ACADEMIC PRESS

Asymmetry in the human primary somatosensory cortex and handedness

Patrick Jung,[a] Ulf Baumgärtner,[a] Thomas Bauermann,[b] Walter Magerl,[a] Jochen Gawehn,[b]
Peter Stoeter,[b] and Rolf-Detlef Treede[a],*

[a] Institute of Physiology and Pathophysiology, Johannes Gutenberg-University, Saarstr. 21, 55099 Mainz, Germany
[b] Institute of Neuroradiology, Johannes Gutenberg-University, Mainz, Germany

Abstract

Brain asymmetry is a phenomenon well known for handedness and language specialization and has also been studied in motor cortex. Less is known about hemispheric asymmetries in the somatosensory cortex. In the present study, we systematically investigated the representation of somatosensory function analyzing early subcortical and cortical somatosensory-evoked potentials (SEP) after electrical stimulation of the right and left median nerve. In 16 subjects, we compared thresholds, the peripheral neurogram at Erb point, and, using MRI-based EEG source analysis, the P14 brainstem component as well as N20 and P22, the earliest cortical responses from the primary sensorimotor cortex. Handedness was documented using the Edinburgh Inventory and a dichotic listening test was performed as a measure for language dominance. Whereas thresholds, Erb potential, and P14 were symmetrical, amplitudes of the cortical N20 showed significant hemispheric asymmetry. In the left hemisphere, the N20 amplitude was higher, its generator was located further medial, and it had a stronger dipole moment. There was no difference in dipole orientation. As a possible morphological correlate, the size of the left postcentral gyrus exceeded that of the right. The cortical P22 component showed a lower amplitude and a trend toward weaker dipole strength in the left hemisphere. Across subjects, there were no significant correlations between laterality indices of N20, the size of the postcentral gyrus, handedness, or ear advantage. These data show that asymmetry of median nerve SEP occurs at the cortical level, only. However, both functional and morphological cortical asymmetry of somatosensory representation appears to vary independently of motor and language functions.
© 2003 Elsevier Science (USA). All rights reserved.

Keywords: Hemispheric asymmetry; Somatosensory cortex; SEP; Source analysis; Morphometry; Handedness

Introduction

Cortical asymmetries are an evolutionary peculiarity, most distinctive in humans (Springer and Deutsch, 1997). The most prominent examples for functional asymmetries of the brain are language and handedness. Approximately 90% of our population show dominant speech processing in the left hemisphere and a great majority prefers to use their right hand (only about 10% are left-handers; Annett, 1973). Language lateralization and handedness are suspected to be related because left-handers exhibit an increased incidence of bilateral or right hemisphere language dominance compared to right-handers (Branch et al., 1964; Hécaen et al.,

1981). Recently, the incidence of speech dominance in the right hemisphere measured by functional transcranial Doppler sonography was found to increase linearly with the degree of left-handedness (Knecht et al., 2000).

In the language system, the functional asymmetry of cortical organization is mainly represented in Broca's and Wernicke's areas (Broca, 1864; Wernicke, 1874). It is still controversial if asymmetry of the planum temporale which includes part of Wernicke's area reflects an anatomical substrate for language specialization (Geschwind and Levitsky, 1968; Foundas et al., 1994; Jäncke and Steinmetz, 1993; Moffat et al., 1998; Beaton, 1997).

In the sensorimotor system, up to now the neurobiological basis for handedness remains widely unclear. Several studies demonstrated a relationship between handedness and anatomical asymmetries, e.g., in the sizes of the frontal

---

* Corresponding author. Fax: +49-6131-3925902.
E-mail address: treede@uni-mainz.de (R.-D. Treede).

and occipital petalia (Bear et al., 1986; Weinberger et al., 1982; LeMay, 1992) and in the surfaces of the plana temporalia and plana parietalia (Steinmetz et al., 1991; Foundas et al., 1995; Jäncke et al., 1994), but only few studies detected asymmetries in brain regions that are directly related to the motor system (White et al., 1994; Amunts et al., 1996, 1997a, b, 2000; Dassonville et al., 1997; Volkmann et al., 1998). In the somatosensory system, even less is known about lateralization than in the motor system. Pneumatic stimulation of the first and fifth digit of both hands revealed a larger distance between dipole positions of the two digits in the left primary somatosensory cortex (SI) in right-handers. A significant correlation between handedness and sizes of hand representation areas was not determined (Sörös et al., 1999). Furthermore, in a magnetoencephalographic study equivalent current dipoles of the somatosensory-evoked field (SEF) components N20m and P30m were stronger in the left SI of both right- and left-handers (Rossini et al., 1994).

A previous EEG study (Buchner et al., 1995) described higher amplitudes of the N20 median nerve somatosensory-evoked potential (SEP; generator: area 3b of primary somatosensory cortex; Allison et al., 1989) over the left scalp in approximately 70% of the exclusively right-handed subjects. The intention of the present study was to clarify if this N20 asymmetry is due to side different subcortical input or to side differences of N20 source locations, source orientations, and/or source strengths by means of dipole source analysis. To verify the hypothesis that functional hemispheric asymmetry is associated with interhemispheric differences in brain structure, the intrasulcal length of the rostral surface of the left and right postcentral gyrus was determined, and its asymmetry was correlated with handedness and N20 asymmetry. Finally, we assessed the relationship of auditory lateralization (speech dominance), handedness, and asymmetry of the N20 SEP component. Some results of the study have been published in abstract form (Jung et al., 2002).

Materials and methods

Subjects

Sixteen subjects (eight females and eight males, ages ranged from 23 to 28 years, mean age: 24.3 years) were included in the study which was approved by the local ethics committee. All subjects gave their written informed consent, according to the Declaration of Helsinki, and were paid for participation. None of them suffered from any neurological or psychiatric diseases.

Subjects were comfortably seated in an electrically shielded, noise- and light-reduced room which had a constant temperature of 24°C. They were instructed to relax and keep their eyes open and fixed to a visual target.

Stimuli

The left and right median nerves were stimulated separately at the wrist with constant-current square-wave pulses of 0.2-ms duration. The stimulus intensity was set at the sum of the individual sensory and motor threshold. Median nerve SEPs were recorded using a 32-channel EEG montage within a time window of 300 ms including a prestimulus interval of 50 ms, bandpass filtered (0.16–500 Hz) and digitized at 2.5 kHz. In order to record the subcortical components N10 and P14 adequately, we additionally chose a 3-channel EEG montage (ipsilateral Erb point-Fz, Fz-ipsilateral A, contralateral P-Fz) with a sampling rate of 10 kHz. In this case, the bandpass was 0.16–3000 Hz and a time window of −7 to 30 ms was analyzed. The interstimulus interval (ISI) was 0.531 s. Subjects were instructed to mentally count the electrical stimuli.

The order of the recording conditions (32-channel vs 3-channel montage, left vs right median nerve stimulation) was counterbalanced across subjects. For each recording condition, two runs of 250 responses were averaged and checked for reproducibility. Data from these two runs were collapsed yielding averages of 500 responses for each condition to achieve a maximal signal-to-noise ratio for amplitude measurements and dipole source analysis.

EEG recording

The EEG was recorded with a 32-channel amplifier (Neurotop, Nihon Kohden) using Ag/AgCl electrodes (5 mm diameter) attached to the scalp with electrode cream (EC2, Grass). A ground electrode was fixed to the forearm ipsilateral to stimulation. All electrode/skin impedances were below 5 kΩ. Electrodes were positioned according to the 10–20 system (Pivik et al., 1993). In addition to the 19 standard positions, the montage included frontocentral (FC5, FC1, FC2, FC6) and centroparietal (CP5, CP1, CP2, CP6) electrodes. We also added electrodes on the zygomatic arch (F9, F10), the preauricular points (T9, T10), and the mastoids (P9, P10) in order to cover the lower parts of the head. All electrodes were referenced to Fz.

Amplitudes were measured baseline to peak. For baseline correction, the mean amplitude of the 5- to 12-ms poststimulus interval was substracted (for the derivation "Erb-Fz": 4 to 8 ms). In order to eliminate low-frequency baseline shifts contaminating EEG signals, we used a high-pass filter (20 Hz, 12 dB/octave, forward filter; Gobbelé et al., 1999). The 32 EEG channels were rereferenced off-line versus the average reference, excluding electrodes contaminated by artifacts.

Dipole source analysis

After recording, each electrode was replaced by a 8-mm-diameter oil capsule (cf. Lagerlund et al., 1993). MR images of each subject were obtained with a 1.5-T scanner (Sie-

mens Magnetom Vision; FLASH 3D, repetition time 14 ms, echo time 4 ms, flip angle 25°, 1-mm slices, 256-mm field of view, 256 × 256 matrix). Subsequently, MR images were aligned to the anterior commissure (AC)–posterior commissure (PC) plane and transformed into Talairach space using AFNI software (Cox, 1996). Individual electrode coordinates were taken as basis for source analysis calculations. For simplification, we designate equivalent current dipoles evaluated by means of source analysis as "dipoles."

For dipole source modeling, we used the Brain Electrical Source Analysis software (BESA; Scherg, 1992) which first calculated the best-fitting ellipsoid of each subject on the basis of the individual electrode coordinates and then adjusted dipole sources using a 4-shell ellipsoidal head model.

Source analysis was initially performed on grand mean EEG data since this provides the best signal-to-noise ratio (16 × 500 averaged responses for each condition). EEG segments were time-locked to the mean N10 latency (Erb potential) to minimize the jitter due to differences in peripheral conduction time. As time window for the dipole fits, onset to peak of the corresponding peaks (P14, N20, P22) in the global field power (i.e., the spatial standard deviation of amplitudes in the different EEG channels as a function of time) was chosen. Dipole sources were fitted in the order of appearance resulting in a 3-dipole model (P14, N20, P22) for each stimulus side with a goodness of fit value (GoF) of >95% in the 10- to 35-ms poststimulus interval.

The same fit procedure was then applied to individual data. In most of the subjects ($n = 9$), an individual fit of all three sources was possible. In subjects where the fit of N20 did not result in stable solutions for both stimulus sides, the time window for P30 was chosen (5 cases), assuming that N20 and P30 are generated in similar locations but inverted dipole orientation (e.g., Allison et al., 1989). If the P30 time window did not lead to stable solutions with an explicit N20 peak in the source waveform, we utilized grand mean location coordinates to fit the N20 source (2 cases). For instable P22 fits, grand mean coordinates were used (3 cases). In that way, stable dipole solutions for every single subject were acquired with a mean GoF of >80% for all three fitted dipole sources in their corresponding time window.

Dipole orientations were determined by BESA's angles ϑ and φ. ϑ corresponds to the angle deviation of dipoles from the vertical axis running from the center of the head to the vertex, and φ expresses the angle deviation of dipoles from the axis passing through the preauricular points. Dipole orientations, coordinates, and source waveforms (dipole strengths) of P14, N20, and P22 were then used for statistical analysis.

Evaluation of functional asymmetries

After excluding any hearing impairments by means of audiometry, each subject performed a dichotic listening test (Jäncke, 1992). Dichotic listening tests are regarded as non-

invasive methods that yield valid estimates of hemisphere speech dominance (Geffen et al., 1981; Zatorre et al., 1989; Hugdahl et al., 1997). A right ear advantage in the dichotic listening test indicates language dominance of the left hemisphere and vice versa. The auditory stimuli were presented to the subjects via headphones from an audio CD. The dichotic stimuli consisted of 6 stop consonants (/b/, /d/, /g/, /p/, /t/ and /k/) that were paired with the vowel /a/ to form 6 consonant-vowel syllables whose volume and basic frequency were equalized. At every dichotic trial, both ears were simultaneously presented a different syllable. Four blocks were presented, each consisting of 30 dichotic trials in a different sequence. Each block was listened to twice, with the headphones reversed the second time to balance headphone asymmetries. The subjects were instructed to mark the consonant of the dichotically presented syllables which was perceived louder or more distinct. Thus, the score for one ear resulted from the sum of the marks indicating a preferential perception of the syllable by the respective ear. From the scores for each ear, a laterality index (LI) was calculated (see "Data evaluation").

Both the direction and the degree of handedness of each subject were determined on the basis of the 10-item version of the Edinburgh Inventory (Oldfield, 1971). For each item (e.g., usage of scissors), the preference was recorded as right only (2–0), left only (0–2), right rather than left (1–0), left rather than right (0–1), or either hand (1–1). On this basis, laterality indices were evaluated (see Data evaluation). Additionally, the subjects were assigned to two handedness groups (LI >80 were classified as "extreme righthanders" and LI ≤80 were considered as "non-righthanders") according to previous suggestion (LeMay, 1992; Habib et al., 1995).

Evaluation of anatomical asymmetries

The intrasulcal length of the anterior wall of the left and right postcentral gyrus was measured as an indicator of the hand representation area in SI in every second of 41 horizontal MR slices (leading to 21 analyzed slices). The applied method has been previously described for the primary motor cortex (MI) by Amunts et al. (1996). In contrast to this study, MR data were not transformed into Talairach space to exclude contortions due to possibly unusual asymmetries or symmetries in the Talairach reference brain. In the present study, morphometric analysis was performed in the AC-PC aligned MR format. In conformity with the Talairach coordinate system, AC was defined as $x = 0$, $y = 0$, and $z = 0$. Negative values indicate locations left (x), caudal (y), and ventral (z) to AC. Thus, horizontal sections extended from $z = 69$ to 29 according to reports that proclaimed an extent of hand representation in MI and SI up to 40 mm in the dorsoventral direction (Sanes et al., 1995; Hluštík et al., 2001). In each horizontal section, the intrasulcal contour of the anterior wall of the postcentral gyrus was traced from the most medial point of the central sulcus

to the most lateral point on the convexity of the postcentral gyrus. In a final step, the entire area (for $z = 69$ to 29) of the anterior wall of the left and right postcentral gyrus was estimated by summing the trapezoidal areas between adjacent sections according to the formula,

$$A = \Delta z \sum_{i=1}^{n-1} (L_i + L_{i+1})/2, \qquad (1)$$

where A is the estimated total area, Δz is the section interval (2 mm), and L_i and $L_i + 1$ are the measured lengths of the rostral wall of the postcentral gyrus in adjacent sections. Moreover, the resultant laterality indices (see Data evaluation) were calculated. To evaluate the relative position of N20 source localizations to the rostral surface of the postcentral gyrus, N20 source locations were retransformed from Talairach space to the original AC-PC aligned format using AFNI software.

Data evaluation

To assess the direction and the degree of auditory lateralization (language dominance), handedness, functional and morphological asymmetry of the somatosensory system, laterality indices (LI) were calculated due to the formula,

$$LI = (R - L)/(R + L) \times 100, \qquad (2)$$

where R is right ear score, right-hand score, mean amplitudes of SEP components following right-sided median nerve stimulation or area of the anterior wall of the left postcentral gyrus, L is left ear score, left-hand score, mean amplitudes of SEP components following left-sided median nerve stimulation or area of the anterior wall of the right postcentral gyrus. Consequently, positive values indicate right ear advantage, hand preference of the right hand, predominant somatosensory processing in the left hemisphere or greater extension of area 3b of SI in the left hemisphere.

All data are presented as mean ± SEM. Data were analyzed using Student's two-tailed paired (to assess side differences) and unpaired (to evaluate gender differences and differences between handedness groups) t tests. P values <0.05 were considered significant.

Results

Early subcortical and cortical SEP components

Neither sensory (1.3 ± 0.1 mA vs 1.2 ± 0.1 mA) nor motor thresholds (3.6 ± 0.2 mA vs 3.6 ± 0.1 mA) were different after right and left median nerve stimulation. Consequently, stimulus intensities were identical for the right and left median nerve, both in absolute current application and in relation to thresholds.

In the 3-channel EEG montage, N10 amplitudes, derived over the distal part of the brachial plexus (Erb point), were also symmetrical after right and left median nerve stimulation (Fig. 1A). Thus, the central nervous system (CNS) received the same input on both sides. In the CNS, amplitudes of the subcortical P14 component, generated in the brainstem (medial lemniscus; Desmedt, 1985), did not differ in side comparison but on the cortical level asymmetries of amplitudes became apparent. The N20 potential showed on average 18 ± 5 % higher amplitudes after right median nerve stimulation ($P < 0.01$). No differences between mean peak latencies after right- and left-sided stimulation were found for all investigated SEP components (Table 1).

In the 32-channel EEG montage, the cortical components N20 and P22 appeared contralateral to stimulation only. Significantly higher amplitudes of the first cortical response N20 were demonstrated for the left-sided electrode positions P3, CP1, and O1 compared to their right-sided counterparts (P4, CP2, O2; all $P < 0.05$). In the EEG channels with maximal N20 deflection (P3 and P4, respectively), the N20 amplitude was on average 31 ± 5 % higher after right median nerve stimulation ($P < 0.001$, Fig. 1B and Fig. 3A). The distances between the Ω region (cortical landmark that represents approximately the hand area of the primary motor cortex; Yousry et al., 1995) and the derivation points P3 and P4 did not differ on both sides (Fig. 1B). Hence, the measured side differences of N20 amplitudes were not an artifact due to unequal electrode placements with reference to landmarks in the sensorimotor region. Amplitudes of the second cortical response (P22) had maximal deflections in the EEG channels C3 and C4, respectively, and were also lateralized. In contrast to N20 asymmetry, significantly higher P22 amplitudes were found after left median nerve

Fig. 1. (A) Grand mean SEP waveforms recorded with the 3-channel EEG montage. Waveforms after right (red line) and left (blue line) median nerve stimulation are illustrated. There were no side differences for the subcortical SEP components N10 (derivation: ipsilateral Erb–Fz; generator: brachial plexus) and P14 (Fz–ipsilateral A; medial lemniscus) while the first cortical SEP component N20 (contralateral P–Fz; area 3b) exhibited significantly higher amplitudes after right compared to left median nerve stimulation ($P < 0.01$). (B) The N20 amplitude asymmetry was also significant in the 32 channel EEG montage ($P < 0.001$). Distances between P3 and P4 recording positions and cortical landmarks in the hand areas of primary motor cortices (Ω regions; Yousry et al., 1995) were not significantly different ($n = 16$). Thus, the illustrated asymmetry of N20 amplitudes may not be explained by asymmetric electrode placements.

Fig. 2. Three-dipole source model of early subcortical and cortical SEP components based on grand mean EEG data after right (A) and left (B) median nerve stimulation. The spatial configuration of the sources in the BESA head model is demonstrated. Time courses of goodness of fit (GoF, gray line), global field power (GFP, black line), and dipole strengths are shown. There were no side differences of the brainstem source (1, blue line) and P22 source (3, green line) activities at peak latencies of 14 and 22 ms, respectively. However, the source waveform of the N20 source (2, red line) was significantly more pronounced at 20-ms peak latency after right compared to left median nerve stimulation ($P < 0.001$).
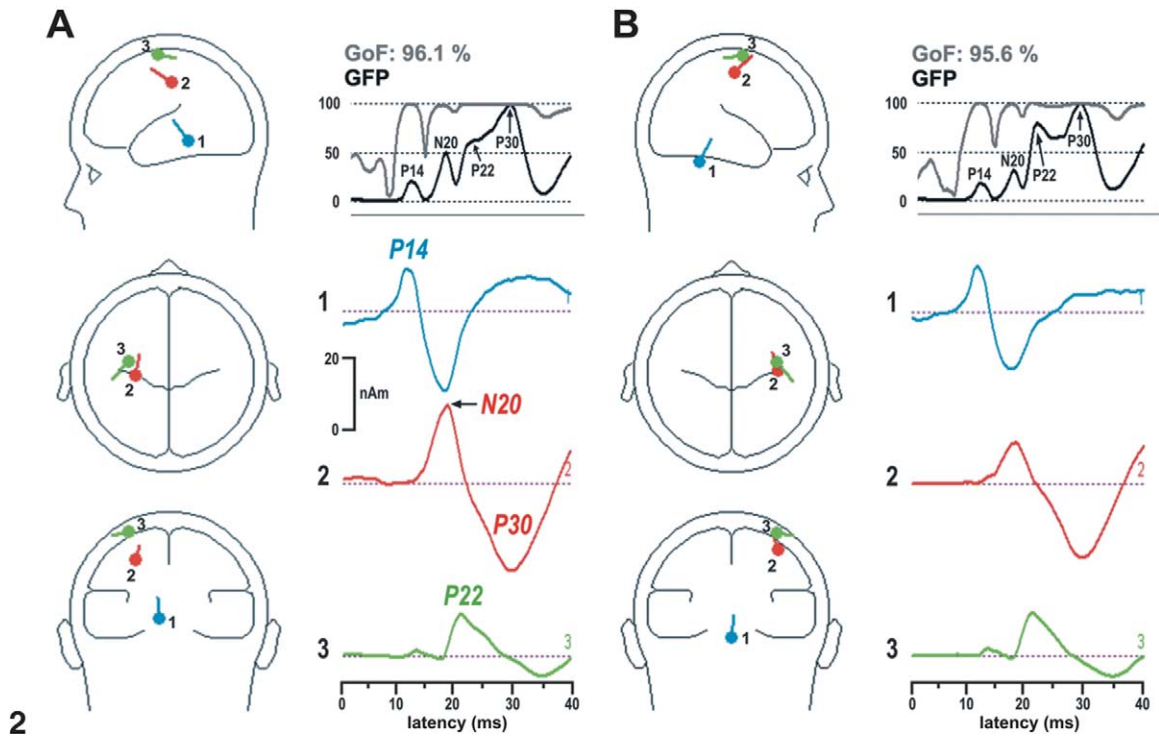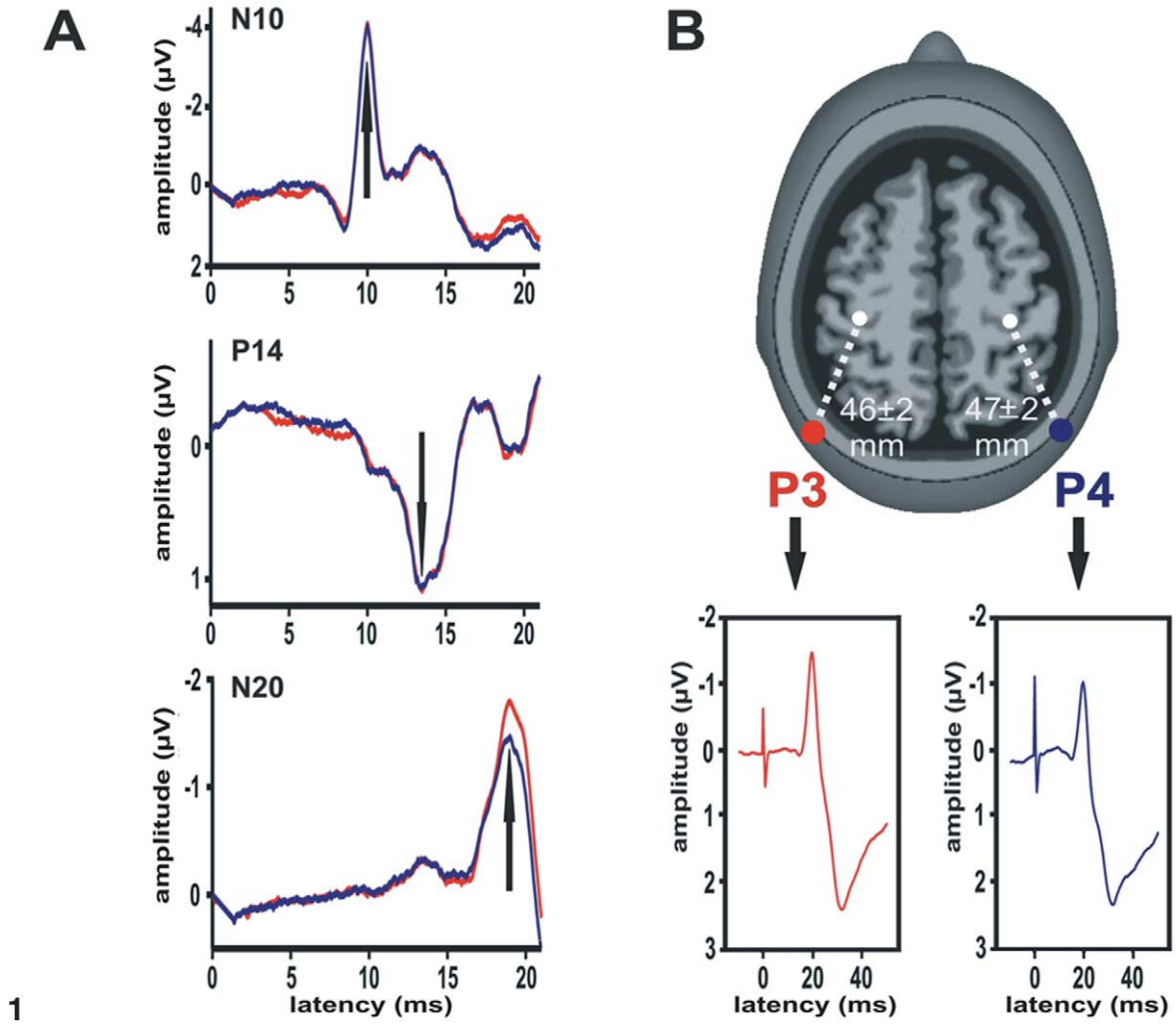
Table 1
Side comparison of SEP peak latencies and amplitudes
(mean ± SEM, $n = 16$)

	rMed	lMed	P values[a]
Peak latencies [ms]			
N10	10.1 ± 0.2	10.2 ± 0.2	n.s.
P14	14.1 ± 0.2	14.1 ± 0.2	n.s.
N20	19.3 ± 0.2	19.2 ± 0.2	n.s.
Amplitudes [μV]			
N10	−4.13 ± 0.38	−4.00 ± 0.33	n.s.
P14	1.16 ± 0.07	1.18 ± 0.06	n.s.
N20	−2.02 ± 0.29	−1.68 ± 0.29	<0.01

Values for median nerve SEP components are referred to the 3-channel EEG montage. rMed, right median nerve stimulation; lMed, left median nerve stimulation.

[a] Student's paired t test.

stimulation (side difference of 21 ± 8 %, $P < 0.05$). No P22 latency differences were detected after right- and left-sided stimulation of the median nerve.

Dipole source analysis

The fit procedure led to stable solutions for the grand mean and for every individual containing a brainstem source (P14) located near midline, the first cortical response (N20) in the contralateral hand area of the primary somatosensory cortex and a second cortical response (P22) located slightly more frontally (Fig. 2).

The dipole location of the P22 source was significantly more anterior (6.3 ± 2.3 mm, $P < 0.05$) and superior (16.7 ± 2.0 mm, $P < 0.001$) in the left hemisphere than the ipsilateral N20 source location. In the right hemisphere, significant differences of P22 and N20 localizations could not be stated.

Table 2 outlines the interhemispheric comparison of mean dipole localizations, mean dipole strengths, and mean dipole orientations. For dipole locations, no significant side differences were found for the P14 and P22 sources. However, the N20 dipole was localized 7.7 ± 2.5 mm more

medial ($P < 0.01$) and therefore less eccentric ($P < 0.05$, Fig. 3C) in the left hemisphere. The P22 source was located slightly more medial (4.2 ± 2.6 mm) in the left sensorimotor region, too, but this difference did not reach significance. Comparing dipole strengths in both hemispheres, no asymmetry was found for the subcortical P14 source whereas at the cortical level hemispheric asymmetry was detected. N20 dipole strengths were considerably more pronounced in the left hemisphere. On average, N20 source activity was 31 ± 6 % stronger in the left SI cortex compared to the right ($P < 0.001$). This clear left hemisphere preponderance of N20 dipole strengths properly reflected the asymmetric N20 amplitudes (Figs. 3A and B) which was supported by the highly significant correlation between the asymmetry of N20 dipole moments and N20 amplitudes across all subjects (Pearson's $r = 0.71$, $P < 0.01$). In contrast, P22 source strengths approached significance with higher dipole moments in the right hemisphere.

Comparing side differences in dipole orientations, no side different angle deviation from midsagittal plane in the frontal plane (ϑ) and in the horizontal plane (φ) was demonstrated for all fitted sources after right- and left-sided median nerve stimulation.

SI morphometry

From $z = 69$ to 29 in the dorsoventral direction (Fig. 4), 15 out of 16 brains showed a greater total area of the anterior wall of the left postcentral gyrus in side comparison; this left hemispheric preponderance was significant in 8 brains. Across all subjects, the rostral area of the postcentral gyrus was significantly larger in the left hemisphere (17.34 ± 0.41 cm^2 vs 15.74 ± 0.34 cm^2, $P < 0.001$, Fig. 3D), mainly because of a further medial extension of the left central sulcus (CS). For $z = 61$ to 29, the left CS ended constantly closer to the interhemispheric fissure compared to the right. On the contrary, the most lateral point of the postcentral gyrus did not differ between the hemispheres in any of the analyzed horizontal slices.

Table 2
Side comparison of dipole source locations, dipole orientations and dipole source strengths.

	P14			N20			P22		
	rMed	lMed	P values[a]	rMed	lMed	P values[a]	lMed	lMed	P values[a]
tlrc x [mm]	−7.6 ± 2.0	−4.2 ± 2.2	n.s.	−37.2 ± 2.1	45.0 ± 2.4	< 0.01	−37.8 ± 1.6	42.0 ± 1.9	n.s.
tlrc y [mm]	−33.5 ± 3.0	−37.2 ± 3.7	n.s.	−23.7 ± 2.1	−21.7 ± 1.9	n.s.	−17.4 ± 1.8	−18.8 ± 2.2	n.s.
tlrc z [mm]	−17.1 ± 5.8	−28.1 ± 6.2	n.s.	52.9 ± 1.5	57.3 ± 2.3	n.s.	69.6 ± 2.3	64.4 ± 3.2	n.s.
ϑ	−35.3 ± 2.4	30.1 ± 3.1	n.s.	74.7 ± 3.3	−70.2 ± 4.3	n.s.	−88.3 ± 4.8	79.0 ± 6.2	n.s.
φ	−82.2 ± 4.5	79.8 ± 5.4	n.s.	68.2 ± 3.0	−65.3 ± 4.2	n.s.	45.4 ± 7.2	−65.4 ± 11.3	n.s.
dm [nAm]	13.4 ± 1.3	13.6 ± 1.4	n.s.	15.7 ± 1.5	10.6 ± 1.5	< 0.001	11.6 ± 2.0	14.8 ± 2.9	n.s.[b]

Values are indicated as mean ± SEM ($n = 16$). rMed, right median nerve stimulation; lMed, left median nerve stimulation; tlrc, talairach head coordinates; ϑ, angle deviation from the vertical axis running from the center of the head to the vertex; φ, angle deviation from the axis passing through the preauricular points; dm, dipole moments.

[a] Student's paired t-test (absolute values were compared for tlrc x, ϑ, φ)

[b] $P = 0.06$

The projection of both N20 dipole sources and the rostral wall of the left and right postcentral gyrus on the frontal plane distinctly illustrated that the left N20 source was located significantly closer to the medial border of the postcentral gyrus than the right N20 source (Fig. 4).

Laterality indices

According to the Edinburgh Inventory, two of the subjects (one male, one female) were considered as left-handed with a score < 0. Thus, the distribution of left-handedness was representative for the general population. The average handedness score was 70 ± 12; 70 ± 9 for men and 70 ± 15 for women, entailing no gender differences. In the dichotic listening test, none of the subjects revealed a left ear advantage. The mean laterality index was 26 ± 6. The performances differed significantly between men and women (11 ± 4 vs 41 ± 5, $P < 0.01$) in which females exhibited a more pronounced right ear advantage than males.

Fifteen out of 16 subjects demonstrated a predomi-

nance of N20 amplitudes over the left scalp which was expressed by a laterality index of 19.6 ± 3.8 across all subjects ($P < 0.001$). Concerning N20 source strengths, all subjects showed stronger dipole moments in the left hemisphere (20.8 ± 4.7, $P < 0.001$). Concordantly, the area of the anterior wall of the postcentral gyrus was larger in the left hemisphere in 15 out of 16 subjects (LI = 4.8 ± 0.8, $P < 0.001$). No gender differences for these asymmetry coefficients were detected. When examining the relationship between handedness scores and laterality indices of N20 amplitudes (Spearman's rank order correlation coefficient $\rho = -0.04$), N20 source strengths ($\rho = -0.09$), N20 eccentricity ($\rho = 0.24$), or SI morphology ($\rho = 0.28$), no significant correlation could be determined. Moreover, correlation between morphological SI asymmetry and N20 laterality ($\rho = -0.07$ for amplitudes, $\rho = -0.16$ for source strengths, $\rho = -0.04$ for eccentricity) was not significant. Ten subjects were classified as "extreme right-handers," six were considered as "non-right-handers" (Habib et al., 1995). There were no evident differences in N20 laterality scores and in macromorphological SI asymmetry between the two groups (Fig. 5). Likewise, no significant correlations between ear advantage and handedness scores ($\rho = 0.03$) and between ear advantage and the laterality indices of N20 eccentricity ($\rho = 0.13$) or SI morphometry ($\rho = -0.07$) were found. The two left-handed subjects (handedness scores: -13 and -80) both had evidence for a left hemisphere dominance in the dichotic listening test (ear advantage: 10 for the weak and 60 for the strong left-hander). The highest, but still not significant, correlations were detected between ear advantage and laterality indices of N20 amplitudes ($\rho = 0.35$, $P < 0.2$) and N20 source strengths ($\rho = 0.46$, $P < 0.1$).
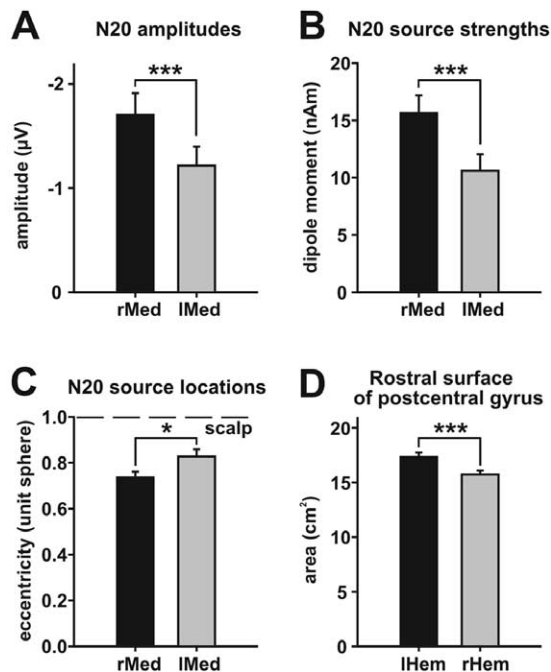
Discussion

Our data documented that asymmetry of median nerve SEP occurs at the cortical level only. No asymmetric tendencies were found neither for the brachial plexus component N10 nor for the brainstem potential P14. In contrast, the first response at the cortical level (N20) was clearly lateralized. The present study clarified that this previously observed cortical asymmetry with higher N20 amplitudes over the left scalp (Buchner et al., 1995) is based on asymmetric dipole strengths and not side different dipole locations or dipole orientations. If N20 sources had equal dipole strengths in both hemispheres, a more eccentric, i.e., less deep, N20 dipole localization in the left hemisphere would entail higher N20 amplitudes over the left scalp. In our data, however, higher N20 amplitudes over the left scalp were determined even though N20 sources were located deeper in the left hemisphere. In contrast, a previous EEG study showed that smaller P40 amplitudes of the tibial nerve SEP in the left compared to the right hemisphere could be at-
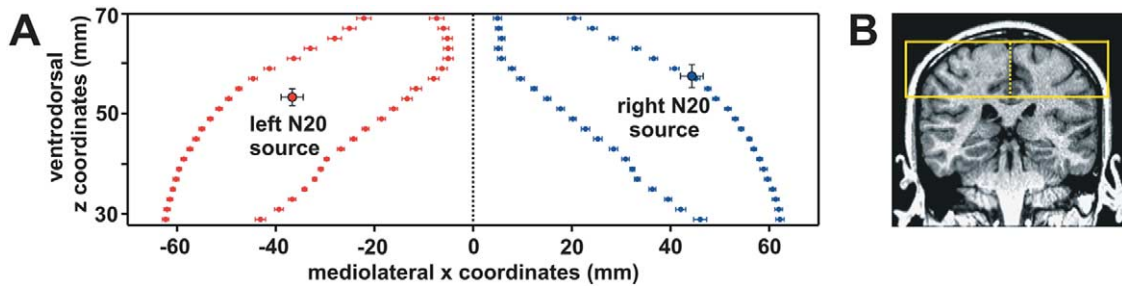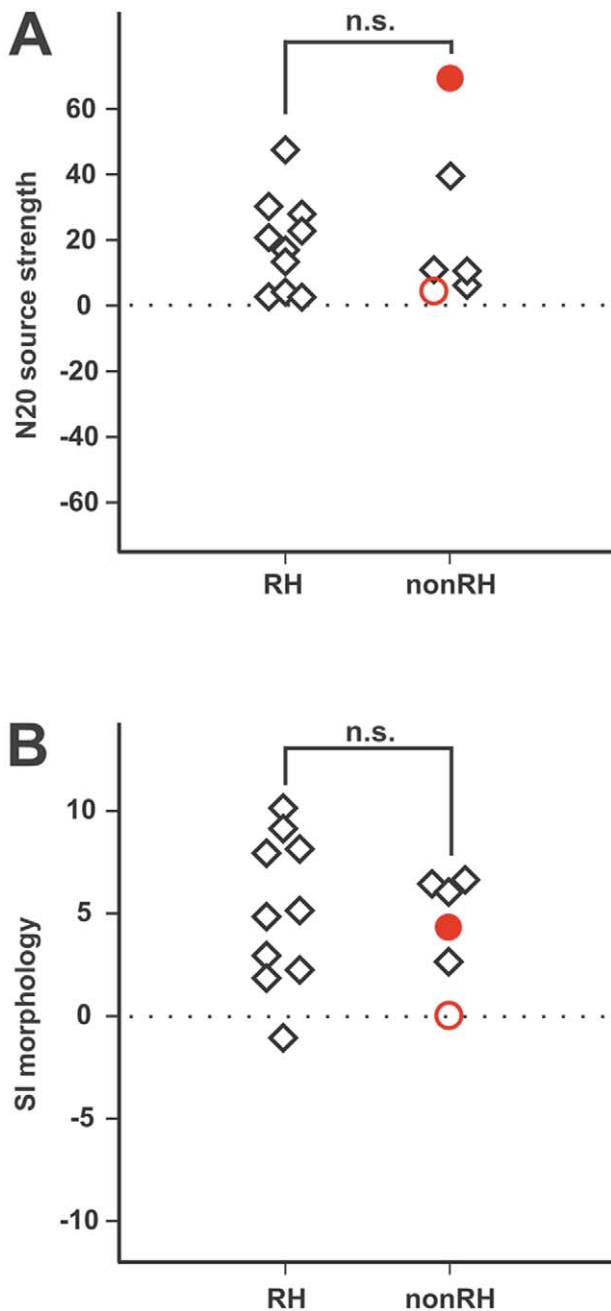

Fig. 3. Side comparison of N20 amplitudes, N20 source strengths, N20 source locations, and SI morphometry (mean $\pm$ SEM, $n = 16$). (A) N20 amplitudes were higher over the left hemisphere (P3-AR) after right median nerve stimulation compared to the right hemisphere (P4-AR) after left median nerve stimulation. (B) N20 source strengths were larger in the left compared to the right hemisphere after contralateral median nerve stimulation. (C) N20 source localizations were less eccentric in the left compared to the right cortex, i.e., left N20 sources were located deeper in the brain. (D) The rostral surface of the postcentral gyrus was significantly larger in the left hemisphere as revealed by morphometric analysis of 21 horizontal MR slices from $z = 69$ to 29. rMed, right median nerve stimulation; lMed, left median nerve stimulation; lHem, left hemisphere; rHem, right hemisphere; *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$

Fig. 4. (A) Frontal projection of medial and lateral borders of the postcentral gyrus in 21 horizontal MR slices ($z = 69$ to 29) and locations of N20 sources in the left (red dots) and right (blue dots) hemisphere (mean $\pm$ SEM, $n = 16$). In side comparison, N20 sources in the left hemisphere were located 4.2 ± 2.6 mm further ventral (n.s.) and 7.7 ± 2.5 mm further medial ($P < 0.01$). The postcentral gyrus was significantly larger in the left than in the right hemisphere ($P < 0.001$). For $z = 61$ to 29, medial borders of the left postcentral gyrus lay constantly closer to the midsagittal plane ($P < 0.05$ for $z = 51, 49, 39, 35, 33, 31$) whereas lateral borders were symmetrical in all horizontal sections. (B) Reprojection of the region sampled in (A) onto a coronal MR image.

tributed to deeper located left P40 dipole sources with a more tangential orientation but not to weaker source strengths (Baumgärtner et al., 1998). In general, source analysis studies exploring cerebral asymmetries with high time resolution are possible with EEG or MEG. To distinguish the influence of different dipole strengths from that of different dipole orientations, it is essential to use EEG for it is sensitive to current flows in all orientations but not MEG which is insensitive to radial current flow (e.g., Schneider et al., 2002).

The leftward N20 asymmetry was distinctive to such an extent that it is of clinical relevance and of importance for cortical reorganization studies. A side difference of more than 50% of N20 amplitudes is commonly considered pathological. In our sample, two healthy subjects showed N20 amplitude side differences of 58.2% and 65.5%, respectively, because of a distinct prevalence in the left cortex. Their median nerve SEP would have been misleadingly classified as pathological by the commonly used criterion.

It is noteworthy that the preponderant N20 response in the left hemisphere is followed by a leftward weaker response, labeled P22. Source activities of P22 in the right hemisphere only tended to be stronger than in the left sensorimotor cortex although P22 amplitudes were significantly higher over the right half of the scalp. This is plausible against the background that P22 dipoles of two-thirds of our subjects showed more radial orientations in the right sensorimotor cortex which entails that P22 electrical potentials were projected more concentrated onto the right half of the scalp. Compared to the first cortical response, reversed

Fig. 5. Distribution of laterality indices (degree of lateralization) of N20 source strengths (A) and SI morphometry (B) of extreme right-handers (RH, handedness score >80, $n = 10$) and non-right-handers (nonRH, handedness score ≤ 80, $n = 6$). Red symbols in the group of non-right-handers are assigned to left-handers ($\bigcirc$, handedness score $= -13$, $\bullet$: handedness score $= -80$). Positive values indicate preponderance of the left hemisphere, i.e., higher N20 responses after right median nerve stimulation and a larger rostral surface of the postcentral gyrus in the left cortex, respectively. No significant differences between handedness groups were found for both N20 and SI lateralization.

brain asymmetry and slightly more frontal location of the second cortical component are in accordance with a previous study by Buchner et al. (1995) who labeled this component as P25. Thus, somatosensory function is not simply processed predominantly in the left hemisphere. Asymmetric somatosensory processing is rather dependent on different SEP components. However, asymmetry of the N20 component was far more pronounced than P22 asymmetry.

In this study, only hemispheric asymmetry of the first two cortical SEP responses, presumably generated in the primary somatosensory cortex, was demonstrated. Knowledge about cortical asymmetry of later SEP components is still insufficient. But there are already indications for a predominant sensory processing in the left secondary somatosensory cortex (Forss et al., 1994; Kany et al., 1997).

The rostral area of the postcentral gyrus was more extended in the left than in the right hemisphere within the dorsoventral coordinates $z = 69$ to 29. This asymmetry of the postcentral gyrus seems to be predominantly caused by a larger hand representation area in the left primary somatosensory cortex by the following lines of evidence: According to previous reports, the region of hand representation accounts for the main portion of the primary sensorimotor cortex in the range of $z = 69$ to 29 (Sanes et al., 1995; Hluštík et al., 2001). This was supported by N20 source localizations in both hemispheres that ranged from $z = 67$ to 41 in our study. Furthermore, a more pronounced hand representation area in the left SI has been previously described on the basis of a larger distance between dipole localizations of the first and fifth digit in the left compared to the right SI (Sörös et al., 1999). In the present study, the larger hand representation area in the left SI was possibly reflected by leftward stronger N20 source strengths after median nerve stimulation.

The distance between the lateral border of the postcentral gyrus and midsagittal plane did not differ in the left and right cortex whereas the medial border lay closer to midsagittal plane in the left hemisphere (Fig. 4). Thus, other functional SI areas could only have been shifted in medioventral or mediodorsal direction by a larger hand area size in the left primary somatosensory cortex. As a consequence, functional displacements of SI areas which lie dorsal to the hand area (e.g., forearm, foot) would be shifted along the course of the postcentral gyrus if its lateroventral-to-mediodorsal course were taken into account (Fig. 4). In fact, a deeper location along the interhemispheric fissure was noted for the SI foot representation area of the left hemisphere (Baumgärtner et al., 1998). However, functional SI regions with a more ventral location in reference to the hand representation area (e.g., face) would be shifted in medioventral direction. For the lateroventral course of the postcentral gyrus runs opposite to a displacement in medioventral direction, such a shift should result in a macrostructural alteration, e.g., a further extension of the rostral wall of the postcentral gyrus toward the interhemispheric fissure. In the present study, the left postcentral gyrus consistently expanded closer to midsagittal plane from $z = 61$ to 29. Actually, this further extension of the left postcentral gyrus toward midline was most pronounced in horizontal MR slices with $z = 39, 35, 33, 31$, i.e., sections beneath the most ventral N20 source localization ($z < 41$). To our knowledge, no interhemispheric comparison of functional SI areas which lie somatotopically ventral to hand representation (e.g., face) has been presented so far. In accordance with our prediction, the face representation area in the left SI should be located further medioventral than in the right SI due to the larger SI hand representation area in the left hemisphere.

Unlike N20 sources, P22 sources were situated in the prerolandic cortex (Fig. 2). In the literature, the origin of the P22 generator still remains controversial. According to our data, the primary motor cortex (area 4) is suggested to be the generator of the P22 potential which is consistent with several studies (Mauguière et al., 1983; Mauguière and Desmedt, 1991; Desmedt and Bourguet, 1985; Deiber et al., 1986; Kawamura et al., 1996) but at variance with other reports which located the generator in area 1 (Allison et al., 1991; Buchner and Scherg, 1991; Kakigi, 1994).

No relationship among handedness, N20 asymmetry, and asymmetric SI morphometry was detected. However, with only one extreme left-hander in our sampling, correlations were not sensitive. But the fact that extreme right-handers who are supposed to exhibit the most pronounced left hemisphere dominance (LeMay, 1992; Habib et al., 1995) did not show any differences in asymmetry of the N20 component or SI morphology compared to non-right-handers indicated no simple direct relationship of handedness to N20 asymmetry or lateralized SI morphology.

Previous studies investigating the relationship between handedness and other structural cerebral asymmetries (planum temporale and parietale, frontal and occipital petalia, sylvian fissure) led to diverse results: Both correlations (Bear et al., 1986; Weinberger et al., 1982; Steinmetz et al., 1991; Foundas et al., 1995; Jäncke et al., 1994) and no correlations (Witelson and Kigar, 1992; Good et al., 2001) were found. If sensorimotor regions or functions were directly investigated as in the present study, no reflection of handedness by structural or functional asymmetries was detected (White et al., 1997; Dassonville et al., 1997; Sörös et al., 1999; Rossini et al., 1994; but Amunts et al., 1996). This is in accordance with our data.

In summary, we have documented that asymmetry of median nerve SEP occurs at the cortical level only. This asymmetry was due to different source strengths and not to source locations or orientations. As a possible morphological correlate of the leftward asymmetry of the N20 SEP component, the total rostral surface area of the left postcentral gyrus exceeded that of the right. However, the degree of lateralization of the N20 response and SI morphology were not related. Moreover, functional and morphological cortical asymmetry of somatosensory representation appears to vary independently of motor (and language) functions.

Acknowledgments

References

Allison, T., McCarthy, G., Wood, C.C., Darcey, T.M., Spencer, D.D., Williamson, P.D., 1989. Human cortical potentials evoked by stimulation of the median nerve. I. Cytoarchitectonic areas generating short-latency activity. J. Neurophysiol. 62, 694–710.

Allison, T., McCarthy, G., Wood, C.C., Stephen, J.J., 1991. Potentials evoked in human and monkey cerebral cortex by stimulation of the median nerve. Brain 114, 2465–2503.

Amunts, K., Jäncke, L., Mohlberg, H., Steinmetz, H., Zilles, K., 2000. Interhemispheric asymmetry of the human motor cortex related to handedness and gender. Neuropsychologia 38, 304–312.

Amunts, K., Schlaug, G., Jäncke, L., Steinmetz, H., Schleicher, A., Dabringhaus, A., Zilles, K., 1997a. Motor cortex and hand motor skills: structural compliance in the human brain. Hum. Brain Mapp. 5, 206–215.

Amunts, K., Schlaug, G., Schleicher, A., Steinmetz, H., Dabringhaus, A., Roland, P.E., Zilles, K., 1996. Asymmetry in the human motor cortex and handedness. NeuroImage 4, 216–222.

Amunts, K., Schmidt-Passos, F., Schleicher, A., Zilles, K., 1997b. Postnatal development of interhemispheric asymmetry in the cytoarchitecture of human area 4. Anat. Embryol. 196, 393–402.

Annett, M., 1973. Handedness in families. Ann. Hum. Genet. 37, 93–105.

Baumgärtner, U., Vogel, H., Ellrich, J., Gawehn, J., Stoeter, P., Treede, R.-D., 1998. Brain electrical source analysis of primary cortical components of the tibial nerve somatosensory evoked potential using regional sources. Electroenceph. Clin. Neurophysiol. 108, 588–599.

Bear, D., Schiff, D., Saver, J., Greenberg, M., Freeman, R., 1986. Quantitative analysis of cerebral asymmetries. Fronto-occipital correlation, sexual dimorphism and association with handedness. Arch. Neurol. 43, 598–603.

Beaton, A.A., 1997. The relation of planum temporale asymmetry and morphology of the corpus callosum to handedness, gender, and dyslexia. a review of the evidence. Brain Lang. 60, 255–322.

Branch, C., Milner, B., Rasmussen, T., 1964. Intracarotid sodium amytal for lateralization of speech dominance. J. Neurosurg. 21, 399–405.

Broca, P., 1864. In: Bulletins et Memoires de la Société Anatomique de Paris, Anatomical Society of Paris, Paris, Vol. 36, pp. 330–357.

Buchner, H., Ludwig, I., Waberski, T., Wilmes, K., Ferbert, A., 1995. Hemispheric asymmetries of early cortical somatosensory evoked potentials revealed by topographic analysis. Electromyogr. Clin. Neurophysiol. 35, 207–215.

Buchner, H., Scherg, M., 1991. Analyse der Generatoren früher kortikaler somatosensibel evozierter Potenziale (N. medianus) mit der Brain Electric Source Analysis. Z. EEG-EMG 22, 62–69.

Cox, R.W., 1996. AFNI: software for analysis and visualization of functional magnetic resonance NeuroImages. Comput. Biomed. Res. 29, 162–173.

Dassonville, P., Zhu, X.-H., Ugurbil, K., Kim, S.-G., Ashe, J., 1997. Functional activation in motor cortex reflects the direction and the degree of handedness. Proc. Natl. Acad. Sci. USA 94, 14015–14018.

Deiber, M.P., Giard, M.H., Mauguière, F., 1986. Separate generators with distinct orientations for N20 and P22 somatosensory evoked potentials to finger stimulation? Electroenceph. Clin. Neurophysiol. 65, 321–334.

Desmedt, J.E., 1985. Critical neuromonitoring at spinal and brainstem levels by somatosensory evoked potentials. Cent. Nerv. Syst. Trauma 2, 169–186.

Desmedt, J.E, Bourguet, M., 1985. Color imaging of parietal and frontal somatosensory potential fields evoked by stimulation of the median or posterior tibial nerve in man. Electroenceph. Clin. Neurophysiol. 62, 1–17.

Forss, N., Hari, R., Salmelin, R., Ahonen, A., Hämäläinen, M., Kajola, M., Knuutila, J., Simola, J., 1994. Activation of the human posterior parietal cortex by median nerve stimulation. Exp. Brain Res. 99, 309–315.

Foundas, A.L., Leonard, C.M., Gilmore, R., Fennell, E., Heilman, K.M., 1994. Planum temporale asymmetry and language dominance. Neuropsychologia 32, 1225–1231.

Foundas, A.L., Leonard, C.M., Heilman, K.M., 1995. Morphological asymmetries and handedness. The pars triangularis and planum temporale. Arch. Neurol. 52, 501–508.

Geffen, G., Caudrey, D., 1981. Reliability and validity of the dichotic monitoring test for language laterality. Neuropsychologia 19, 413–423.

Geschwind, N., Levitsky, W., 1968. Human brain: left-right asymmetries in temporal speech regions. Science 161, 186–187.

Gobbelé, R., Buchner, H., Scherg, M., Curio, G., 1999. Stability of high-frequency (600 Hz) components in human somatosensory evoked potentials under variation of stimulus rate—evidence for a thalamic origin. Clin. Neurophysiol. 110, 1659–1663.

Good, C.D., Johnsrude, I., Ashburner, J., Henson, R.N., Friston, K.J., Frackowiak, R.S., 2001. Cerebral asymmetry and the effects of sex and handedness on brain structure: a voxel-based morphometric analysis of 465 normal adult human brains. NeuroImage 14, 685–700.

Habib, M., Robichon, F., Lévrier, O., Khalil, R., Salamon, G., 1995. Diverging asymmetries of temporo-parietal cortical areas: a reappraisal of Geschwind/Galaburda theory. Brain Lang. 48, 238–258.

Hécaen, H., De Agostini, M., Monzon-Montes, A., 1981. Cerebral organization in left-handers. Brain Lang. 12, 261–284.

Hluštík, P., Solodkin, A., Gullapalli, R.P., Noll, D.C., Small, S.L., 2001. Somatotopy in human primary motor and somatosensory hand representations revisited. Cereb. Cortex 11, 312–321.

Hugdahl, K., Carlsson, G., Uvebrant, P., Lundervold, A.J., 1997. Dichotic-listening performance and intracarotid injections of amobarbital in children and adolescents. Arch. Neurol. 54, 1494–1500.

Jäncke, L., 1992. Ein deutscher dichotischer Konsonant-Vokal-Recall- und Monitoring-Test. Reliabilität und Vergleich beider Prozeduren. Z. Neuropsychol. 3, 143–156.

Jäncke, L., Schlaug, G., Huang, Y., Steinmetz, H., 1994. Asymmetry of the planum parietale. NeuroReport 5, 1161–1163.

Jäncke, L., Steinmetz, H., 1993. Auditory lateralization and planum temporale asymmetry. NeuroReport 5, 169–172.

Jung, P., Baumgärtner, U., Magerl, W., Treede, R.-D., 2002. Hemispheric asymmetry of cortical generators of the median nerve somatosensory evoked potential. Brain Topogr. 14, 345–346 (abstract).

Kakigi, R., 1994. Somatosensory evoked magnetic fields following median nerve stimulation. Neurosci. Res. 20, 165–174.

Kany, C., Treede, R.-D., 1997. Median and tibial nerve somatosensory evoked potentials: middle-latency components from the vicinity of the secondary somatosensory cortex in humans. Electroenceph. Clin. Neurophysiol. 104, 402–410.

Kawamura, T., Nakasato, N., Seki, K., Kanno, A., Fujita, S., Fujiwara, S., Yoshimoto, T., 1996. Neuromagnetic evidence of pre- and post-central cortical sources of somatosensory evoked responses. Electroenceph. Clin. Neurophysiol. 100, 44–50.

Knecht, S., Drager, B., Deppe, M., Bobe, L., Lohmann, H., Floel, A., Ringelstein, E.B., Henningsen, H., 2000. Handedness and hemispheric language dominance in healthy humans. Brain 123, 2512–2518.

Lagerlund, T.D., Sharbrough, F.W., Jack, C.R., Erickson, B.J., Strelow, D.C., Cicora, K.M., Busacker, N.E., 1993. Determination of 10–20

system electrode locations using magnetic resonance image scanning with markers. Electroenceph. Clin. Neurophysiol. 86, 7–14.

LeMay, M., 1992. Left-right dissymmetry, handedness. AJNR 13, 493–504.

Mauguière, F., Desmedt, J.E., 1991. Focal capsular vascular lesions can selectively deafferent the prerolandic or the parietal cortex: somatosensory evoked potentials evidence. Ann. Neurol. 30, 71–75.

Mauguière, F., Desmedt, J.E., Courjon, J., 1983. Astereognosis and dissociated loss of frontal or parietal components of somatosensory evoked potentials in hemispheric lesions. Detailed correlations with clinical signs and computerized tomographic scanning. Brain 106, 271–311.

Moffat, S.D., Hampson, E., Lee, D.H., 1998. Morphology of the planum temporale and corpus callosum in left handers with evidence of left and right hemisphere speech representation. Brain 121, 2369–2379.

Oldfield, R.C., 1971. The assessment and analysis of handedness: the Edinburgh Inventory. Neuropsychologia 9, 97–113.

Pivik, R.T., Broughton, R.J., Coppola, R., Davidson, R.J., Fox, N., Nuwer, M.R., 1993. Guidelines for the recording and quantitative analysis of electroencephalographic activity in research contexts. Psychophysiology 30, 547–558.

Rossini, P.M., Narici, L., Martino, G., Pasquarelli, A., Peresson, M., Pizzella, V., Tecchio, F., Romani, G.-L., 1994. Analysis of interhemispheric asymmetries of somatosensory evoked magnetic fields to right and left median nerve stimulation. Electroenceph. Clin. Neurophysiol. 91, 476–482.

Sanes, J.N., Donoghue, J.P., Thangaraj, V., Edelman, R.R., Warach, S., 1995. Shared neural substrates controlling hand movements in human motor cortex. Science 268, 1775–1777.

Scherg, M., 1992. Functional imaging and localization of electromagnetic brain activity. Brain Topogr. 5, 103–111.

Schneider, P., Scherg, M., Dosch, H.G., Specht, H.J., Gutschalk, A., Rupp, A., 2002. Morphology of Heschl's gyrus reflects enhanced activation in the auditory cortex of musicians. Nature Neurosci. 5, 688–694.

Sörös, P., Knecht, S., Imai, T., Gurtler, S., Lutkenhoner, B., Ringelstein, E.B., Henningsen, H., 1999. Cortical asymmetries of the human somatosensory hand representation in right- and left-handers. Neurosci. Lett. 271, 89–92.

Springer, S.P., Deutsch, G., 1997. Left Brain, Right Brain: Perspective from Cognitive Neuroscience, fifth ed. Freeman, New York.

Steinmetz, H., Volkmann, J., Jäncke, L., Freund, H.-J., 1991. Anatomical left-right asymmetry of language-related temporal cortex is different in left- and right-handers. Ann. Neurol. 29, 315–319.

Valeriani, M., Restuccia, D., Di Lazzaro, V., Le Pera, D., Scerrati, M., Tonali, P., Mauguière, F., 1997. Giant central N20-P22 with normal area 3b N20-P20: an argument in favour of an area 3a generator of early median nerve cortical SEPs? Electroenceph. Clin. Neurophysiol. 104, 60–67.

Volkmann, J., Schnitzler, A., Witte, O.W., Freund, H.-J., 1998. Handedness and asymmetry of hand representation in human motor cortex. J. Neurophysiol. 79, 2149–2154.

Weinberger, D.R., Luchins, D.J., Morishisa, J., Wyatt, R.J., 1982. Asymmetrical volumes of the right and left frontal and occipital regions of the human brain. Neurology 11, 97–100.

Wernicke, C., 1874. Der aphasische Symptomenkomplex. Franck & Weigert, Breslau.

White, L.E., Andrews, T.J., Hulette, C., Richards, A., Groelle, M., Paydarfar, J., Purves, D., 1997. Structure of the human sensorimotor system. II. Lateral symmetry. Cereb. Cortex 7, 31–47.

White, L.E., Lucas, G., Richards, A., Purves, D., 1994. Cerebral asymmetry and handedness. Nature 368, 197–198.

Witelson, S.F., Kigar, D.L., 1992. Sylvian fissure morphology and asymmetry in men and women: bilateral differences in relation to handedness in men. J. Comp. Neurol. 323, 326–340.

Yousry, T., Schmid, U.D., Jassoy, A.G., Schmidt, D., Eisner, W.E., Reulen, H.-J., Reiser, M.F., Lissner, J., 1995. Topography of the cortical hand area: prospective study with functional MR imaging and direct motor mapping at surgery. Radiology 195, 23–29.

Zatorre, R.-J., 1989. Perceptual asymmetry on the dichotic fused words test and cerebral speech lateralization determined by the carotid sodium amytal test. Neuropsychologia 27, 1207–1219.