (Josse and Tzourio-Mazoyer, 2004). During development, myelination seems to occur earlier in the left hemisphere (Paus et al., 1999), and observations were made in the temporal lobe of thicker myelin sheaths in the left hemisphere as compared to the right (Anderson et al., 1999). Besides, leftward WM asymmetry could arise from a greater myelination, allowing faster conduction times, on the left side (Zatorre and Belin, 2001; Anderson et al., 1999; Paus et al., 1999). This could also favor the processing of speech sounds in this hemisphere, along with the auditory cortical asymmetry. Furthermore, Golestani observed a dependence of the capacity to learn novel speech sounds on parietal WM, particularly on the left hemisphere (Golestani et al., 2002), associated with a backward shift of the parieto-occipital fissure. The occipital fissure was also more posterior in the left hemisphere, an anatomical finding that seems to be retrieved here. Overall, the results indicate that WM asymmetries in locations corresponding to language related fiber bundles are congruent with the left hemispheric specialization for language.

Rightward GM asymmetries and brain function

Rightward anatomical asymmetries and their possible relationships with brain function were less studied, relatively to leftward asymmetries and language. Here, GM asymmetries overall favored the right hemisphere, notably in the parietal, temporal and occipital lobes, and also in the orbital region. One needs to be careful as regards the interpretation of these asymmetries, as they may be counterparts of leftward WM asymmetries, yet, hemispheric specialization also concerns several other functions, such as emotional and visuospatial processing (Mesulam, 1999), lateralized in the right hemisphere. Visuospatial asymmetries may no lesser than language possess anatomical correlates. A lesion of the right parietal lobe is generally associated with unilateral neglect (Heilman et al., 1985). It has for instance been hypothesized that the rightward asymmetry of the posterior ascending ramus of the sylvian fissure, the planum parietale, would be a structural marker of the lateralization of visuospatial functions to the right hemisphere (Jancke et al., 1994). Here, the fact that the parietal lobe was, overall, rightward asymmetric in grey matter volume is also a possible correlate of this functional asymmetry. This may also be the case for the rightward grey matter asymmetries in the occipital region, mostly composed of visual cortex. More generally, the observed leftward WM/rightward GM hemispheric asymmetries observed in the temporo-parieto-occipital junction, and the co-occurring sulcal pattern differences (petalia, sylvian fissure asymmetries) might be congruent with the fundamental functional difference (language versus visuospatial) between the two hemispheres. More GM in the parietal lobe would benefit to visuospatial functions, while opposite WM volume asymmetries could be useful to other processes in the left hemisphere.

Conclusion

In young adult males, the left-handed exhibited variations in anatomical asymmetry, paralleling the variations of functional asymmetries in the motor or language networks that characterize this group. Considering the existing variability in the topography of atypical hemispheric specialization for speech in a comparable population (Tzourio-Mazoyer et al., 2004), the present results favor the hypothesis that the establishment of language functional networks and hand dominance, rather than strictly determined, would be merely biased towards the classic pattern (Annett, 1998) by relatively advantaging structural (GM and WM) asymmetries. Atypical and heterogeneous cortical functional representations, which appear to concern part of the normal left-handed population, would then emerge as ad hoc solutions when some of the early anatomical asymmetries that would induce the left hemispheric specialization for speech would be less marked or absent. Alternatively, it is possible that some structural asymmetry differences between left- and right-handed subjects also reflect structural adaptations to early deviances from the usual and structurally expected functional pattern.

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