Structure of the Human Sensorimotor System. II: Lateral Symmetry

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We have evaluated the lateral symmetry of the human central sulcus, brainstem and spinal cord using quantitative histological and imaging techniques in specimens from 67 autopsy cases. Our purpose was to determine whether the preferred use of the right hand in the majority of humans is associated with grossly discernible asymmetries of the neural centers devoted to the upper extremities. In the accompanying report, we described a consistent set of morphological features in the depths of the central sulcus that localize the sensorimotor representation of the distal upper extremity. Measurements of the cortical surface in this region, and indeed throughout the entire central sulcus, showed no average lateral asymmetry. Cytoarchitectonic measurements of area 4 and area 3 confirmed this similarity between the left and right hemispheres. The medullary pyramids, which contain the corticospinal tracts, were also symmetrical, as were the cross-sectional areas of white and gray matter in the cervical and lumbar enlargements of the spinal cord. Finally, we found no lateral difference in the size and number of motor neurons in the ventral horns at these levels of the cord. Based on these several observations, we conclude that the preferred use of the right hand in humans occurs without a gross lateral asymmetry of the primary sensorimotor system.

Introduction

Individual humans vary greatly in their talents for a wide variety of behaviors. However, the way this variation is instantiated in the nervous system is not known. Thus, arguments continue about the linkage – if any – between brain size and intelligence, and there is little consensus about how a skilled or habitual behavior is realized in underlying neural circuitry (see Geschwind and Galaburda, 1985; Peters, 1991b; Ungerleider, 1995). One supposition is that extraordinary performance is based on a commensurately greater allocation of circuitry in corresponding neural centers, such that preferred behaviors are represented by more neurons, more synapses, more supporting glial cells and, therefore, the occupancy of more territory in the brain (reviewed in Purves *et al.*, 1996). Such a relationship between brain circuitry and behavior is clear among different mammalian species, where especially proficient sensory and motor functions are reflected in (and presumably predicated upon) the relative extent of related cortical and subcortical circuitry. Thus, the cortical representations of the distal forelimbs are disproportionately large in raccoons compared to other carnivores (Welker and Seidenstein, 1959), whereas in rats and mice, a remarkable amount of cortical circuitry is devoted to the representation of the facial whiskers (Woolsey and Van der Loos, 1970). In another rodent, the star-nosed mole, much of the somatic sensory cortex is devoted to special appendages on the snout that assist these animals in foraging (Catania *et al.*, 1993; Catania and Kaas, 1995). Although the principle that specialized or preferred behavior is associated with a commensurately greater allocation of neural circuitry is well documented in these and many other examples across species, it is uncertain how – or if – this rule applies to variations in behavior among members of the same species, including humans.

An attractive context in which to explore the quantitative relationship of neural circuitry and performance in humans is handedness. Our reasons for choosing this particular lateralized behavior are several. First, because the relevant neural structures reside in the two sides of the same nervous system, each specimen serves as its own control for global variations (e.g. differences in brain size) that might confound comparisons among individuals. Second, hand preference is a robust behavior that has been present for at least thousands of years (Coren and Porac, 1977). Moreover, its distribution in the general population is well known; approximately 9 out of 10 of us are right-handed when tested by questionnaires (Oldfield, 1971; Gilbert and Wysocki, 1992) or by actual performance (Provins and Cunliffe, 1972; Bishop, 1989; Peters, 1991a). Third, much is already known about the control and representation of manual behavior in the primate sensorimotor system (e.g. Kaas, 1990; Zeffiro, 1990; Lemon, 1993; Lawrence, 1994; Sanes *et al.*, 1995). Finally, the right hand of right-handers is larger than the left hand, a difference that presumably reflects activity-dependent hypertrophy and implies differential use of the two hands (Purves *et al.*, 1994).

In the accompanying report (White *et al.*, 1997), we characterized the morphology of the human central sulcus and the cytoarchitecture of the primary sensorimotor cortex harbored in its banks, including the region that contains the sensorimotor representation of the distal upper extremity. We also described and validated morphometric methods for measurement of the central sulcus and the primary sensorimotor cortex. Here, we have used these measurements – as well as a variety of other quantitative morphometric, cytoarchitectonic and imaging techniques – to assess lateral differences in the size of several neural structures related to the upper extremity: area 4 (primary motor cortex), area 3 (primary somatic sensory cortex), the corticospinal tract in the medullary pyramids, and the cervical enlargement of the spinal cord. Based on cross-species comparisons, our hypothesis was that the preferred use of the right hand in the majority of humans is associated with a greater amount of neural circuitry allocated to the representation and control of the right upper extremity relative to the left. Thus, we expected to find, on average, more sensorimotor cortex in the left hemisphere, a larger left medullary pyramid, and more white and gray matter and larger motor neurons in the right side of the cervical enlargement of the spinal cord compared to the corresponding neural centers related to the left hand. Contrary to our expectation (and our preliminary findings – White *et al.*, 1994), the results we report here indicate that, on average, the two sides of the human primary sensorimotor system are symmetrical.

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Materials and Methods

Specimens

Brains and spinal cords were obtained at autopsy from the Duke University Medical Center in conformity with University guidelines and regulations. The specimens were taken from a total of 67 individuals of either sex who had died of non-neurological causes (Table 1). Forty-two brains were used for analysis of the central sulcus (including 22 brains from a preliminary study – White *et al.*, 1994), 20 brains for measurement of the medullary pyramids, and 27 spinals cords for assessment of the cervical and lumbar enlargements. The spinal cords were dissected through the foramen magnum with the aid of a special instrument designed for this purpose (Shandon-Lipshaw, Pittsburgh PA; catalog no. 610). All brains and spinal cords were removed within 24 h of death and placed in 10% formalin for at least a week prior to further processing. Each specimen was initially identified only by its autopsy case number; thus detailed information pertaining to gender, age and medical history was unknown to us until the analysis was complete. Subsequent review of the autopsy records confirmed that both upper and lower extremities were intact in every subject.

An inherent limitation in this study is the lack of information about handedness. Determination of hand preference post-mortem was not possible because this information is not usually included in patient records, and contacting next of kin was often not permissible. We assume, however, that all but a few of the brains and spinal cords were from right-handed individuals, simply because ~90% of humans are right-handed (see above). Given our sample sizes, we considered this an acceptable limitation since our goal was to compare the left and right sides of the sensorimotor system in relation to the hand preference of the majority of humans, rather than to compare the nervous systems of left-handed and right-handed individuals.

Analysis of Sensorimotor Cortex

Twenty brains (cases 1–20, see Table 1) were dissected and Nissl-stained sections prepared and traced by camera lucida, as described in the accompanying paper (see Fig. 1, White *et al.*, 1997).

Surface Measurements of the Central Sulcus

In order to assess the size of the central sulcus, two investigators independently measured the extent of cortical surface in the anterior and posterior walls of the sulcus and the overall length of the fundus (see White *et al.*, 1997). The extent of cortical surface in the central sulcus was defined and measured in each section tracing (see Fig. 1, White *et al.*, 1997). The length measurements of the cortical surface were used to estimate the total surface area of the banks of the central sulcus by assuming that the linear contours from adjacent sections define the two parallel sides of a trapezoid. Thus, the surface area was estimated by summing the trapezoidal areas between adjacent sections according to the formula:

$$A = d/2 \sum_{i=1}^{n-1} (L_i + L_{i+1}) \tag{1}$$

where A is the estimated cortical area, d is the section interval (1 mm), and L_i and L_{i+1} are the measured lengths of cortical surface in the central sulcus in adjacent sections. In addition to the 20 brains obtained for our present study, data from a preliminary investigation of 22 specimens (cases 22–43, see Table 1), which did not include an assessment of cortical surface area (White *et al.*, 1994), were reanalyzed using formula (1). Thus, a total of 42 brains were evaluated for asymmetry of the cortical surface in the central sulcus. All other cortical measurements described below were obtained using the set of 20 brains obtained for the accompanying study (White *et al.*, 1997) (i.e. cases 1–20).

The total length of the central sulcus was determined by first reconstructing the pre- and post-central gyri, and then measuring the length of the fundus in three-dimensional space (see Fig. 1, White *et al.*, 1997). Thus, the coordinates of the fundus of the central sulcus were

Table 1
Summary data of autopsy cases from which specimens were obtained

Case	Sex	Age (years)	Brain weight (g)	Central sulcus	Medullary pyramid	Cervical enlargement	Lumbar enlargement
1	M	71	1313	+	–	–	–
2	M	39	1200	+	–	–	–
3	M	76	1300	+	–	–	–
4	M	32	1440	+	–	–	–
5	F	60	1340	+	+	–	–
6	F	86	1160	+	+	–	L3–S1
7	F	75	1063	+	+	–	–
8	F	79	1530	+	+	–	–
9	M	61	1488	+	+	–	L2–S2
10	M	68	1430	+	+	–	–
11	M	76	1370	+	–	–	–
12	M	66	1310	+	–	–	–
13	M	75	1340	+	–	–	–
14	M	13	1470	+	+	–	–
15	M	73	1250	+	–	–	–
16	M	74	1149	+	+	–	–
17	F	28	1380	+	–	–	–
18	M	66	1303	+	–	T1	L2–S2
19	F	67	1240	+	–	–	–
20	M	51	1400	+	–	T1	L2–S2
21	M	73	1337	–	+	–	L3–S1
22	M	68	1450	+	–	–	–
23	M	58	1340	+	–	–	–
24	F	45	1180	+	–	–	–
25	F	71	1210	+	–	–	–
26	F	71	1420	+	–	–	–
27	M	72	1230	+	–	–	–
28	M	68	1410	+	–	–	–
29	M	71	1310	+	–	–	–
30	M	47	1500	+	–	–	–
31	F	55	1250	+	–	–	–
32	M	77	1430	+	–	–	–
33	F	17	1250	+	–	–	–
34	M	56	1650	+	–	–	–
35	F	76	1060	+	+	–	–
36	M	36	1375	+	+	–	–
37	M	70	1300	+	+	–	–
38	F	49	1280	+	+	–	–
39	M	45	1280	+	+	–	–
40	M	62	1500	+	+	–	–
41	M	50	1510	+	+	–	–
42	M	62	1330	+	+	–	–
43	M	73	1155	+	+	–	–
44				–	+	–	–
45				–	+	–	–
46	F	29	1220	–	–	C8–T1	L1–S1
47	F	55	1484	–	–	–	L1–S1
48	F	48	1150	–	–	C8–T1	L2–S2
49	M	61	1317	–	–	T1	–
50	M	59		–	–	T1	L1–S1
51	M	66	1473	–	–	C5–T1	L1–S1
52	F	49		–	–	C4–Tl	–
53	M	51	1376	–	–	T1	–
54	F	67	1410	–	–	C5–T1	L1–S2
55	F	64	1360	–	–	C4–T1	L2–S1
56	M	59	1205	–	–	C4–C5	L2–S1
57	F	46	1140	–	–	C4–C7	L2–S2
58	F	49	1313	–	–	C4–T1	L3–S2
59	F	47		–	–	–	L2–S3
60	F	50		–	–	–	L2–S4
61	F	85	1128	–	–	C4–T1	–
62	M	65	1323	–	–	C4–T1	L2–S1
63	M	62	1473	–	–	C4–T1	L2–S1
64	F	74	1042	–	–	–	L2–S1
65	F	76	1192	–	–	C4–T1	–
66	M	49	1435	–	–	C4–T1	–
67	F	58	1265	–	–	C4–T1	–
Mean ± SD							
All subjects ($n = 67$)		59.6 ± 15.5	1320 ± 130				
Males ($n = 38$)		60.6 ± 14.1	1364 ± 109				
Females ($n = 27$)		58.4 ± 17.5	1253 ± 132				

Gender, age and brain weight (unfixed) of subjects were obtained from the autopsy reports; the reports were not available for cases 44 and 45. Brain weight was not recorded for cases 50, 52, 59 and 60. A '+' indicates that the central sulci or the medullary pyramids were excised and examined. Linear measurements of the extent of cortical surface in the walls of the central sulcus from cases 22–43 were reported previously (White *et al.*, 1994), but are reanalyzed in this study using methods to estimate the extent of cortical surface area in the central sulcus. The mean brain weight for males was significantly greater than the corresponding value for females ($P < 0.01$; two-sample *t*-test).

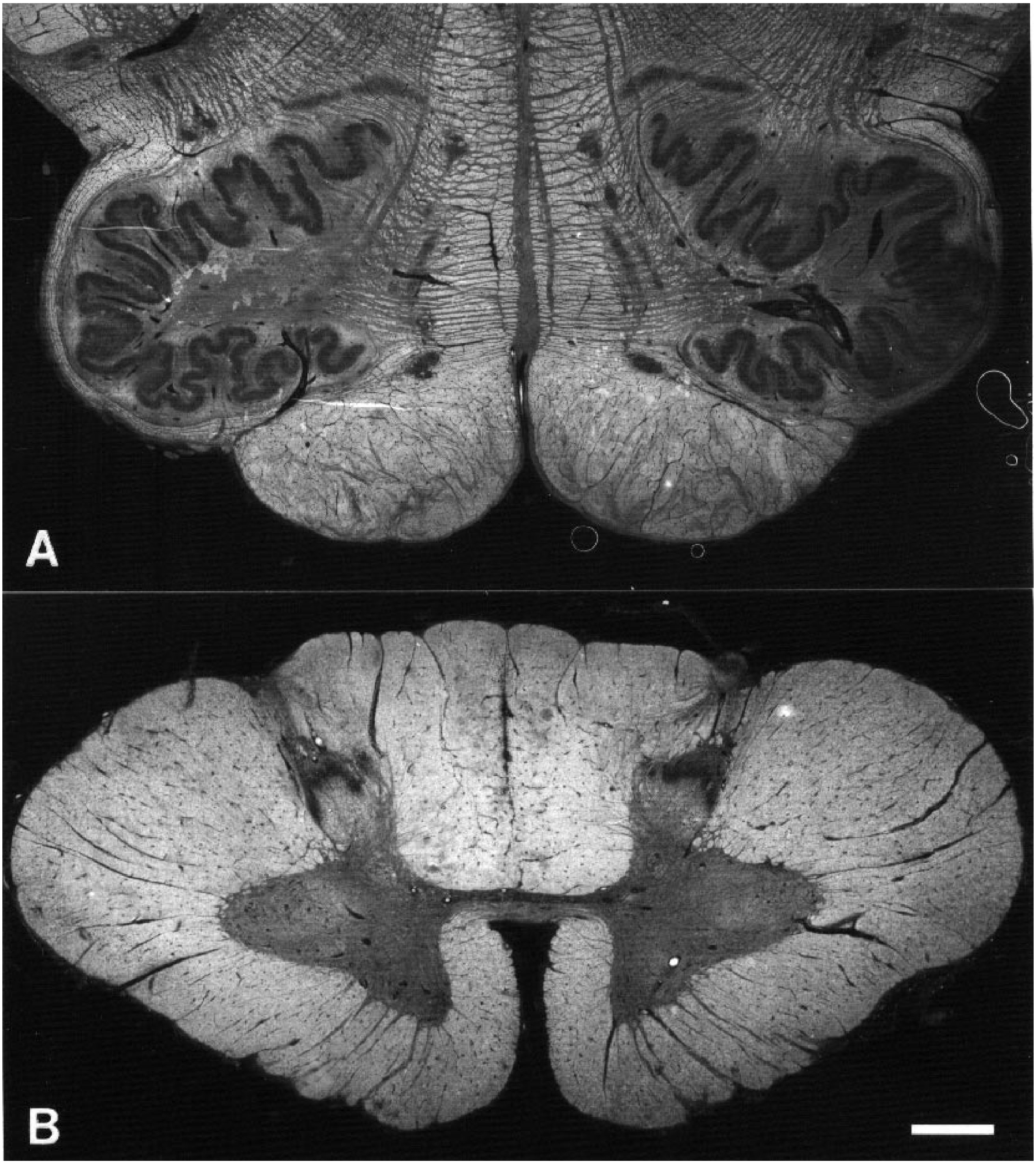

Figure 1. Subcortical sensorimotor structures measured. (*A*) Photomicrograph of the pyramidal tract printed directly from an unstained, wet-mounted cross-section at the mid-olivary level of the medulla. The pyramids were defined dorsally by the transverse fibers of the olives in the medial lemniscus. The ventromedial fissure and the ventrolateral surface of the medulla form the medial and lateral borders of the pyramid. (*B*) Cervical enlargement of the spinal cord. Photomicrograph printed directly from an unstained, wet-mounted cross-section of the cord at the C8 level. The gray and white matter of the spinal cord are easily discriminated and measured in such preparations. Scale bar = 1 mm.

determined in serial section, and the total length of the fundus (L_f) was then calculated according to the formula:

$$L_f = \sum_{i=1}^{n-1} \sqrt{\left(x_i - x_{i+1}\right)^2 + \left(y_i - y_{i+1}\right)^2 + \left(z_i - z_{i+1}\right)^2} \qquad (2)$$

where x_i, y_i and z_i are Cartesian coordinates for the *i*th section.

Cytoarchitectonic Measurements

We next used the stained sections to define and measure the extent of the primary motor cortex, area 4, and a major portion of the primary somatic sensory cortex, area 3. The cytoarchitectonic criteria that were used for the definition of the boundaries between adjacent fields and a quantitative assessment of their reliability are described in detail in the accompanying report (White *et al.*, 1997). In each camera lucida tracing of the central sulcus, the linear extent and area of these cytoarchitectonic fields were measured independently by two investigators using a digitizing tablet and Bioquant IV morphometric software (see Fig. 1, White *et al.*, 1997). The linear extents of areas 4 and 3 were determined by measuring the length of the layer V contour line contained in each cortical field; the area was assessed by tracing the perimeter of the field bounded by the pial surface, white matter, and the anterior and posterior cytoarchitectonic borders. The total areal extent of each cytoarchitectonic division was estimated by substituting linear measurements of the length of layer V in each cortical subdivision from adjacent sections into formula (1). The total volume of each cortical division was determined using Cavalieri's estimator of morphometric volume (Uylings *et al.*, 1986; Rosen and Harry, 1990):

$$V_C = d\sum_{i=1}^{n} a_i - t\,a_{\max} \qquad (3)$$

where V_C is Cavalieri's estimated cortical volume, d is the section interval (1 mm), a_i is the area of the cytoarchitectonic field in the ith section, t is the section thickness (200 or 50 μm), and $a_{\max}$ is the maximum value of a_i in the set of measurements from a given hemisphere.

Data Analysis

For each cortical structure measured, we used the average of two independent assessments (see White *et al.*, 1997) to determine the degree of asymmetry between hemispheres. Asymmetry was expressed in terms of percentage difference, where:

$$\text{Percentage difference} = \{\text{left} - \text{right}/[(\text{left} + \text{right})/2]\} \times 100 \qquad (4)$$

The distribution of percentage difference values obtained for each structure was then subjected to the Shapiro–Wilk test for normality, using SAS statistical software (SAS Institute Inc., Cary, NC). Because several subsets of data were not normally distributed, non-parametric statistical procedures were employed in our analysis of the cortical (and subcortical – see below) data. Thus, the median (50th percentile) and interquartile range (range of values between the 25th and 75th percentiles) of each subset of measurements was determined; in addition to these parameters, the non-parametric 95% confidence interval of the median (Conover, 1980) was calculated for each median percentage difference value. To examine the significance of all hemispheric differences, Wilcoxon signed rank tests were applied to the percentage difference values obtained for each cortical parameter measured. Finally, multivariate linear regression analysis was performed to determine if gender and age were significant factors in our analysis of asymmetry. For reasons of clarity and efficiency, tables are used to present median values, interquartile ranges and 95% confidence intervals of the median differences for each structure examined, whereas data from individual specimens are displayed in series of scattergrams. To facilitate any further analysis, the actual measurements of each specimen are provided in an Appendix.

Analysis of the Medullary Pyramids

The medulla was dissected away from the rest of the brain in 20 specimens (see Table 1) by making transverse cuts at the rostral and caudal extent of the inferior olives. This block of medullary tissue (~2 cm in length) was placed in graded concentrations of buffered sucrose (up to 30%) for 1 week. The tissue was then frozen quickly on dry ice and sectioned transversely in a cryostat (–20°C) at 40 μm. Sections were saved at 0.8 mm intervals and mounted unstained in an aqueous medium. To minimize bias, the order of the slides from individual specimens was randomized; as a further precaution, we obscured right and left by inverting half the sections.

The unstained, hydrated sections were used to assess the area occupied by corticospinal fibers in each medullary pyramid. Images of each section were printed on photographic paper at a magnification of 15× (Fig. 1*A*). The areas of the right and left pyramids were measured using a digitizing tablet and Bioquant IV morphometric software. For each specimen, the area measurements from each side of every section through the inferior olives were summed, and mean values for left and right sides determined. Lateral differences in the areas of the pyramids were expressed as percentage differences and compared as described for the cortical measurements.

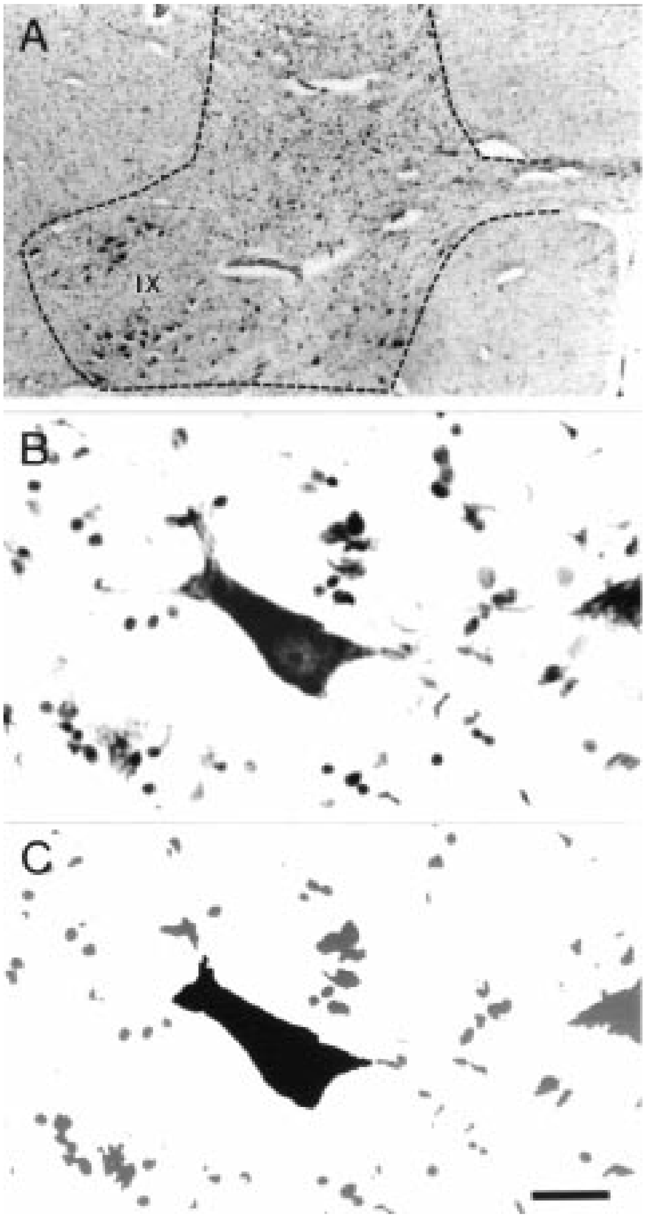

Figure 2. Automated measurement of motor neuron cell body size following video-enhanced image processing and analysis. (*A*) Photomicrograph of a Nissl-stained cross-section from the ventral horn (dotted outline) of the cervical enlargement (C7). (*B*) Higher magnification photomicrograph of a representative motor neuron in (*A*). (*C*) Digitized image after background subtraction and digital thresholding. Only motor neurons with a distinct nucleolus were selected for measurement. IX = Rexed's lamina IX. Scale bar = 0.5 mm in (*A*) and 25 μm in (*B*) and (*C*).

Analysis of the Spinal Cord

Following removal of the dura, portions of the spinal cord containing the cervical and/or lumbar enlargements from 27 specimens (see Table 1)

Table 2
Measurements of cortical surface area in the central sulcus

	Presumptive hand region sample			Entire central sulcus		
	Left (mm^2)	Right (mm^2)	Percentage difference	Left (mm^2)	Right (mm^2)	Percentage difference
Data from set of 20 human brains						
Median	1571.6	1565.1	2.4	3329.0	3201.85	0.75
Interquartile range	284.4	141.9	10.6	636.4	379.0	11.8
95% confidence interval of the median (*m*)			$-1.7 \le m \le 5.3$			$-2.4 \le m \le 5.7$
P			>0.4			>0.4
Data from preliminary study of 22 human brains (White et al., 1994)						
Median	1533.9	1514.1	–1.7	2804.1	2805.8	–1.4
Interquartile range	420.7	282.4	13.5	457.9	682.7	16.9
95% confidence interval of the median (*m*)			$-8.5 \le m \le 3.1$			$-7.4 \le m \le 2.4$
P			>0.3			>0.2
Combined data from 42 human brains						
Median	1549.8	1556.0	–0.3	2968.4	3107.8	–0.7
Interquartile range	267.5	215.8	12.5	734.3	581.9	14.5
95% confidence interval of the median (*m*)			$-3.3 \le m \le 2.9$			$-3.8 \le m \le 2.6$
P			>0.9			>0.6

All *P*-values indicate the level of statistical significance as assessed by Wilcoxon signed rank tests.

were cut transversely into longitudinal blocks ~2 cm in length and placed in graded concentrations of buffered sucrose (up to 30%) for 1 week. The tissue was then frozen quickly on dry ice and sectioned transversely in a cryostat. Two consecutive 40 μm sections were saved at 0.8 mm intervals for further processing. One series was mounted unstained in an aqueous medium; the other series was mounted on subbed slides, allowed to dry and stained with cresyl violet acetate. To minimize bias, the order of the slides from individual specimens was randomized; as a further precaution, we obscured right and left by inverting half the sections. The rostral and caudal extents of the cervical and lumbar enlargements were determined by the presence of motor neurons in the lateral columns of the ventral horn (see below).

The unstained, hydrated sections were used to assess the amount of white and gray matter in each hemicord (Fig. 1*B*), as described for the analysis of the medullary pyramids. For each specimen, the hemicord areas of white and gray matter from every section through the cervical and lumbar enlargements were summed separately and mean values determined. Lateral differences in the areas of white and gray matter were expressed in terms of percentage difference and assessed as described for the cortical measurements.

To determine the number and size of motor neurons in each hemicord, the ventral horn was examined in the Nissl-stained sections throughout the cervical and lumbar enlargements using a compound microscope (80×). Motor neurons were recognized by their large size (diameter >20 μm), multipolar shape, abundance of Nissl bodies and location in lamina IX of the ventral horn (Truex and Taylor, 1968; Tomlinson *et al.*, 1973; Schoenen and Faull, 1990). Both alpha and gamma motor neurons were included in the analysis by these criteria (Kawamura *et al.*, 1977; Abdel-Maguid and Bowsher, 1979). To ensure that the same motor neuron was not counted twice, only motor neuron profiles containing nucleoli were counted and measured.

The images of the Nissl-stained sections were transferred to an image analyzer (Image 1, Universal Imaging, Media, PA) by means of a CCD camera (VE-CCDX, Dage MTI, Michigan, IN) and subjected to background subtraction and digital thresholding. All motor neuron profiles containing a nucleolus were selected from the digitized image and measured automatically (Fig. 2). For every section through the cervical or lumbar enlargement, the average cross-sectional area and number of motor neurons were determined. Average values were then calculated for both hemicords, expressed in terms of percentage differences, and assessed as described above for the cortical measurements.

Results

Gender and Age

For each cortical and subcortical structure measured, multivariate linear regression modeling showed that gender and age were not significant factors in our assessment of lateral symmetry. Thus, the direction and degree of asymmetry evident in our measurements of the human primary sensorimotor system were not systematically different between the genders or among specimens taken from subjects of different ages. The relatively small sizes of our samples, however, especially with respect to the question of age, limits the conclusions that can be drawn from these data regarding gender and age effects.

Symmetry of the Presumptive Hand Region

In the accompanying paper (White *et al.*, 1997), we described a structurally distinct region in the depth of the central sulcus, which – based on recent functional imaging data – appears to mark the location of the representation of the distal upper extremity in the human sensorimotor cortex. Accordingly, our quantitative analysis of sensorimotor cortical asymmetry in relation to handedness has focused on this morphological feature, which we refer to as the 'presumptive hand region'. In order to sample this region in each hemisphere, we defined a 3 cm segment of the central sulcus (spanning 30 consecutive sampled sections) centered on the gyral bridge that characterizes the center of this structure (see Fig. 5, White *et al.*, 1997). Samples of this size were chosen because recent investigations of the human motor cortex with functional magnetic resonance imaging indicate that the extent of the posterior precentral gyrus over which magnetic resonance changes are observed during voluntary movements of the digits and wrist is about three centimeters (Sanes *et al.*, 1995).

Measurements of the Cortical Surface in the Central Sulcus

Measurements of the extent of cortical surface area in this 3 cm sample of the presumptive hand region showed only a very slight

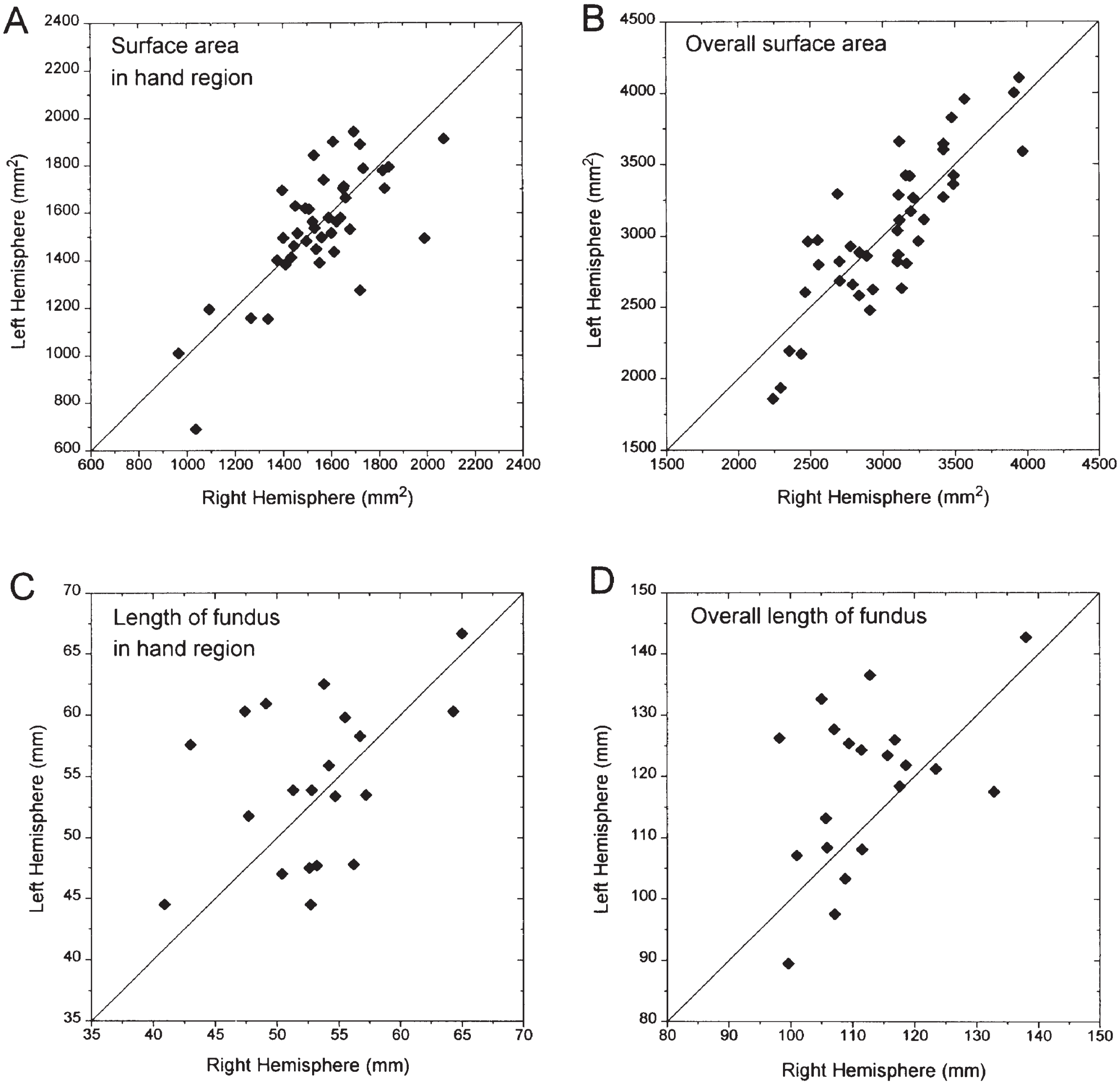

Figure 3. Symmetry of the human central sulcus. (*A*) Measurements of the extent of cortical surface in the walls of the central sulcus in the 3 cm sample of the presumptive hand region. In this and the other panels, each symbol represents the measurements obtained from the left and right hemispheres of the same specimen; the diagonal line has a slope of 1 and thus represents symmetry. Note the scattering of symbols to either side of the diagonal line. (*B*) Measurements of the extent of cortical surface in the walls of the entire central sulcus. As in the presumptive hand region (*A*), individual specimens are clustered along the diagonal line indicating no overall average asymmetry of the cortical surface in the central sulcus. Panels (*A*) and (*B*) contain data from 42 specimens (see Methods). (*C*) Measurements of the length of the fundus of the central sulcus in the presumptive hand region from 20 brains. No median lateral asymmetry was evident. (*D*) Measurements of the overall length of the fundus of the central sulcus in 20 brains. In 14 of 20 specimens, the overall length of the left central sulcus was greater than the right, which yielded a median percentage difference that approached — but failed to achieve — statistical significance (see Table 3).

leftward median asymmetry that failed to reach statistical significance (Table 2; see also Table A1). To extend this observation, we reanalyzed data from the set of 22 brains of our preliminary study that were sectioned in a modified axial plane (White *et al.*, 1994). The results from these brains showed a very small median rightward asymmetry that again failed to reach statistical significance (see Table 2). It should be noted that our preliminary analysis of a portion of this same data set suggested an asymmetry in favor of the left hemisphere (White *et al.*, 1994). This asymmetry was mainly evident in modified axial sections taken from the superior 1–2 cm of the hemisphere. Given our present understanding of the location of the sensorimotor representation of the distal upper extremity, it is now apparent that the asymmetrical portion of the central sulcus in our preliminary study was largely superior to the presumptive hand region. Moreover, because we did not, at that time, appreciate the morphology of the presumptive hand region, our means of aligning and comparing data from the two hemispheres was not based upon comparing homologous structural features of the central sulcus. Therefore, it is possible that the asymmetry we did find in the upper portion of the central sulcus was an artifact of the method used to register measurements obtained from the two central sulci. The present analysis of these two sets of brains shows that there is no measurable median asymmetry of the cortical surface in the region of the hand representation in the central sulcus (Fig. 3*A*; see Table 2). Furthermore, the 95%

Table 3
Length of the fundus of the central sulcus in 20 human brains

	Presumptive hand region sample			Entire central sulcus		
	Left (mm)	Right (mm)	Percentage difference	Left (mm)	Right (mm)	Percentage difference
Median	53.9	53.0	2.6	121.5	110.4	4.6
Interquartile range	12.3	6.1	15.4	17.9	11.4	14.8
95% confidence interval of the median (m)			$-4.0 \le m \le 8.5$			$-0.2 \le m \le 10.5$
P			>0.4			>0.05

All P-values indicate the level of statistical significance of percentage difference values, as assessed by Wilcoxon signed rank tests. The overall length of the central sulcus was significantly correlated with the extent of cortical surface in the central sulcus (Spearman correlation coefficient = 0.67; $P < 0.01$), the total combined area of areas 4 and 3 (Spearman correlation coefficient = 0.57; $P < 0.01$), and the total combined volume of areas 4 and 3 (Spearman correlation coefficient = 0.40; $P < 0.05$).

confidence intervals of the median differences (see Table 2) suggest that any average asymmetry in the human population – if one exists – is very small, of the order of a few percent.

In addition to assessing the median asymmetry in our sample, we also evaluated the direction and degree of asymmetry evident in individual brains. Twenty-one of the 42 brains examined yielded positive percentage difference values (toward leftward asymmetry), whereas 21 had negative percentage difference values (toward rightward asymmetry). This distribution of positive and negative values is obviously different from the distribution of right- and left-handedness in the human population (see above). The percentage difference values for individual specimens from the two sets of brains studied ranged from –39.8 (case 27) to 19.3 (case 25) (see Table A1). The majority of specimens, however, were distributed near the median value. Thus, although obvious asymmetry was found in the presumptive hand region of some specimens, the majority of specimens displayed little or no lateral difference between the hemispheres (see Fig. 3*A*).

Measurements of the Fundus of the Central Sulcus

The length of the fundus of the central sulcus in each hemisphere was measured in the 20 brains sectioned orthogonal to the central sulcus (see Fig. 1). The results again showed no median asymmetry in the presumptive hand region, despite a trend toward leftward asymmetry in the length of the entire central sulcus (Table 3; see Fig. 3*C*; Table A2; Falk *et al.*, 1991). Presumably, this overall trend mainly involved segments of the central sulcus medial and/or lateral to the region of the hand representation.

Measurements of Area 4 and Area 3

We next assessed the extent of the primary motor cortex, area 4, and a major portion of the primary somatic sensory cortex, area 3, in the same set of 20 brains (i.e. cases 1–20). Our measurements of cortical area and volume for each cytoarchitectonic field yielded much the same result as our analysis of the cortical surface: both parameters produced very slight positive median percentage difference values (toward leftward asymmetry) that failed to achieve statistical significance (Tables 4 and 5; Figs 4*A*,*B* and 5*A*,*B*). The 95% confidence intervals of the median percentage differences for the volume of area 4 and area 3 (see Tables 4 and 5) again suggest that any asymmetry of areas 4 and 3 in the population from which this sample was drawn is very small. The ranges of percentage difference values for the area and volume of areas 4 and 3 in individual specimens were comparable to the range determined for measurements of the cortical surface area in the central sulcus, and, with the exception of the volume of area 4, about as many specimens displayed a bias in favor of the left hemisphere as the right (see Tables A3 and A4). Thus, we found no significant median asymmetry in the primary sensorimotor cortex, including the primary motor cortex, which is, arguably, the neural center most relevant to the behavior in question. However, of all our measurements of the presumptive hand region, the volume of area 4 did yield the largest median asymmetry (see Table 4), with 14 specimens having positive percentage difference values (toward leftward asymmetry) and six specimens having negative values (toward rightward asymmetry). Of these latter six, three specimens (cases 8, 11 and 16) displayed moderate rightward asymmetries (percentage differences were –10.3, –11.6 and –16.9 respectively; see Table A3), any one of which had sufficient influence to keep the median percentage difference from reaching statistical significance.

Symmetry of the Entire Sensorimotor Cortex

In addition to our assessment of symmetry of the sensorimotor cortex in the region of the hand representation, we also measured the overall extent of the cortical surface in the central sulcus, as well as area 4 and area 3 in the paracentral lobule and along the entire central sulcus. The results were consistent with the more restricted analysis of the presumptive hand region. Thus, measurements of the cortical surface in the entire central sulcus and the overall extents of areas 4 and 3 showed no statistically significant median asymmetries between the two hemispheres (see Tables 2–5 and Figs 3*B*,*D*, 4*C*,*D* and 5*C*,*D*). As with our analysis of the presumptive hand region, obvious asymmetry was detected in some specimens, but the majority of percentage difference values were distributed near the median for each cortical structure measured. Moreover, about equal numbers of brains had positive percentage difference values as negative values.

Symmetry of Subcortical Sensorimotor Centers

Our measurements at the cortical level suggest that – at least in the region of the hand representation – the primary sensorimotor cortex is allocated symmetrically to the left and right hemispheres in most human brains. In order to extend and confirm this conclusion, we investigated the structure of the medullary pyramids and the cervical and lumbar enlargements of the spinal cord.

Medullary Pyramids

The structure of the medullary pyramids was examined in 20 human brainstems (see Table 1). The pyramids of the medulla are formed primarily by bundles of corticospinal tract fibers that originate in ipsilateral cerebral cortex. The axons of the

Table 4

Cytoarchitectonic measurements of area 4 in 20 human brains

	Presumptive hand region sample			Entire central sulcus		
	Left	Right	Percentage difference	Left	Right	Percentage difference
Measurements of cortical area (mm^2)						
Median	521.6	521.2	3.0	1276.6	1249.7	1.0
Interquartile range	55.4	63.6	12.7	145.3	215.6	13.9
95% confidence interval of the median (*m*)			$-2.0 \leq m \leq 7.0$			$-2.3 \leq m \leq 6.9$
P			>0.2			>0.3
Measurements of cortical volume (mm^3)						
Median	1995.8	1985.6	3.2	4958.4	4752.1	1.0
Interquartile range	252.2	238.9	8.5	677.5	556.5	10.9
95% confidence interval of the median (*m*)			$-1.4 \leq m \leq 6.9$			$-1.4 \leq m \leq 6.3$
P			>0.1			>0.2

All *P*-values indicate the level of statistical significance of percentage difference values, as assessed by Wilcoxon signed rank tests. The percentage difference values for measurements of area and volume in the sample of the presumptive hand region are significantly correlated (Spearman correlation coefficient $= 0.84$; $P < 0.01$), as are the percentage difference values for overall measurements of area and volume (Spearman correlation coefficient $= 0.86$; $P < 0.01$).

Table 5

Cytoarchitectonic measurements of area 3 in 20 human brains

	Presumptive hand region sample			Entire central sulcus		
	Left	Right	Percentage difference	Left	Right	Percentage difference
Measurements of cortical area (mm^2)						
Median	781.0	810.1	–1.0	1697.5	1668.1	2.8
Interquartile range	167.6	127.0	11.9	242.7	189.6	8.3
95% confidence interval of the median (*m*)			$-3.1 \leq m \leq 5.2$			$-2.8 \leq m \leq 4.7$
P			>0.6			>0.4
Measurements of cortical volume (mm^3)						
*M*edian	1846.2	1898.8	1.5	3738.0	3582.4	0.7
Interquartile range	356.5	270.0	10.8	831.2	641.4	14.1
95% confidence interval of the median (*m*)			$-5.1 \leq m \leq 4.0$			$-3.3 \leq m \leq 5.8$
P			>0.8			>0.5

All *P*-values indicate the level of statistical significance of percentage difference values, as assessed by Wilcoxon signed rank tests. Length and area measurements of cytoarchitectonic fields area 3a and area 3b were determined separately and then summed for each section measured; hemispheric totals were determined for area 3 based on these combined measurements. The percentage difference values for measurements of area and volume in the sample of the presumptive hand region are significantly correlated (Spearman correlation coefficient $= 0.73$; $P < 0.01$), as are the percentage difference values for overall measurements of area and volume (Spearman correlation coefficient $= 0.78$; $P < 0.01$).

corticospinal system, which arise from the motor and premotor areas in the frontal lobe and from a portion of the parietal lobe (Holmes and May, 1909; Brown and Fang, 1961; Jane *et al.*, 1967), form a compact fasciculus in the ventral medulla. Although the pattern of decussation is quite variable from subject to subject, human pyramidal tract fibers typically cross into the contralateral hemicord at the spinomedullary junction, with only a small number remaining uncrossed (Yakovlev and Rakic, 1966). In this component of the study, we measured the cross-sectional area of the pyramids in the segment of the medulla that contains the inferior olives (i.e. rostral to the pyramidal decussation). In accordance with our measurements of the sensorimotor cortex, we detected no median lateral bias in the size of the medullary pyramids in the two sides of the brainstem (Table 6; Figure 6; Table A5).

Spinal Cord

Finally, we examined the structure of the spinal cord for evidence of lateral asymmetry in 20 specimens (see Table 1). The spinal cord is enlarged in the two regions along its rostral–caudal axis that supply innervation to the limbs. The cervical enlargement extends from spinal segments C4 to T1, giving rise to the spinal nerves that form the brachial plexus. The lumbar enlargement gives rise to the spinal nerves that supply the lower limbs, and extends from spinal segments L1 to S3 (Tomlinson *et al.*, 1973). Spinal segments vary in length along the spinal cord, averaging 13 mm in the cervical region, 26 mm in the midthoracic region and diminishing from 15 to 4 mm in the lumbosacral region (Gray, 1973). Although the majority of our specimens extended from upper cervical segments to the filum terminale, the entire cervical or lumbar enlargement could not be examined in every case because of damage incurred at autopsy.

No significant asymmetry was found in independent measurements of the white and gray matter areas of each hemicord (Table 7; Fig. 7*A*,*B*; Table A6). We also measured the number and size of spinal motor neurons to assess the possibility of lateral bias in these cells. No consistent asymmetry was evident in either parameter (Table 8; Fig. 7*C*,*D*; Table A7). We also investigated the lumbar enlargement, which provides innervation to the lower limbs. Although footedness is a weaker lateralized behavior than handedness, approximately 8 out of 10 humans prefer to use the right foot for a variety of tasks (Coren, 1992). The overall size of the cord and its constituent motor

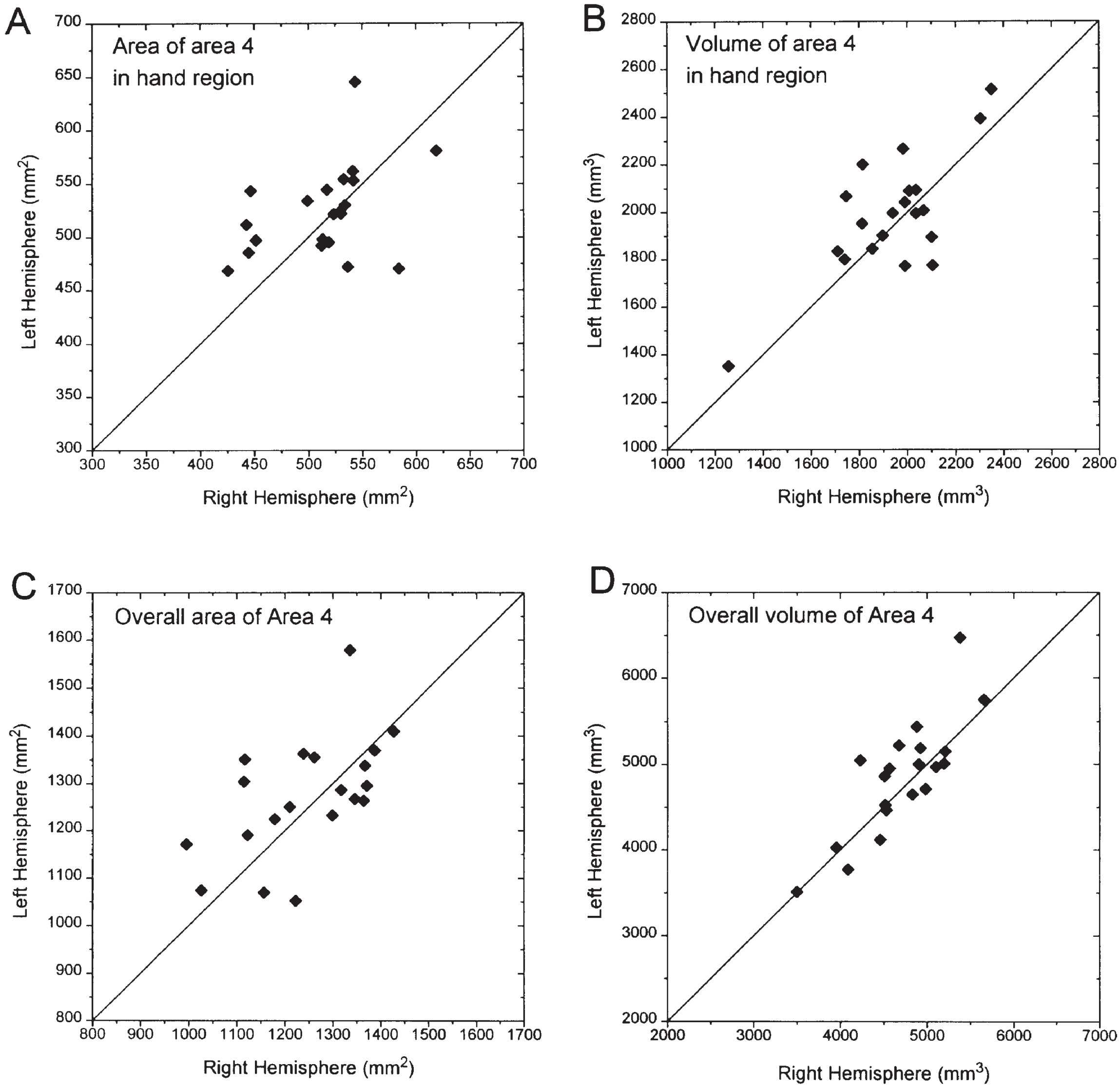

Figure 4. Symmetry of area 4 (primary motor cortex) in 20 human brains. (*A*) Measurements of the area of cytoarchitectonic field area 4 in the 3 cm sample of the presumptive hand region. (*B*) Measurements of the volume of area 4 in the 3 cm sample of the presumptive hand region. (*C*) Measurements of the overall area of area 4 in the paracentral lobule and the precentral gyrus along the entire length of the central sulcus. (*D*) Measurements of the overall volume of area 4 in the paracentral lobule and the precentral gyrus along the entire length of the central sulcus. For each of these sets of measurements, the symbols are distributed above and below the diagonal line representing symmetry, with no significant bias toward either side. Conventions are the same as in Figure 3.

neurons at the level of the lumbar enlargement was, like its cervical counterpart, symmetrical in all respects (see Tables 7 and 8; Fig. 8; Tables A8 and A9).

Although we found no evidence of lateral bias in the spinal cord, there were significant differences between the lumbar and cervical enlargements. Compared to the cervical enlargement, there was about a 2-fold increase in the number of motor neurons in each section of the lumbar enlargement (Wilcoxon signed rank test; $P < 0.01$). This increase in motor neuron number was reflected in the cross-sectional area of gray matter, which was 45% larger in the lumbar spinal cord ($P < 0.01$) than in the cervical spinal cord. Indeed, in both the cervical and the lumbar enlargements of the cords examined, there was a significant correlation (Spearman correlation coefficient = 0.58; $P < 0.01$) between motor neuron number in any given specimen and the cross-sectional area of gray matter, indicating that our gross measurements of the spinal cord provide a reasonable reflection of the number of motor neurons. Motor neurons in the lumbar enlargement were also larger than those in the cervical enlargement (46%; $P < 0.01$). These differences in neuronal size probably reflect the average size of motor units in muscles of the upper and lower extremities. For example, the average number of muscle fibers innervated by motor neurons supplying the human brachioradialis is ~400; for the gastrocnemius muscle the number is ~2000 (Feinstein *et al.*, 1955; Stuart and Enoka, 1983).

Interindividual Variation in Size

Although the distribution of areas 4 and 3 along the length of the central sulcus is highly consistent among individuals (see White *et al.*, 1997), we found much interindividual variation in the overall extent of areas 4 and 3. For both cytoarchitectonic fields, there was a nearly 2-fold range in cortical area and volume (see

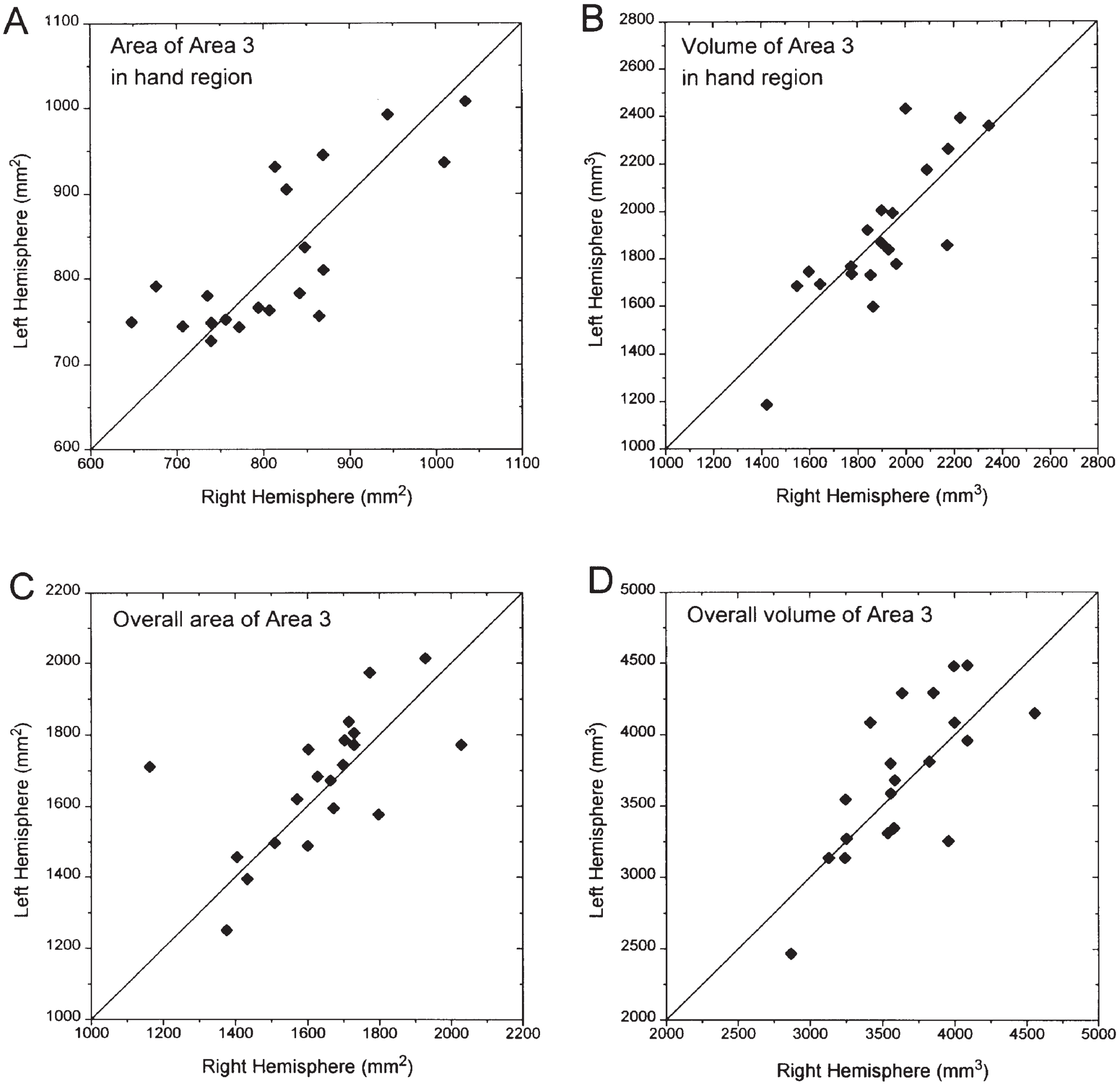

Figure 5. Symmetry of area 3 (primary somatic sensory cortex) in 20 human brains. (*A*) Measurements of the area of cytoarchitectonic field area 3 in the 3 cm sample of the presumptive hand region. (*B*) Measurements of the volume of area 3 in the 3 cm sample of the presumptive hand region. (*C*) Measurements of the overall area of area 3 in the paracentral lobule and the post-central gyrus along the entire length of the central sulcus. (*D*) Measurements of the overall volume of area 3 in the paracentral lobule and the post-central gyrus along the entire length of the central sulcus. As was the case for area 4 (primary motor cortex) (see Fig. 4), the symbols in each panel are distributed symmetrically about the diagonal line representing symmetry. Conventions are the same as in Figure 3.

Tables A3 and A4), which is greater than the range in overall brain size for these same 20 specimens (see Table 1). This amount of variation in the extent of cytoarchitectonic fields among individuals is comparable to the differences in the size of the human primary visual cortex (i.e. area 17) (Stensaas *et al.*, 1974; Murphy, 1985; Leuba and Kraftsik, 1994) and the rodent somatic sensory cortex (Riddle and Purves, 1995).

Similar to the variation in primary sensorimotor cortex, the size of the medullary pyramids varied ~2-fold among individuals (see Table A5). Given this amount of cortical and pyramidal variation, we investigated the relationship between the total amount of area 4 and area 3 and the cross-sectional area of the ipsilateral pyramid in the eight brains (16 hemispheres) from which both the central sulcus and the medulla were excised (see Table 1). Our results showed a weak (non-significant) correlation between the cross-sectional area of the pyramids and the total amount of areas 4 and 3 in the entire central sulcus (correlation with cortical area: Spearman correlation coefficient

Table 6
Cross-sectional area of the medullary pyramids in 20 human brains

	Area of pyramid (mm^2)		Percentage difference
	Left	Right	
Median	13.8	13.9	–1.6
Interquartile range	2.6	2.5	7.8
95% confidence interval of the median (*m*)			$-4.3 \leq m \leq 1.9$
P			>0.1

The *P*-value indicates the level of statistical significance of percentage difference values, as assessed by Wilcoxon signed rank tests.

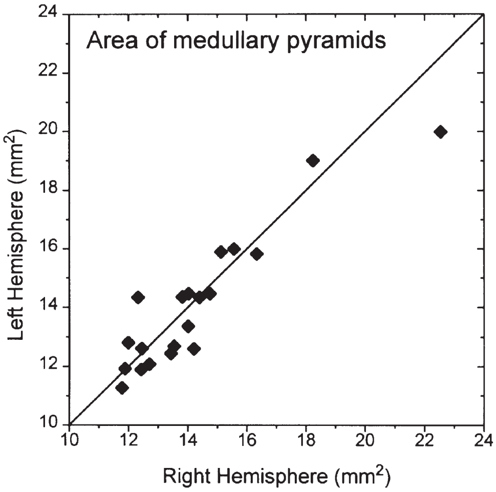

Figure 6. Symmetry of the medullary pyramids in 20 human brains. The symbols representing measurements of the cross-sectional areas of left and right pyramids from individual specimens are distributed symmetrically about the diagonal line. Conventions are the same as in Figure 3.

= 0.42; correlation with cortical volume: Spearman correlation coefficient = 0.48). A much stronger relationship, however, was found between pyramidal area and the extent of areas 4 and 3 in the 3 cm sample of the presumptive hand region (correlation with cortical area: Spearman correlation coefficient = 0.63; $P < 0.05$; correlation with cortical volume: Spearman correlation coefficient = 0.69, $P < 0.01$). Significant interindividual variability was also observed in the cervical and lumbar enlargements of the spinal cord, where a 2-fold range in the area of white and gray matter was detected (see Tables A6 and A8).

Discussion

Asymmetry in the human sensorimotor system was first reported by Flechsig (1876), who concluded that the uncrossed ventral pathway of the pyramidal tract was more often larger on the right side of the spinal cord than the left in those cases (40%) in which he found a lateral difference. Yakovlev and Rakic (1966) extended Flechsig's observations, reporting that the human corticospinal tract is often asymmetric at birth, the left medullary pyramid being on average larger and decussating higher than the right in most neonates. The same pattern of higher left-sided decussation was found in >70% of adult specimens (Kertesz and Geschwind, 1971). More recently, a rightward bias in the size of the corticospinal tract in the cervical spinal cord was reported in 55% of specimens, with 26%

Table 7
Cross-sectional area of white and gray matter in the cervical and lumbar enlargements of the human spinal cord

	Area of white matter (mm^2)			Area of gray matter (mm^2)		
	Left	Right	Percentage difference	Left	Right	Percentage difference
Cervical enlargement						
Median	25.8	25.3	–1.1	5.5	5.6	–1.0
Interquartile range	3.9	4.1	10.4	1.3	1.4	4.6
95% confidence interval of the median (m)			$-5.0 \leq m \leq 2.2$			$-1.5 \leq m \leq 2.5$
P			>0.6			>0.4
Lumbar enlargement						
Median	17.0	16.9	0.6	9.1	9.1	0.3
Interquartile range	2.5	2.0	5.1	2.1	2.4	3.6
95% confidence interval of the median (m)			$1.0 \leq m \leq 2.6$			$-1.2 \leq m \leq 1.6$
P			>0.4			0.5

All P-values indicate the level of statistical significance of percentage difference values, as assessed by Wilcoxon signed rank tests.

Table 8
Cross-sectional area and number of motor neurons in the cervical and lumbar enlargements of the human spinal cord

	Cell area (mm^2)			Number/section		
	Left	Right	Percentage difference	Left	Right	Percentage difference
Cervical enlargement						
Median	1111.5	1159.0	–2.1	3.1	3.5	–0.8
Interquartile range	251.5	270.5	8.3	2.4	3.5	27.6
95% confidence interval of the median (m)			$-4.2 \leq m \leq 1.4$			$-7.3 \leq m \leq 12.0$
P			>0.3			>0.4
Lumbar enlargement						
Median	1882.0	1919.0	0.4	8.7	9.4	0.5
Interquartile range	167.0	216.0	10.2	6.2	6.7	20.0
95% confidence interval of the median (m)			$-3.5 \leq m \leq 2.3$			$-3.7 \leq m \leq 7.4$
P			>0.6			>0.4

All P-values indicate the level of statistical significance of percentage difference values, as assessed by Wilcoxon signed rank tests.

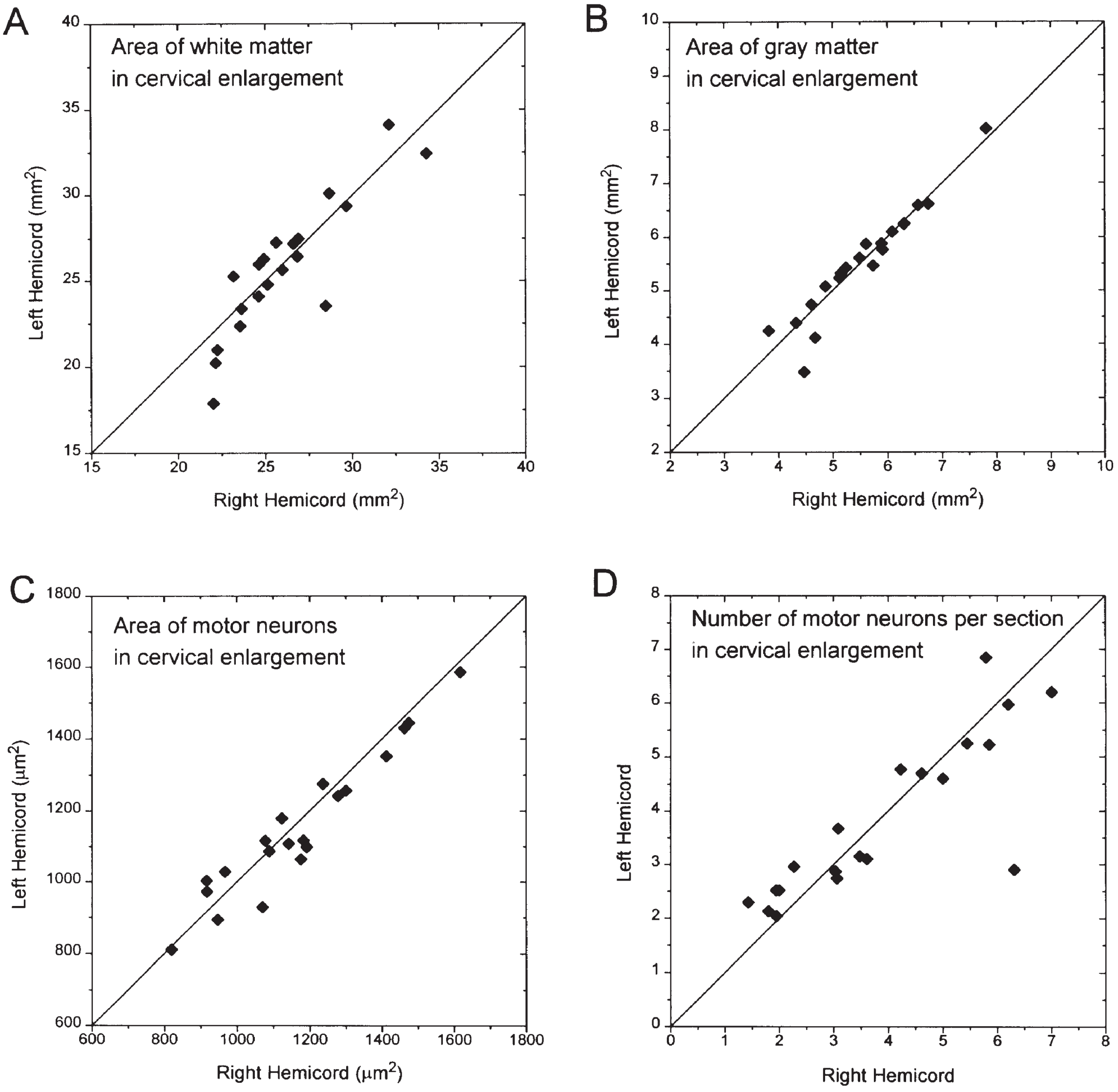

Figure 7. Symmetry of the cervical enlargement of the human spinal cord. (*A*) Cross-sectional area of white matter in the cervical enlargements of 20 human spinal cords. (*B*) Cross-sectional area of gray matter in the cervical enlargements of 20 human spinal cords. (*C*) Somal area of motor neurons in the ventral horn of the cervical enlargements of 20 human spinal cords. (*D*) Number of motor neurons in the ventral horn of each 40 μm section taken from the cervical enlargements of 20 human spinal cords. The distribution of symbols representing the overall area of white and gray matter in the 20 cervical enlargements and their constituent motor neurons was symmetrical.

showing no asymmetry and 19% showing larger corticospinal tracts on the left side of the cord (Nathan *et al.*, 1990; see also Yakovlev and Rakic, 1966). In a preliminary study, we reported a leftward asymmetry in the extent of cortical surface in the upper portion of the central sulcus (White *et al.*, 1994; see also Foundas *et al.*, 1995).

Although these earlier studies suggested a population asymmetry in the human sensorimotor system, it is apparent from our present analysis of three levels of the neuraxis that any average lateral difference, if one exists at all, must be very slight. We could detect no average lateral bias in primary motor (area 4) or somatic sensory (area 3) cortex in the region of the upper limb representation, or throughout the entire central sulcus (see also Rademacher *et al.*, 1993). Likewise, we found no consistent lateral bias in the medullary pyramids or the cervical enlargement of the spinal cord. Thus, the preferred use of the right hand in the majority of the human population occurs with little or no reflection of this functional asymmetry in the gross structure of these sensorimotor centers. In principle, this conclusion might still allow quantitative lateral differences in the underlying neural elements of the primary sensorimotor system, including neurons, dendritic branches and synapses. Although this possibility should not be dismissed, the correlation that we noted between gray matter area and the number of motor neurons in the cervical spinal cord, as well as evidence from other studies (e.g. Barasa, 1960; Rockell *et al.*, 1980; Szentágothai, 1993; Leuba and Kraftsik, 1994), indicate that significant differences in the numbers of any of these cellular parameters would have been reflected in the macroscopic structure of the regions we measured. Thus, our failure to find any gross lateral asymmetry – together with the symmetry of those neuronal parameters that we did measure in the spinal

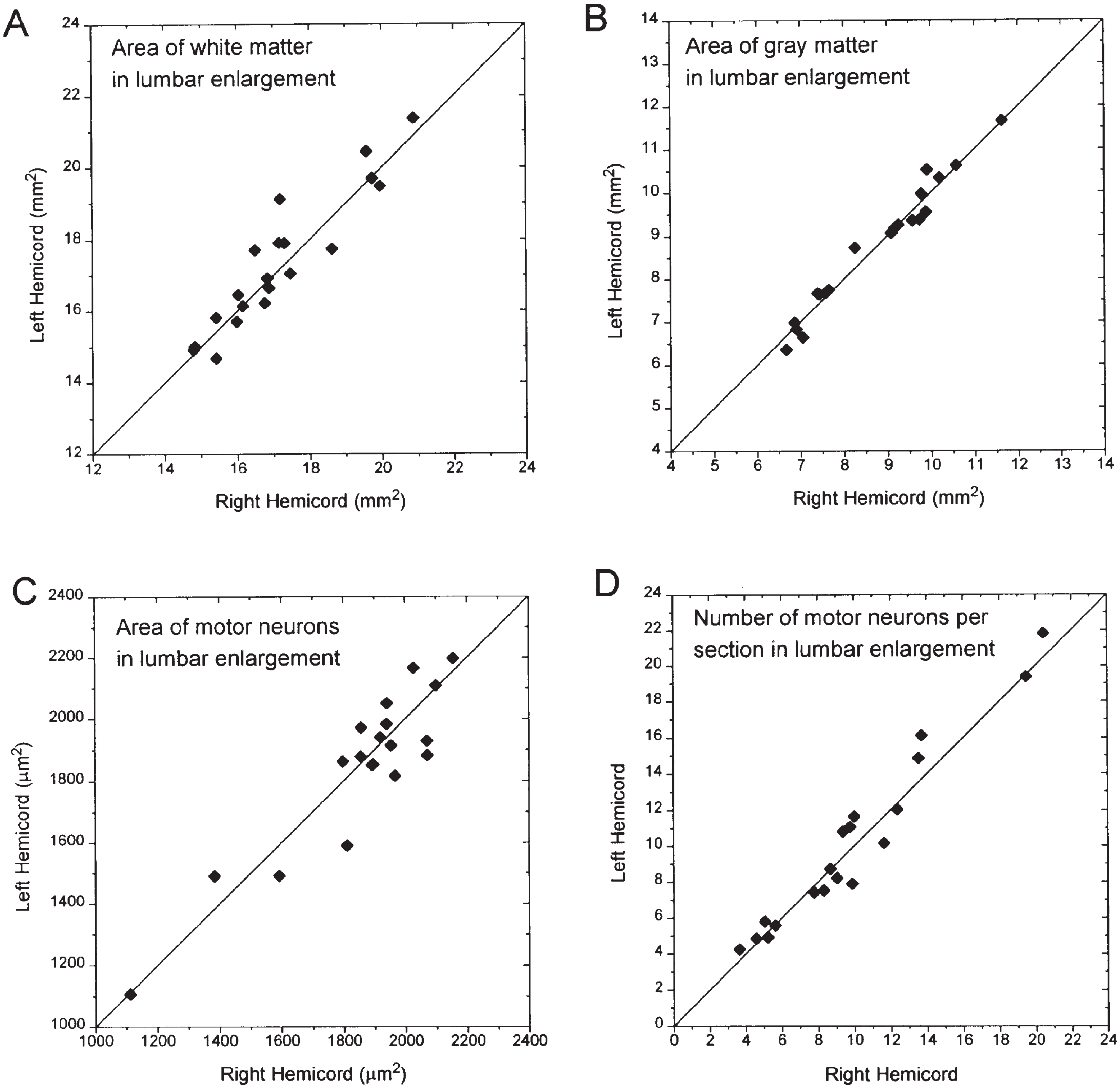

Figure 8. Symmetry of the lumbar enlargement of the human spinal cord. (*A*) Cross-sectional area of white matter in the lumbar enlargements of 20 human spinal cords. (*B*) Cross-sectional area of gray matter in the lumbar enlargements of 20 human spinal cords. (*C*) Somal area of motor neurons in the ventral horn of the lumbar enlargements of 20 human spinal cords. (*D*) Number of motor neurons in the ventral horn of each 40 μm section taken from the lumbar enlargements of 20 human spinal cords. The distribution of bilateral measurements of the overall size of the cord and its constituent motor neurons at the level of the lumbar enlargement was, like its cervical counterpart, symmetrical in all respects.

cord – implies that any lateral difference in the distribution and size of cellular elements in the human primary sensorimotor system is likely to be, on average, quite small.

These results admit at least three explanations of the neurobiological basis of handedness. One interpretation is that, despite our finding of sensorimotor symmetry, handedness is in fact explained by gross asymmetries of the primary sensorimotor centers in favor of the regions that represent and control the preferred hand and arm. This conclusion would require that right- and left-handers display opposite asymmetries and that our sample contained a sufficient number of specimens from left-handers to obscure an asymmetry present in the majority subsample of specimens from right-handers. We consider this an improbable explanation of our results since there is evidence that undermines the assumption that right- and left-handers are simple opposites (see Peters, 1995; Purves *et al.*, 1994). Moreover, our samples appear to have been sufficiently large to represent any average asymmetry present in the right-handed majority without seriously over-representing left-handers. Nonetheless, in the absence of behavioral information about handedness, this explanation cannot be excluded.

A second interpretation is that no asymmetry is evident in the primary sensorimotor system simply because the differences between the right and left hemispheres related to handedness are localized elsewhere. Peters (1991a, 1995), for example, has argued that the neural asymmetries responsible for handedness may be found not in the 'executing motor machinery' (primary sensorimotor structures), but in the neural systems responsible for planning and coordinating the cooperative movements of the digits and hands. According to this conception of handedness, the superior skills of the right hand in the majority of humans derive from hemispheric differences in neuronal circuitry in the supplementary motor and premotor cortices, prefrontal associational cortex, cerebellum and/or basal ganglia. Although involvement of each of these regions is entirely plausible, it seems unlikely that a sensorimotor behavior as robust as handedness would not be well represented throughout the primary sensorimotor system. Indeed, recent human studies using functional mapping techniques have demonstrated changes in the primary sensorimotor cortex with the acquisition of skilled manual behavior (Karni *et al.*, 1994; Elbert *et al.*, 1995; Ungerleider, 1995). Furthermore, given what is known about trophic dependencies between neurons and their targets (Purves, 1988), a disproportion anywhere in the sensorimotor system should be reflected throughout.

A third interpretation of our results, and the one we favor, is that the capabilities of the left primary sensorimotor cortex that underlie right-handedness are balanced by other less obvious (but equally important) capabilities of the right primary sensorimotor cortex. In this view, the basis of lateralized behaviors such as handedness may lie, not in any gross structural asymmetry, but in the differential specialization of homologous regions in the two cerebral hemispheres.

Conclusion

We undertook this work with the overall goal of understanding the quantitative relationship between neural circuitry and behavior in humans. Our hypothesis at the outset was that proficient or preferred behaviors – for which human handedness serves as a model – are instantiated in a commensurate elaboration of the corresponding neural circuitry. This simple idea is supported by a wealth of comparative neurological studies that demonstrate the relationship between specialized sensorimotor behavior and its central representation among diverse species (see Introduction for specific examples). Despite this abundance of circumstantial evidence (see also Peters, 1991b), our detailed examination of the structure of the sensorimotor system at three levels of the neuraxis has shown no evidence of an average lateral asymmetry that might provide an anatomical basis for handedness in the human population. Nonetheless, the principle that specialized behavior is reflected in more extensive central circuitry remains a compelling explanation of extraordinary performance. Laterally specialized behavior, however, may not provide an appropriate context for this rule, simply because both sides of the brain are driven to make the most of the available cortical space. Thus, our results emphasize that one must be especially cautious about the assumption that lateral asymmetries of cortical function, whether related to language (Broca, 1861; Geschwind and Levitsky, 1968; Sperry, 1982), vision (Jackson, 1958, Kimura and Durnford, 1974; Sperry, 1982), or any other behavior will be manifested in a gross asymmetry of the amount of related neural circuitry in the two hemispheres.

Notes

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Appendix

Table A1

Cortical surface area in the central sulcus of 42 human brains

Case	Presumptive hand region sample		Entire central sulcus	
	Left (mm^2)	Right (mm^2)	Left (mm^2)	Right (mm^2)
1	1615.2	1508.2	3425.3	3159.8
2	1495.9	1400.9	2886.0	2838.7
3	1713.3	1652.9	3362.3	3487.4
4	1402.4	1374.4	2869.8	3106.3
5	1739.8	1569.4	3602.5	3421.3
6	1462.8	1445.3	2966.1	3243.9
7	1436.6	1612.2	3272.6	3418.5
8	1515.6	1600.8	3110.2	3116.1
9	1942.7	1695.1	3958.1	3567.1
10	1889.4	1722.0	4106.2	3946.0
11	1580.0	1638.6	3642.8	3419.9
12	1514.4	1459.7	2861.8	2888.8
13	1662.6	1661.1	3286.5	3109.2
14	1498.6	1560.8	3424.8	3489.9
15	1563.2	1522.0	2660.7	2792.5
16	1391.4	1551.2	2823.5	3101.0
17	1793.7	1840.9	3589.5	3969.1
18	1448.9	1537.3	3295.6	2687.7
19	1843.1	1528.4	3659.9	3116.4
20	1787.7	1734.2	3827.8	3477.9
22	1536.3	1531.0	2808.8	3165.1
23	1413.7	1433.6	2581.6	2834.9
24	1383.5	1410.9	2824.0	2699.6
25	1694.6	1396.2	2605.1	2462.8
26	1704.1	1823.3	3039.5	3100.4
27	692.0	1036.0	2192.7	2353.2
28	1901.1	1608.2	2799.4	2556.3
29	1010.3	964.9	1934.6	2290.8
30	1579.9	1589.4	2171.4	2435.5
31	1157.3	1265.4	1858.0	2239.4
32	1629.2	1450.6	3115.5	3284.6
33	1702.4	1650.2	3420.7	3186.7
34	1778.9	1815.8	3268.8	3211.3
35	1482.5	1497.1	2686.4	2702.7
36	1194.1	1092.5	2970.7	2550.6
37	1273.9	1719.9	3172.2	3194.2
38	1618.3	1493.0	2929.5	2776.7
39	1154.0	1336.8	2623.3	2930.7
40	1912.6	2070.6	4003.3	3908.3
41	1563.4	1622.1	2963.8	2482.4
42	1531.5	1678.6	2475.8	2910.1
43	1494.1	1989.1	2633.4	3129.7

Cases 1–20 were sectioned in a plane that was orthogonal to the course of the central sulcus and the dorsolateral convexity of the hemisphere (see Fig. 1 of White *et al.*, 1997). Cases 22–43, which were cut in a modified axial plane, are from a preliminary study (White *et al.*, 1994). For this data set, linear measurements of the extent of cortical surface in each histological section were taken from our previous analysis and inserted into formula (1) to estimate the cortical surface area in the banks of the central sulcus (see Methods). The absolute values of cortical surface area are often less in this set of 22 brains than in the present of set 20 brains shown above (cases 1–20). This is because in our early studies, a greater amount of tissue was lost at the top and bottom edges of every block, as compared to our present method of cutting. Nonetheless, since the two hemispheres were treated equally, this excessive loss of tissue should not effect our assessment of asymmetry.

Table A2
Length of the fundus of the central sulcus measured in 20 human brains

Case	Presumptive hand region sample		Entire central sulcus	
	Left (mm)	Right (mm)	Left (mm)	Right (mm)
1	62.5	53.8	118.4	117.6
2	58.3	56.7	103.3	108.8
3	60.3	47.4	126.0	116.8
4	44.5	40.9	113.2	105.7
5	55.9	54.2	117.5	132.8
6	47.7	53.2	121.8	118.6
7	59.8	55.5	125.4	109.4
8	47.5	52.6	108.1	111.5
9	53.9	51.3	136.5	112.8
10	66.7	65.0	142.8	138.0
11	51.8	47.7	124.3	111.4
12	47.0	50.4	89.5	99.6
13	53.5	57.2	107.1	101.0
14	44.5	52.7	123.4	115.6
15	53.9	52.8	97.6	107.1
16	57.6	43.0	126.3	98.2
17	60.3	64.3	121.2	123.4
18	47.8	56.2	108.4	105.9
19	60.9	49.1	132.6	105.0
20	53.4	54.7	127.7	107.0

Table A3
Cytoarchitectonic measurements of area 4 in 20 human brains

Case	Presumptive hand region sample				Overall			
	Area (mm^2)		Volume (mm^3)		Area (mm^2)		Volume (mm^3)	
	Left	Right	Left	Right	Left	Right	Left	Right
1	468.3	425.2	1351.8	1255.4	1170.8	995.2	3511.4	3497.9
2	561.9	541.2	1995.2	2035.7	1354.8	1260.9	4948.6	4566.8
3	544.6	517.2	1951.5	1811.6	1294.9	1370.1	4646.0	4830.5
4	485.4	444.5	1834.9	1709.9	1267.1	1345.7	4968.3	5100.2
5	511.4	442.5	2066.9	1746.2	1362.7	1238.5	5438.8	4880.0
6	497.1	451.4	1800.2	1738.8	1073.5	1026.0	4026.4	3953.4
7	530.2	533.7	1996.4	1938.9	1262.8	1364.0	4708.5	4980.9
8	471.9	536.3	1893.7	2100.2	1249.7	1209.9	5190.0	4921.3
9	645.2	543.2	2514.1	2349.6	1578.7	1335.2	6472.0	5379.7
10	554.4	532.5	2006.9	2067.3	1337.2	1366.8	5005.0	5191.7
11	495.0	518.9	1772.0	1989.9	1369.5	1386.7	5151.4	5208.6
12	491.9	512.1	1845.0	1854.2	1286.0	1317.2	4998.8	4904.9
13	534.1	498.9	2093.9	2035.7	1190.1	1122.0	4858.2	4508.0
14	497.9	513.0	1900.4	1897.3	1232.2	1298.9	4461.9	4529.8
15	553.1	541.7	2266.5	1982.0	1069.2	1156.5	4115.4	4460.1
16	470.1	583.6	1775.0	2103.6	1051.9	1222.6	3770.3	4090.3
17	521.2	523.4	2090.3	2007.0	1224.5	1178.6	4524.5	4516.0
18	521.9	530.0	2041.1	1989.1	1303.6	1114.3	5046.9	4231.0
19	543.3	446.6	2200.0	1813.7	1350.4	1116.1	5223.3	4673.7
20	580.9	618.6	2392.4	2303.8	1409.9	1426.9	5749.5	5657.3

Table A4
Cytoarchitectonic measurements of area 3 in 20 human brains

Case	Presumptive hand region sample				Overall			
	Area (mm^2)		Volume (mm^3)		Area (mm^2)		Volume (mm^3)	
	Left	Right	Left	Right	Left	Right	Left	Right
1	992.2	944.2	1776.0	1960.0	1972.9	1773.5	3342.8	3579.5
2	779.6	735.2	1185.5	1421.5	1495.9	1508.6	2466.1	2866.4
3	765.9	793.9	2003.3	1898.8	1593.9	1672.1	3811.2	3825.9
4	744.3	706.4	1683.2	1547.3	1619.2	1570.7	3542.9	3244.3
5	905.0	826.5	2173.4	2087.2	1784.7	1702.7	4085.2	3998.7
6	762.5	806.7	1594.8	1863.4	1576.0	1797.7	3250.6	3955.8
7	756.1	864.2	1729.1	1854.2	1716.2	1698.5	3678.0	3585.2
8	782.4	841.8	1854.9	2171.6	1672.3	1664.0	3959.0	4087.6
9	945.0	869.0	2390.0	2226.4	1837.0	1714.5	4482.7	4087.2
10	1007.7	1034.2	2260.4	2176.6	2013.9	1928.3	4477.9	3995.0
11	743.1	771.9	1734.6	1775.0	1488.0	1600.6	3306.7	3537.2
12	727.4	739.5	1766.0	1771.9	1393.6	1432.8	3267.8	3251.6
13	836.6	847.7	1837.4	1928.8	1683.4	1627.6	3586.3	3558.9
14	752.0	756.4	1745.0	1596.9	1772.2	1729.2	3798.0	3556.5
15	748.2	739.8	1919.8	1840.8	1250.5	1375.4	3133.3	3240.5
16	791.0	675.9	1691.4	1644.4	1455.7	1404.3	3132.5	3128.4
17	936.3	1009.7	2357.1	2345.8	1772.5	2028.0	4151.4	4556.0
18	749.3	647.5	1864.6	1898.8	1711.6	1162.2	4085.4	3416.4
19	931.5	813.5	2429.5	1999.6	1759.3	1602.3	4287.7	3636.4
20	809.9	869.4	1992.2	1945.7	1805.0	1729.2	4291.3	3852.6

Table A5

Cross-sectional area of the medullary pyramids at the level of the inferior olives

Case	Area of pyramid (mm^2)	
	Left	Right
5	12.61	12.45
6	11.92	11.88
7	11.89	12.42
8	12.44	13.43
9	15.82	16.33
10	14.46	14.03
14	12.07	12.70
16	13.36	14.01
21	14.46	14.75
35	12.80	11.99
36	12.60	14.21
37	14.33	12.32
38	14.33	14.39
39	14.35	13.82
40	19.01	18.24
41	15.99	15.56
42	19.98	22.54
43	11.27	11.78
44	15.89	15.12
45	12.68	13.54

Table A6

Cross-sectional area of white and gray matter in the cervical enlargement of the spinal cord

Case	Area of white matter (mm^2)		Area of gray matter (mm^2)	
	Left	Right	Left	Right
18	25.66	25.97	5.46	5.74
20	24.77	25.12	4.11	4.67
46	24.08	24.62	5.42	5.24
48	26.43	26.84	6.25	6.31
49	23.52	28.46	4.73	4.60
50	20.23	22.13	3.48	4.47
51	27.48	26.90	5.76	5.91
52	27.27	25.62	6.10	6.09
53	25.27	23.16	4.24	3.82
54	26.30	24.91	5.87	5.61
55	27.19	26.61	6.24	6.30
56	30.10	28.67	5.23	5.12
57	32.43	34.29	6.61	6.75
58	25.97	24.63	5.61	5.49
61	20.98	22.23	4.39	4.32
62	23.37	23.62	5.88	5.89
63	34.10	32.14	6.59	6.56
65	17.88	22.00	5.07	4.86
66	22.36	23.54	5.32	5.15
67	29.37	29.66	8.01	7.81

Table A7

Cross-sectional area and number of motor neurons in the cervical enlargement of the human spinal cord

Case	Cell area (mm^2)		Number / section	
	Left	Right	Left	Right
18	1276	1237	5.23	5.85
20	1586	1617	6.20	7.00
46	1063	1176	4.60	5.00
48	1352	1412	6.84	5.79
49	1430	1462	3.67	3.08
50	1444	1474	2.90	6.31
51	1242	1278	5.97	6.20
52	1178	1123	2.29	1.43
53	1028	967	4.77	4.23
54	1107	1142	4.70	4.61
55	1098	1192	3.15	3.48
56	929	1070	2.13	1.80
57	810	819	2.87	3.03
58	1086	1089	5.25	5.44
61	1257	1300	2.74	3.06
62	972	917	3.10	3.61
63	1002	916	2.04	1.95
65	1117	1183	2.96	2.27
66	893	946	2.52	1.94
67	1116	1078	2.52	2.00

Table A8

Cross-sectional area of white and gray matter in the lumbar enlargement of the spinal cord

Case	Area of white matter (mm^2)		Area of gray matter (mm^2)	
	Left	Right	Left	Right
6	14.68	15.41	6.35	6.67
9	17.71	16.49	8.72	8.25
18	16.13	16.15	9.17	9.16
20	15.70	15.98	9.37	9.73
21	21.37	20.88	11.66	11.63
46	19.48	19.95	7.68	7.58
47	19.70	19.73	10.34	10.19
48	19.12	17.18	10.52	9.91
50	16.91	16.83	6.98	6.86
51	17.74	18.61	6.63	7.05
54	14.91	14.79	6.82	6.90
55	16.45	16.02	7.64	7.43
56	17.91	17.15	9.54	9.88
57	16.22	16.76	7.75	7.65
58	15.01	14.82	9.96	9.77
59	17.05	17.46	9.06	9.08
60	17.90	17.30	9.25	9.24
62	15.81	15.41	7.66	7.39
63	20.44	19.58	10.62	10.58
64	16.64	16.88	9.35	9.57

Table A9

Cross-sectional area and number of motor neurons in the lumbar enlargement of the human spinal cord

Case	Cell area (mm^2)		Number/section	
	Left	Right	Left	Right
6	1983	1940	10.14	11.64
9	2050	1941	14.86	13.54
18	1816	1966	19.38	19.48
20	1851	1892	8.71	8.67
21	2197	2155	21.82	20.45
46	1878	1856	8.19	9.04
47	2108	2099	10.79	9.36
48	2166	2027	16.13	13.70
50	1853	1895	7.41	7.77
51	1929	2070	7.50	8.31
54	1914	1953	12.03	12.37
55	1863	1797	4.24	3.64
57	1107	1112	5.80	5.04
58	1971	1857	11.64	10.00
59	1882	2071	7.87	9.87
60	1941	1919	11.04	9.75
62	1490	1383	5.58	5.63
63	1590	1811	4.84	4.58
64	1491	1592	4.91	5.21

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