Structural and Functional Asymmetry in the Human Parietal Opercular Cortex

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List of abbreviations:

CS = central sulcus; ECD = equivalent current dipole; FO = frontal operculum; GA = grand average; GFP = global field power; ICC = intraclass correlation coefficient; INS = insula; LI = laterality index; l/rMN = left/right median nerve; NRH/RH = inconsistent/consistent right-handers; OIC = operculoinsular cortex; a/pPO = anterior/posterior portion of the parietal operculum; PSS = posterior subcentral sulcus; PT = planum temporale; RPS = regional probe source; RS = regional source; SF = sylvian fissure; SI = primary somatosensory cortex; SIIc/i = contra-/ipsilateral secondary somatosensory cortex; Tc/i = contra-/ipsilateral temporal electrode positions

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Abstract

In this combined EEG and MRI study, the asymmetry of functional and structural measures in the human parietal operculum (PO) were investigated. Median nerve SEP recordings showed maximum scalp potentials over contra- (N80, N110) and ipsilateral (N100, N130) temporal electrode positions. In accordance, MRI-coregistered source analysis revealed two electrical sources in the contra- (N80, N110), and two in the ipsilateral (N100, N130) PO. The dipole orientations of the contra- and ipsilateral sources with earlier peak activation, N80 and N100, were more tangential than those of the later peaking N110 and N130 sources. The most prominent contralateral N110 source exhibited pronounced left lateralized dipole strengths in the 80 – 120 ms latency range, in contrast to symmetrical N80 and ipsilateral source responses. The asymmetry of the N110 source activity explained both the asymmetry of N110 and N100 scalp potentials. Morphometric analysis demonstrated no interhemispheric differences in the sizes of the anterior PO (aPO), containing the cytoarchitectonic areas OP3 and OP4, but left lateralized sizes of the posterior PO (pPO), which encompasses the anatomically defined areas OP1 and OP2. The N110 source was located in the pPO, and its asymmetry was significantly correlated with the structural pPO asymmetry but not with handedness and auditory lateralization. Thus, both structural and functional asymmetries exist in the human PO, and they are closely related to each other but not to measures of brain asymmetry in other functional systems, i.e. auditory lateralization and handedness.

Keywords: brain asymmetry, dipole source analysis, operculum, secondary somatosensory cortex, median nerve
Introduction

In humans, innocuous somatosensory stimuli elicit earliest and most prominent cortical activations in the contralateral primary somatosensory (SI) and bilateral operculoinsular cortex (OIC) (Backes et al. 2000; Burton et al. 1993; Coghill et al. 2001; Hari and Forss 1999; Maldjian et al. 1999). The OIC comprises multiple cortical regions, i.e. the insula (INS), the frontal operculum (FO), the retroinsular cortex, the parietal operculum (PO) and the secondary somatosensory cortex (SII). The latter two are often used as synonyms. Predominant MEG and EEG responses in the OIC occur in the latency range of 70-150 ms following Aβ fibre stimulation of the hand and were mostly attributed to SII (García-Larrea et al. 1995; Hari et al. 1983; Hoechstetter et al. 2001; Kany and Treede 1997; Mima et al. 1998). Most previous MEG and EEG investigations using spatio-temporal source analysis described only one electrical source within the OIC whose location largely varied in the anterior-posterior direction between studies (Forss et al. 1994; Hari et al. 1983; Hoechstetter et al. 2001; Mauguière et al. 1997; Mima et al. 1998; Stancak et al. 2002). Similarly, laser stimulation of nociceptive Aδ afferents exhibited large variations of dipole source locations in the supra-sylvian cortex (García-Larrea et al. 2003). Subdural EEG recordings and MEG source analysis in a patient with a left frontal brain tumor revealed two different hand somatosensory areas within the OIC (Mima et al. 1997). The two electrical sources were about 1.5 cm apart. The more anteromedially located source was maximally active at 85 ms, the activity of the posterior source peaked at 110-125 ms. FMRI and PET studies confirmed these results in healthy subjects, demonstrating activation foci in both PO (i.e. the SII region) and the more anteriorly located INS or FO after somatosensory stimulation (Disbrow et al. 2000; Ferretti et al. 2003; Gelnar et al. 1999). Disbrow et al. (2000) proposed a further functional subdivision of the human SII region/PO into two different somatosensory areas (PV
and SII), analogous to previous findings in non-human primates (Burton et al. 1995; Krubitzer et al. 1995). The anatomical basis for this was recently provided in a postmortem study in which four different cytoarchitectonic areas (OP1-4) in the human SII region/PO were identified (Eickhoff et al. 2006a). Eickhoff and coworkers (2006a) pointed out that i) the functional ‘PV area’ corresponds to the cytoarchitectonic ‘area OP4’, ii) the ‘SII area’ is equivalent to ‘area OP1’, and iii) the areas PV and SII denote individual areas within the ‘SII region’. The finding of at least two active regions within the OIC during innocuous and painful stimulation thus yielded a possible explanation for the large anterior-posterior variability of electrical operculoinsular source locations in MEG/EEG studies. Stancak et al. (2005) further clarified this issue by utilizing high spatial accuracy of fMRI as a basis for high temporal resolution EEG source analysis. They found two electrical sources in the fronto-parietal operculum located about 2.5 cm apart. The anterior source in the frontal operculum showed a peak latency of about 80 ms and was tangentially oriented, the posterior source in the parietal operculum peaked at about 120 ms and was rather radially oriented. Different peak latencies and orientations of SEP generators in the opercular cortex have already been proposed by Allison et al. (1989) who found an early response at 100 ms of tangential and a later one at 125 ms of radial orientation in their intracranial EEG recordings. The differences of dipole orientations between the two operculoinsular sources also elucidated the frequent observation of earlier peak latencies of operculoinsular responses in MEG (70-90 ms) (Forss et al. 1994; Hoechstetter et al. 2001; Simões et al. 2002) than EEG studies (110-130 ms) (Kany and Treede 1997; Kunde and Treede 1993; Stancak et al. 2002) because MEG is only sensitive to tangential current flows (Hämäläinen et al. 1993) and EEG is more sensitive to radial than tangential dipolar electrical sources.
Few studies have investigated hemispheric asymmetry of operculoinsular responses. One previous EEG study (Kany and Treede 1997) reported higher N110 amplitudes over left- than right-sided temporal electrode positions after non-painful median nerve (MN) stimulation. In MEG, higher dipole strengths were determined for left operculoinsular sources in side comparison (Alary et al. 2002; Forss et al. 1994; Simões et al. 2002). A left-hemisphere dominance of supra-sylvian dipole sources was also described in nociceptive processing (Schlereth et al. 2003).

In this study, we aimed at investigating hemispheric asymmetry of the different electrical sources in the human OIC using MRI-coregistered spatio-temporal EEG source analysis. FMRI and PET were not chosen due to their limited temporal resolution. EEG was favored over MEG in this study, because it records scalp potentials resulting from both tangential and radial intracranial current flows and thus has the potential to detect operculoinsular responses with both peak latencies at 70-90 ms (tangential) and 110-130 ms (radial). In addition, morphometry of the parietal opercula in both hemispheres was executed to evaluate the relation between functional and structural lateralization measures in the human opercular cortex. Finally, we tested if these measures were correlated with well known lateralized brain functions in humans, i.e. handedness and speech dominance.

**Materials and Methods**

**Subjects**

We investigated 16 healthy subjects (ages ranged from 23 to 28 years, mean age: 24.3 years; 8 female). The study was approved by the local ethics committee and conducted with the informed consent of each subject.
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 and EEG recording**

Constant-current square-wave pulses of 0.2-ms duration were delivered in separate runs to either the left (lMN) or the right (rMN) median nerve at the wrist. The stimulus intensity was set at the sum of the individual sensory and motor threshold and was occasionally adjusted to elicit a non-painful sensation. Symmetric activation of both median nerves was verified by recording the N10 potential at Erb’s point (Jung et al. 2003). The interstimulus interval (ISI) varied between 2 and 5 s. For the recording of the median nerve SEP, a time window of 300 ms including a 50 ms prestimulus interval, a bandpass filter of 0.16–500 Hz, a sampling rate of 2.5 kHz and a 32-channel-EEG montage were chosen. In addition to the standard 19 positions of the 10-20 system (Pivik et al. 1993), EEG electrodes were added in the frontocentral (FC5, FC1, FC2, FC6) and centroparietal (CP5, CP1, CP2, CP6) region, on the zygomatic arch (F9, F10), the preauricular points (T9, T10), and the mastoids (P9, P10) in order to increase electrode densities around primary and secondary somatosensory cortices which were expected to evoke highest cortical activities. SEP amplitudes were measured baseline to peak versus the average reference. The baseline was defined as the mean amplitude of the 5 to 12 ms poststimulus interval. Artifacts were rejected visually in all single trials before averaging. For each stimulus side, about 500 trials were averaged per subject. The order of conditions (2 runs each for left and right MN stimulation) was systematically balanced across subjects.

**MR image acquisition and normalization**
Structural T1-weighted images were acquired (FLASH 3D, TR 14 ms, TE 4 ms, flip angle 25°, 256-mm field of view, 256 x 256 matrix, voxel size 1.0 mm³) on a 1.5 Tesla Siemens Magnetom Vision scanner. The MR images were aligned to the anterior commissure (AC)–posterior commissure (PC) plane and transferred into Talairach space using Brain Voyager (www.brainvoyager.com). Prior to MRI acquisition, each EEG electrode was replaced by vitamin E capsules to later determine its spatial coordinates on MRI. The individual electrode coordinates in Talairach space were the basis for calculation of the best-fitting 4-shell ellipsoidal head model in BESA (Brain Electrical Source Analysis software) (Scherg 1992) which was then used for dipole source analysis.

**Dipole source analysis**

The dipole source modeling was data-driven and was first performed on the basis of Grand Average (GA) EEG data since this provided the highest signal-to-noise ratio (SNR) with 16 x 500 averaged trials per stimulus side. Our fit strategy consisted of sequentially adding either a single regional source (brainstem, SI) or a symmetrical pair of regional sources (SII) to the model. A regional source (RS) is a source with three single dipoles at the same location but with orthogonal orientations that can represent the electrical activity of a small volume of the brain irrespective of its orientation. Fitting a RS thus involves three degrees of freedom (location only) whereas a single dipole has 5 degrees of freedom (location and orientation). Dipole orientation is determined in later steps by orthogonal rotation of the RS; in this way, one orientation is identified that explains the strongest activity in that region. In many cases (here: P14, P30, N60) the other two orientations do not explain any activity. In other cases (here: all SII sources) a second orientation explains another part of the activity and only the third orientation can be neglected. The sequential fit strategy
described below was terminated if the Goodness-of-Fit value (GoF) was > 95 % in the analysis time window (10-150 ms). In a final step, all cortical sources were refitted in the 10-150 ms time interval. Stability of the source model was assumed if all sources moved less than 2 cm in all spatial directions. Validity of the source model was tested by adding 15 regional probe sources (RPS) which were uniformly distributed and predefined by BESA’s default source montage “BR_Brain Regions_LR.bsa”. Five RPS were located midsagittally in the frontopolar, frontal, central, parietal and occipital region, and 5 symmetrical RPS were at lateral frontal, central, parietal, anterior temporal and posterior temporal regions in right and left hemispheres. In the next step, RPS with an Euclidean Distance of < 3 cm to one of our fitted RS (i.e. RPS in the lateral central and posterior temporal regions) were switched off since these RPS were likely to pick up activity that was already sufficiently represented by the nearby fitted sources. The remaining 11 RPS increased the GoF within the 10-150 ms latency range by less than 2 %, and showed no relevant activity in their source waveforms or source activity waveforms that were very similar to one of the fitted sources. Hence, no probe sources were identified that picked up relevant residual activity. A similar fit strategy was then applied to every individual.

SEP components were identified as peaks in the Global Field Power (GFP, i.e. the spatial standard deviation of amplitudes in the different EEG channels as a function of time) and modeled in the order of their GFP appearance. One RS was fitted for the subcortical P14 and another RS for the cortical P30 component in their onset-to-peak time intervals in the GFP. Another two symmetrical RS were fitted for a later GFP peak arising over a latency range of 70-110 ms in which the predominant SII activity was presumed (Hoechstetter et al. 2001). Two symmetrical RS were chosen since SII is activated bilaterally by unimanual somatosensory input (Disbrow et al. 2001;
Hari et al. 1983; Eickhoff et al. 2008) and its responses show no significant
topographical differences to ipsi- and contralateral stimuli in either hemisphere
(Wegner et al. 2000). The RS of the P14 and P30 component were located in the
brainstem and contralateral primary (S1c) cortex, respectively (Fig. 2A). The sources
that were fitted in the 70-110 ms time window were localized in contra- (SIIc) and
ipsilateral (SIIi) secondary somatosensory cortices (Fig. 2A). Finally, RS were rotated
such that a single orientation explained maximum activity during the time window of
the source fit. RS were then converted into three orthogonal orientated equivalent
current dipoles (ECDs) and those ECDs showing no relevant deflections in their
source waveforms were rejected from the source model. Thus, a model with one
ECD in the brainstem, one in area 3b of S1c, two ECDs in SIIc and two in SIIi was
obtained (Fig. 2A). It was evident that this source model could not sufficiently explain
our scalp SEP data at a latency of 60 ms (N60 component). Thus, another RS was
fitted at that latency and finally converted into a single ECD. It has been recently
described (Jung et al. 2008) that its putative generator is area 1 of S1c (Fig. 2A).
Since the present study was designed to investigate middle and late latency SEP
components, dipole fits of the earliest SEP components N20 and P22 were not
included in the source model because i) the high pass filter settings were not optimal
to fit these components (cf. Jung et al. 2003), ii) the SNR is much higher for the later
P30 and N60 components at a relatively long and variable ISI between 2 and 5 s,
and iii) the P30 and the N60 ECDs sufficiently explain electrical activity at 20 and 22
ms, respectively (cf. Jung et al. 2008).
In the case of instable RS fits on individual data, spatial coordinates of GA dipole
solutions were used (2 x for P14 after rMN stimulation, 4 x for N60 for each stimulus
side, symmetrical SII locations in 2 subjects). If the SII source modeling was instable
after MN stimulation at one side (1 x rMN, 3 x IMN), spatial SII coordinates fitted for
stimulation of the other MN were inserted for that individual. This approach is based on the assumption that the same part of SII is activated from both stimulus sides; this assumption was based on the existence of bilateral receptive fields in individual neurons, and was verified in those 10 subjects for whom SII source location fits were available for both median nerves. In these subjects, no significant differences in the paired t test were found for the left SII source location after contralateral rMN and ipsilateral IMN stimulation and vice versa. To give equal weight to each subject and to both stimulus sides, symmetric SII locations of either the right or left stimulus side were randomly chosen in subjects where stable SII RS fits were possible for both the rMN and the IMN (10 subjects) and in the two subjects for whom GA SII coordinates had to be inserted. Thus, for the final source analysis, bilateral symmetric SII locations of rMN data were used in 8 subjects, and of IMN data in the remaining 8 subjects. By this approach, interhemispheric differences are restricted to dipole orientations and strengths. This strategy was favored over the utilization of both rMN and IMN individual SII location fits in these subjects because source modeling is less reliable in detecting small location shifts. In contrast, source orientation fits are much more reliable and robust. Hence, the orientations were fitted to both individual rMN and IMN data in all subjects. By this strategy, we excluded the detection of falsely lateralized source activities in those subjects where SII locations were slightly deeper in one than the other hemisphere. Deeper source locations in one hemisphere would result in higher source strengths even if the scalp potentials were symmetrical.

ECD orientations were denoted as unit vectors whose direction was specified by its components in the x, y, and z directions. The scalar product was calculated to determine the angle between a data-driven fitted SII dipole orientation and a hypothetical SII dipole directly pointing at a particular electrode (T3 or T4); that
hypothetical orientation would lead to maximal projection of the dipole source activity on an EEG lead between that electrode and the common average reference.

**Measures of functional hemispheric asymmetry**

Dichotic listening tests are regarded as non-invasive tools that yield valid estimates of hemispheric speech dominance (Geffen and Caudrey 1981; Hugdahl et al. 1997). After hearing impairments were excluded by audiometry, dichotic listening tests were performed in all subjects. The dichotic stimuli were simultaneously presented via headphones to both ears and consisted of different consonant-vowel syllables whose volume and basic frequency were equalized. Four blocks of 30 dichotic trials in different sequences were presented and 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. A right ear advantage indicates left hemisphere dominance of auditory processing and vice versa. Handedness was evaluated according to the 10-item version of the Edinburgh Inventory (Oldfield 1971). Subjects were classified into two handedness groups of either consistent (RH, LI > 80) or inconsistent (NRH, LI ≤ 80) right-handers, according to previous suggestions to analyze the relation between handedness and other structural-functional measures in small sample sizes (LeMay 1992; Habib et al. 1995).

**MRI morphometry**

The size of the parietal operculum (PO) was measured on AC-PC aligned MR images. The AC was defined as x = 0, y = 0, z = 0, in conformity with the Talairach coordinate system (Talairach and Tournoux 1988). The PO was further subdivided into an anterior (aPO) and a posterior (pPO) area. The anterior and posterior borders
of aPO and pPO were defined on sagittal MRI slices, in line with the common borders between the cytoarchitectonic PO areas OP4 and OP1 that were reported by Eickhoff et al. (2006a), i.e. the y level of the lateral end of the central sulcus (CS) corresponded to the anterior border of aPO, and the conjunction of the Sylvian Fissure (SF) with the posterior subcentral sulcus (PSS) was the posterior border of aPO and anterior limit of pPO, the posterior limit of SF was concordant with that of pPO. Thus, it was assumed that aPO primarily contained the cytoarchitectonic areas OP3 and OP4, and pPO predominantly encompassed areas OP1 and OP2 (Eickhoff et al. 2006a). The most medial point of the SF or circular sulcus of insula represented the medial limits of aPO and pPO, lateral limits were indicated by the lip of SF at the hemispheric surface. Using the freeware image analysis program ImageJ, the contour of the upper wall of SF was traced on coronal images in 2 mm steps between the anterior border of aPO and the posterior limit of pPO. Finally, the area of aPO and pPO was calculated by summing the trapezoidal areas between adjacent sections (cf. Jung et al. 2003).

**Statistical analysis**

Mean source waveforms and their 95% confidence intervals were calculated by using the bootstrap BCₐ method (Efron and Tibshirani 1993; Hoechstetter et al. 2001). Significance was assumed at latencies where the confidence intervals did not include the baseline.

Laterality indices (LI) were computed to assess the direction and degree of auditory lateralization (speech dominance), handedness, asymmetry of strengths of SII sources and PO asymmetry, due to the following formula:

\[
LI = \frac{R-L}{R+L} \times 100
\]
where R is right ear score, right hand score, left-hemispheric strength or eccentricity of SII sources and PO areas and L indicates the same measures of the other side. Thus, positive values indicate right ear advantage, right hand preference, higher left SII source strengths or greater extension of the PO area in the left hemisphere.

Paired two-tailed t tests were performed to test for interhemispheric differences of ECD orientations, strengths as well as aPO and pPO sizes. Unpaired two-tailed t tests were used to estimate differences between handedness groups. Spearman’s linear regression analysis was utilised to test for correlations between asymmetric measures (ear advantage, handedness, SII source strength, PO area). The intra- and interrater reliability of the PO borders were assessed by interclass correlation coefficients (ICC).

All data are presented as mean \( \pm \) SEM unless otherwise stated. Statistical significance was assumed if \( p < 0.05 \).
Results

Scalp potentials of long latency SEP components

Our analysis was focused on scalp potentials in the 70-150 ms poststimulus interval (long latency range). A detailed study on earlier SEP components, generated in SIc, has been recently published (Jung et al. 2008). In the long latency range, highest amplitudes were measured over T3 and T4 EEG electrodes after MN stimulation (Fig. 1) and maximum amplitudes were recorded at 110 ms (N110) at contralateral temporal electrode positions (Tc). An earlier and less prominent peak over Tc was also visible at about 80 ms (N80) in the GA scalp potential waveforms (Fig. 1A) but it was only delineable from the N110 potential in 7 out of 16 subjects. Maximum amplitudes over ipsilateral temporal electrode sites (Ti) were determined at 100 ms (N100) and 130 ms (N130, Fig. 1A). In interhemispheric comparison, contralateral N80 scalp potentials revealed no differences but higher amplitudes of the contralateral N110 and ipsilateral N100 components were recorded at left temporal electrode positions (Table 1, Fig. 1). As a result, contralateral N110 potentials were stronger than ipsilateral N100 amplitudes after stimulation of the right MN (-4.01 ± 0.44 μV vs. -1.36 ± 0.24 μV, p < 0.001) but similar after left-sided stimulation (-2.08 ± 0.40 μV vs. -2.80 ± 0.28 μV, n.s.) (Table 1). In the case of N130 scalp potentials, no reliable latency and amplitude measurements were possible on individual basis, due to their superimposition with the N140 vertex negativity in most subjects (García-Larrea et al. 1995; Kunde and Treede 1993).

Source analysis of long latency SEP components

Spatio-temporal source analysis revealed two electrical generators of dipolar shape in both the contra- (N80, N110) and the ipsilateral (N100, N130) SII region/PO (Fig. 2A). Their Talairach coordinates in mm were x = |−41.1| ± 1.6, y = −31.5 ± 2.1, z =
Both sources in SIIc showed peaks in their source waveforms at 80 ms (Fig. 2B), explaining the N80 scalp potential. In addition, the N110 scalp potential was reflected by another later and more prominent peak at 110 ms in the source activity waveform of the N110 SIIc ECD (Fig. 2B).

Although the interindividual variability of SII source orientations was relatively high, N110 ECDs demonstrated a significantly stronger projection to contralateral temporal electrode positions (Tc, i.e. T3 or T4) than N80 ECDs by virtue of their source orientation. To assess how well N80 and N110 sources projected to Tc, we measured the angle between the source orientations and a vector pointing directly at Tc. This angular deviation between our modeled SIIc source orientations and the orientations of sources with the same location but with optimal radial negative projection onto Tc was significantly smaller for N110 than N80 ECDs (47 ± 6° vs. 64 ± 5°, p < 0.04). In the ipsilateral SII, N100 ECDs accounted for N100 deflections on the scalp and N130 ECDs reflected the N130 scalp potentials (Fig. 2B) which were only clearly visible on grand averaged but not on individual EEG recordings. Although the source solutions that were analyzed on the basis of GA scalp potentials showed a more radial orientation of the N130 than the N100 ECD (Fig. 2B), this could not be confirmed in the analysis of individual source models. Here, no difference of N100 and N130 ECD orientations in projection to Ti was determined (58 ± 6° vs. 61 ± 5°, n.s.).

In left-right comparison, SIIc and SIIi sources showed no significant differences of peak latencies or dipole orientations but dipole strengths were clearly stronger in the left than in the right hemisphere for the N110 ECD (Table 2, Fig. 3A), and well explained amplitude asymmetry of the corresponding N110 scalp SEP component. Contributions of dipole location were not assessed due to our analysis strategy (see
Methods). In contrast, asymmetric N100 potentials with higher amplitudes over the left than the right Ti could not be attributed to side different dipole strengths or orientations of the accordant N100 ECD. Their asymmetry was primarily based on higher positive voltage production of contralateral N110 ECDs at the right than the left Ti at 100 ms (Fig. 3B) which was the case in 15 out of 16 subjects in a semiquantitative analysis of scalp voltage maps. Thus, the asymmetry of N110 ECD strengths accounted for the amplitude asymmetry of both N110 and N100 scalp potentials.

**Auditory lateralization, handedness and opercular morphometry**

All subjects showed a right ear advantage in the dichotic listening test. The corresponding LI was 26.0 ± 5.7. The mean handedness score was 69.7 ± 12.2. Six of our 16 subjects were assigned as inconsistent right-handers including two left-handers. Thus, left-handedness (12.5 %) was distributed as in the general population (Annett 1973). The results of morphometry are illustrated in Fig. 4. The intra- and interrater reliability of the PO borders were high, i.e. ICC values for intra- and interrater reliability were 0.917 and 0.907 (anterior aPO border), 0.913 and 0.823 (border between aPO and pPO), 0.945 and 0.884 (posterior pPO border), 0.999 and 0.999 (medial borders of aPO and pPO), and 1.000 and 0.999 (lateral borders of aPO and pPO). The aPO area did not significantly differ between left and right hemispheres (4.57 ± 0.28 cm² vs. 4.36 ± 0.28 cm²). Moreover, the anterior-to-posterior extent of the aPO was similar in both hemispheres (anterior border, CS-SF: y = -10.1 ± 1.0 mm, left; y = -10.2 ± 0.6 mm, right; posterior border, PSS-SF: y = -20.3 ± 1.1 mm, left; y = -19.7 ± 1.1 mm, right). The posterior limit of SF lay about 8 mm further posterior in the left than in the right hemisphere (y = -47.2 ± 1.4 mm vs. -39.4 ± 1.1 mm, p < 0.0001), in accordance with previous reports (Falkai et al. 1992;
Steinmetz et al. 1989). This resulted in a larger left pPO area (9.13 ± 0.41 cm² vs. 7.04 ± 0.41 cm², p < 0.005), detected in 14 out of 16 subjects. SII ECD sources were clearly located in the pPO in both hemispheres (Fig. 4C).

Relation between measures of structure and function in perisylvian cortex

N80 and N110 ECD strengths were not correlated with aPO or pPO sizes, neither in the left nor right hemisphere (all $\rho < 0.47$, n.s.). However, laterality indices (LI) between pPO size and SIIc source strengths were significantly related ($\rho = 0.51$, $p < 0.05$ for N80 ECD and $\rho = 0.69$, $p < 0.005$ for N110 ECD, Fig. 5). No such correlations were found for neither ipsilateral SII nor for combined ipsilateral and contralateral responses. Interestingly, the LI of N110 ECDs showed no correlation with the left hemispheric pPO size ($\rho = -0.02$, n.s.) but was strongly negatively correlated with the pPO size in the right hemisphere ($\rho = -0.84$, $p < 0.0001$). Similarly, the LI of pPO size was only moderately correlated with the pPO size in the left ($\rho = 0.53$, $p < 0.05$) but strongly negatively correlated with its size in the right hemisphere ($\rho = -0.80$, $p < 0.0001$). Thus, the pPO size in the right hemisphere seemed to determine functional and structural asymmetry in the posterior parietal operculum, i.e. the smaller the pPO area in the right cerebrum, the higher is the degree of pPO asymmetry.

Relation between left lateralized measures of perisylvian cortex and other functional systems

Auditory lateralization was neither related to the PO asymmetry nor to the LI of SIIc ECD strengths (all $\rho < 0.4$, n.s.). Moreover, no significant correlation was found between any of the structural and functional measures of the perisylvian cortex and
handedness (all $\rho < 0.3$). RH and NRH showed no significant differences in any LIs of the perisylvian cortex measures (all $p > 0.1$).

Our source analysis on early and middle latency SEP components has been recently published (Jung et al. 2008), where we described lateralized dipole strengths of the S1c source in area 3b at 20 ms (N20). The current and the previously published analysis were performed in the same subjects under the same experimental conditions. Hence, it was valid to correlate the laterality indices of the area 3b source strengths at 20 ms with those of the maximum N110 source strengths. The relation between the asymmetries of early S1c (N20) and SIIc (N110) processing was not significant ($\rho = 0.27$).
Discussion

Asymmetry of long latency scalp potentials

The lateralization of MN SEP components in the 70-150 ms latency range has received little notice in the literature. It has only been investigated in one previous EEG study (Kany and Treede 1997). In accordance with this previous study, we recorded maximum scalp potentials at 110 ms (N110) over contralateral temporal electrode positions (Tc) and determined significantly higher N110 amplitudes over the left than right scalp (Fig. 1, Table 1). Moreover, we detected an additional earlier N80 scalp potential that was also maximal at Tc but less prominent and consistent (only definable in 7/16 subjects) than the N110 SEP component. The N80 component showed no lateralized amplitudes. The asymmetry of ipsilateral long latency SEP components was analyzed for the first time. In this analysis, N100 amplitudes were stronger over the left than the right side of the scalp. An ipsilateral N130 SEP component was distinctly visible on GA data at temporal electrode positions (Fig. 1) but not sufficiently delimitable in the scalp potential waveforms of most subjects due to its interference with the N140 vertex negativity (García-Larrea et al. 1995; Kany and Treede 1997).

Number and localization of electrical sources in the operculo-insular cortex

We used regional sources (RS) for source analysis. A RS represents all cortical activity within a 3 cm sphere whose center is the RS location. In this study, two out of three RS components in the OIC showed relevant activity in their source waveforms in the 70-150 ms latency range, both contra- (N80, N110) and ipsilaterial (N100, N130) to MN stimulation. There are two possible explanations for this observation. First, relevant activity of two RS components might reflect a single generator whose extensive activation area comprises predominant dipolar current flows in two almost
orthogonal directions due to cortical folding. Second, it may represent two different generators in close spatial relationship. We definitely favor the latter possibility for the following reasons. First, the two contralateral RS components (N80, N110) showed different functional behaviour, which would not be expected from a single generator. N110 source activity was distinctly asymmetric whereas N80 strengths were not lateralized (Fig. 3A). Second, previous imaging studies on somatosensory processing reported evidence for at least two different generators in the OIC, one in the INS/FO and at least one in the SII region/PO, whose locations were only 0.9–2.5 cm apart from each other (Disbrow et al. 2000; Ferretti et al. 2003; Ledberg et al. 1995; Stancak et al. 2005). Thus, activity of these close-by cortical regions may be sufficiently described by one RS. This assumption was further supported by similar findings concerning ECD peak latencies and orientations of operculoinsular sources in this EEG work and that of Stancak et al. (2005). The previous report described one tangentially oriented ECD in the contralateral FO peaking at about 80 ms and one rather radially oriented ECD in the contralateral PO with a 120 ms-peak latency. This fits well with the present finding of two RS components in the OIC showing i) maximum activity at 80 (N80) and 110 ms (N110), and ii) on average more radially oriented N110 than N80 ECDs. The N110 component presumably dominated source location fitting due to the higher sensitivity of EEG to radial current flows. Thus, the RS of the OIC was located in the PO in this study, and not in the FO or INS. An additional attempt to find stable dipole solutions with two ECDs in different locations during the time window of maximum OIC activation was not successful due to the known difficulties in EEG to differentiate multiple simultaneously active cortical areas with high spatial resolution.

Alternative to activations in the INS/FO and the SII region/PO, N80/N100 and N110/N130 sources might indicate activation of two different functional areas within
the SII region/PO, as there is evidence for two separate somatotopic body representations on human PO in the functional areas PV and SII (Disbrow et al. 2000) and in their structural correlates OP1 and OP4 (Eickhoff et al. 2007), respectively. Further, the spatial accuracy of both EEG and MEG may not be sufficient to separate activity of areas in close neighborhood, e.g. INS/FO and aPO, and thus activity in both areas might be reflected by one tangentially oriented RS component, i.e. N80 or N100 in this study, if the main current flow in these areas is similarly oriented. However, again, the findings of the recent fMRI-constrained EEG source analysis study of Stancak and co-workers (2005) argue for a more probable location of N80 and N100 sources in the INS/FO than in the frontal SII subarea aPO, PV or OP4, because the properties (peak latencies, dipole orientations) of their contralateral INS/FO and SII/PO sources were strikingly similar to ours.

**Ipsilateral electrical activity in the operculo-insular cortex**

For source analysis in the opercular cortex, the current fit strategy to choose RS and the constraint of symmetrical locations enabled us to even analyse ipsilateral source components with a relatively low SNR. However, the present observation of two electrical sources (N100 and N130) in ipsilateral OIC after MN stimulation is novel and supported by previous fMRI studies which demonstrated bilateral foci of activation in both the INS/FO and the SII region/PO (Disbrow et al. 2000; Ferretti et al. 2007). In addition, intracerebral recordings in primates identified bilateral tactile receptive fields in a relevant proportion of neurons in the insula (Robinson and Burton 1980a) and SII (Robinson and Burton 1980b; Whitsel et al. 1969). This was further supported in MEG commonly showing bilateral somatosensory activation in the OIC (Simões and Hari 1999; Wegner et al. 2000). Moreover, the mean peak latency difference of 15-20 ms between contralateral N80 and ipsilateral N100 as well
as contralateral N110 and ipsilateral N130 sources is concordant with previous EEG and MEG studies (García-Larrea et al. 1995; Hari and Forss 1999). The analysis of GA data demonstrated that N100 ECDs are rather tangentially and N130 ECDs are rather radially oriented, similar to their contralateral counterparts N80 and N110 (Fig. 2A). Thus, N80 and N100 as well as N110 and N130 sources may represent contra- and ipsilateral activation in the INS/FO and the SII region/PO, respectively. The fibre pathways that mediate bilateral activation in OIC are still under debate (Forss et al. 1999; Stancak et al. 2002); the corpus callosum is one eligible structure (Disbrow et al. 2003) and the current 15-20 ms-latency delay of ipsilateral responses is in line with the anticipated transcallosal conduction time (Jung and Ziemann 2006; Meyer et al. 1998).

**Functional asymmetry in the operculo-insular cortex**

The asymmetry of the contralateral N110 SEP component with higher amplitudes over the left than the right side of the scalp (Fig. 1, Table 1) was explained by the lateralized N110 source activation in the contralateral SII area (Fig. 3A, Table 2). In contrast, the asymmetry of ipsilateral N100 SEP amplitudes was not caused by lateralized N100 source strengths but was, again, due to the lateralized N110 source activity. The latter showed high source activation at N100 peak latency (Fig. 2B) and projected higher positive voltage on ipsilateral temporal electrode positions after rMN than IMN stimulation (Fig. 3A). Amplitudes of the contralateral N80 SEP component showed no significant side differences (Table 1). However, the analysis of N80 peak amplitudes was little reliable because i) they were superimposed with the up slope of the N110 SEP component, ii) the statistical power in detecting side differences of N80 scalp potentials was reduced because their delineation was only possible in 44% of our subjects and iii) the results based on individual scalp potential waveforms
were inconsistent with GA data which argued strongly for asymmetric N80 SEP components (Fig. 1A). In source analysis, the N80 ECDs showed equivalent peak latencies to N80 scalp potentials (Tables 1 and 2). The strength of the operculo-insular N80 ECDs was not lateralized (Fig. 3A) which is discrepant to results of some MEG studies that found higher source strengths in the left than in the right OIC (Forss et al. 1994; Simões et al. 2002; Wegner et al. 2000). In these studies, only one ECD was fitted in the OIC. Hence it is likely that both N80 and N110 source activities were depicted and superimposed in the source waveform of the single ECD.

This study showed that N110 source activities had already been significantly lateralized at maximum N80 source strengths (Fig. 3A). As a result, the asymmetry of the single operculoinsular ECD with maximum source activity at about 80 ms in these MEG studies might have been pretended by the projected pronounced asymmetry of the N110 generator in this time range.

The N110 ECD location was attributed to the contralateral SII area (Fig. 4). The SII area is regarded as a higher-order association area in somatosensory processing, producing rather complex computations of tactile stimuli and being crucially involved in functions like vibrotactile discrimination (Brody et al. 2002), haptic object recognition (Haggard 2008) and integration of tactile information from the two body halves (Dijkerman and de Haan 2007). The SII area receives input from multiple cortical areas, i.e. the thalamus, the different areas of SI, the posterior parietal cortex, the insula, the premotor cortex and the SII area of the opposite hemisphere. In contrast, earliest cortical somatosensory processing in area 3b of SI is mediated via direct thalamic projections and is supposed to concern relatively simple features such as stimulus location and duration (Dijkerman and de Haan 2007). The N20 component reflects the earliest cortical response in area 3b of SI after contralateral MN stimulation. It shows left hemisphere dominance (Jung et al. 2003; Jung et al.
2008; Theuvenet et al. 2005), as it was also demonstrated for SIIc processing at 110 ms (N110) in this study. However, the asymmetry of cortical activity in area 3b at 20 ms showed no correlation with the asymmetry of SII activity at 110 ms. This lack of a simple linear relation between asymmetries in area 3b and area SII could be anticipated because i) not only area 3b but multiple cortical areas project to the SII area, ii) initial processing steps within SI may precede the information transfer from SI to SII, iii) subsequent processing in SI, as reflected by the P30 and N60 MN SEP components, did not show functional lateralization (Jung et al. 2008), and iv) the stimulus features proceeded in area 3b and SII are quite different.

The N110 response presumably reflects an early processing stage in the SII area. Thus, in analogy to SI, its left hemisphere dominance might rapidly resolve in further processing. As a consequence, functional lateralization in these areas would be blurred in fMRI and PET studies due to the low temporal resolution of these imaging techniques.

**Structural asymmetry of the parietal operculum and its relation to function**

The human operculum is usually separated into two parts, i.e. a frontal (FO) and a parietal (PO) portion. In this study, the PO was morphometrically analyzed and further subdivided into an anterior (aPO) and a posterior (pPO) area, according to the cytoarchitectonic borders in the human PO as defined by Eickhoff et al. (2006a). The aPO contains the cytoarchitectonic areas OP3 and OP4, the pPO encompasses areas OP1 and OP2. The cytoarchitectonic PO areas OP1-4 were reported to show no significant volume differences between the two hemispheres (Eickhoff et al. 2006b). In accord with this, no interhemispheric differences in aPO size were measured. However, the pPO size was significantly larger in the left than in the right hemisphere (Fig. 4C). The discrepancy between the lateralization of the pPO and the
cytoarchitectonic areas OP1 and OP2 is easily explained. First, the cytoarchitectonic area OP1 fills in most of the pPO and it demonstrated a strong trend towards larger volumes in the left than in the right hemisphere (Eickhoff et al. 2006b). Second, areas OP1 and OP2 never reached the posterior end of the SF (Eickhoff et al. 2006a), but the latter was defined as the posterior border of the pPO in this study because Eickhoff and co-workers (2006a) did not specify a precise macroscopical landmark for the posterior end of areas OP1 and OP2. The left lateralized pPO size was even expected since the SF is known to be 7-8 mm longer in the left than in the right hemisphere (Falkai et al. 1992; Steinmetz et al. 1989). However, as a limitation, one has to take into account that manual morphometry requires subjective determination of anatomical boundaries and thus considerable anatomical expertise. Hence, one might argue that automated image processing methods (e.g. voxel-based morphometry) would have been a more appropriate approach to draw valid conclusions about PO asymmetry. However, both intra-rater reliability (ICC 0.913-1.000) and inter-rater reliability (ICC 0.823-0.999) were high and similar to each other. It has also been shown that manual and automated measures provide complementary information about brain morphology (Eckert et al. 2005).

Our dominant RS component in the long latency range (N110) was clearly localized in the pPO (Fig. 4C). Projected onto probabilistic maps of the cytoarchitectonic areas in the human PO, SII source locations in this study could be predominantly attributed to area OP1, which also represents the most likely functional localization of SII in human functional imaging studies (Eickhoff et al., 2006b) and corresponds to the SII area in monkeys (Burton et al. 1995; Krubitzer et al. 1995). Although N110 source strengths were not correlated with absolute values of pPO size in both hemispheres, a significant linear relation between LIs of maximum N110 source activation and pPO size was found (Fig. 5). On a microstructural level, asymmetric ECD strengths may
be the consequence of i) more dense activation of neurons within the same area, ii) higher synchronization of neuronal firing rates within the same area, and iii) a larger area of neuronal activation in one hemisphere compared to the other. The strong correlation between the LIs of PO size and N110 ECD strengths in this study suggests the latter possibility as the most likely one for the lateralized N110 source activation. Interestingly, pPO asymmetry and its link between structure and function were mainly determined by the pPO size in the right hemisphere. Previous studies provided evidence for a decline in right hemisphere function as an effect of aging (right hemi-aging model) (Dolcos et al. 2002), resulting in an increase of left lateralized and a decrease of right lateralized brain functions. The right hemi-aging model and the present observation point at a potentially crucial role of the right hemisphere in determining brain asymmetry.

Neither absolute nor LI values of the aPO size and the N80 source activity were significantly correlated. This missing link between aPO structure and N80 function further supports the above-mentioned notion that the N80 source component is more likely generated in FO than in aPO.

**Asymmetry in the parietal operculum, handedness and auditory lateralization**

Beside structural and functional measures of PO asymmetry, we evaluated the most prominent examples of (left lateralized) brain asymmetry, i.e. handedness via the Edinburgh Inventory and speech dominance via the dichotic listening test. We found no linear relationship between the degree of handedness, the degree of auditory lateralization and measures of PO asymmetry. These findings are in line with the notion that most measures of brain asymmetries are not linearly related, which particularly applies for correlations between asymmetries of different functional systems. For instance, the association of handedness and speech dominance is only
mild, since not only about 95% of the right-handers but also about 70% of the left-handers show left hemispheric language dominance (Corballis 2003). Similarly, the cerebral dominance for language is not or only moderately related to structural brain asymmetries. Among all known asymmetric brain structures, the strongest relation to speech dominance was described for the planum temporale (PT). A left lateralized PT asymmetry was predominantly determined in subjects with left hemispheric dominance for language (Foundas et al. 1994), but right hemispheric speech dominance was not associated with reversed PT asymmetry. Moreover, the degree of PT asymmetry was not significantly related to the degree of lateralized speech processing (Tzourio et al. 1998). In terms of handedness, both evidence for and against a relation of handedness with other structural cerebral asymmetries (planum temporale and parietale, frontal and occipital petalia, sylvian fissure) has been previously reported (Bear et al. 1986; Foundas et al. 1995; Steinmetz et al. 1991; but Good et al. 2001). However, most studies found significant correlations with handedness if structures of the motor system (primary motor cortex, pyramidal tract, spinal motor neurons) were directly investigated (Amunts et al. 1996; Melsbach et al. 1996; Nathan et al. 1990; but White et al. 1997). Likewise functional measures of the primary motor cortex were lateralized and reflected the degree of handedness (Dassonville et al. 1997; Volkmann et al. 1998). Similar results would be awaited for the somatosensory system due to its high interconnection with the motor system. However, lateralized structural and functional measures in primary and secondary somatosensory cortices have previously not been proved to be significantly correlated with the degree of handedness (Jung et al. 2003; Jung et al. 2008; Rossini et al. 1994; Simões et al. 2002; Sörös et al. 1999). In accordance with this, we failed to show a linear correlation between handedness and measures of asymmetric structure and function in area SII (pPO). In addition, consistent right-handers, who
are supposed to exhibit the most pronounced left hemisphere dominance (Habib et al. 1995; LeMay 1992), showed no differences in area SII/pPO asymmetry compared to inconsistent right-handers, and area SII/pPO asymmetry was not reversed in the two left-handers of our sample (Fig. 5). Thus, our findings further support that processing in somatosensory regions is less linked to handedness than in motor areas.

**Conclusions**

Spatiotemporal source analysis is essential to clarify the different causes of asymmetric EEG scalp potentials. The asymmetry of scalp potentials may be the result of i) side different source locations and orientations (P40 SEP component after tibial nerve stimulation in Baumgärtner et al. (1998)), ii) lateralized source strengths (N20 MN SEP component in Jung et al. (2003); N110 MN SEP component in this study), and iii) asymmetric projection of distant source activities (N100 MN SEP component in this study). The present study confirmed the findings of two different generators in the contralateral OIC, one showing its peak response about 30-40 ms earlier (N80) and a more tangential ECD orientation than the other (N110), that have been previously reported (Stancak et al. 2005), and extended the analysis to their associated cortical responses in the ipsilateral OIC (N100, N130). The focus of this study was the investigation of asymmetries of source generators in the contra- and ipsilateral operculoinsular cortices. We found that only one (N110) of the two contralateral operculoinsular sources was lateralized, and none of the ipsilateral ones. The N110 source was clearly located in the pPO (SII area) and its asymmetry was linearly linked to the structural pPO asymmetry but not to measures of brain asymmetry in other functional systems. The findings demonstrate a dominant role of the left SII area in the processing of contra- but not ipsilateral somatosensory stimuli.
and further suggest bilateral and symmetric activations of more anteriorly located
cortical generators in the OIC, i.e. areas INS/FO or PV/OP4.

Acknowledgments

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References


Burton H, Fabri M, and Alloway K. Cortical areas within the lateral sulcus connected to cutaneous representations in areas 3b and 1: a revised interpretation of


Figure Legends

**Figure 1.** (A) Grand averaged SEP recorded at electrode sites T3 and T4 (against average reference) after right (solid line) and left (dotted line) median nerve (MN) stimulation (recording epoch, -50–250 ms). Amplitudes were maximal at temporal electrode positions in the 70–130 ms latency range. Peak amplitudes were measured after 80 (N80) and 110 (N110) ms over temporal electrodes positioned contralateral to stimulation. Ipsilateral to stimulation, peak amplitudes were recorded at latencies of 100 ms (N100) and 130 ms (N130). (B) Profile of N110 amplitudes (mean ± SEM) in the centrotemporal electrode row after right (black diamonds) and left (white circles) MN stimulation. In interhemispheric comparison, higher N110 amplitudes were recorded over the left than right temporal region, both after contra- (p < 0.01) and ipsilateral (p < 0.001) MN stimulation. With respect to the stimulated nerve, the N110 component revealed higher amplitudes at contra- than ipsilateral temporal electrode sites after right (p < 0.001) but not left MN stimulation.

**Figure 2.** (A) Dipole source locations (spheres) and orientations (currents flow from the sphere to the end of the dipole vector) based on Grand Average EEG data after right MN stimulation. Source analysis revealed 7 dipolar sources, one located in the brainstem (P14 in grey colour), two in the contralateral SI cortex (P30, area 3b in dark blue and N60, area 1 in light blue), two in the contralateral (red, N80, N110) and two in ipsilateral (green, N100, N130) SII cortices. (B) Mean (solid line) waveforms of cortical sources and their 95% confidence intervals (shaded areas) in the left hemisphere during the poststimulus interval of 10–150 ms. In the contralateral SI cortex, the P30 source (dark blue) was not only significantly active in the early 16–70 ms but also in the late 90–140 ms latency interval; the N60 source (light blue) was active between 45 and 80 ms. Significant activation of both N80 and N110 sources in
contralateral SII cortex started at about 55 ms but activity of N80 sources peaked (80 ms) and ended (115 ms) earlier than of N110 sources. Sources in the ipsilateral SII cortex responded in the 80–120 ms latency range, with highest dipole strengths at 100 ms (N100), and between 110 and 140 ms, with peak activation at 130 ms (N130). In the late 70–150 ms latency range, N110 source responses were the strongest among all cortical sources.

**Figure 3.**

(A) Mean difference waveforms between left and right homologous cortical sources and their 95% confidence intervals (shaded areas) in the 10–150 ms poststimulus interval. Significance was assumed if the 95% confidence interval did not include the baseline (horizontal dashed line). The N110 source exhibited higher activity in the left than right hemisphere between 75 and 120 ms whereas all other cortical sources (SI: P30, N60; SIIc: N80; SIII: N100, N130) showed no relevant interhemispheric differences in their dipole strength during the first 150 ms after MN stimulation. (B) Scalp voltage topography at the peak latency of SIII source activity after left (left column) and right (right column) MN stimulation based on Grand Average EEG data. Raw data (upper row) showed higher negative voltages over T3 than T4 electrodes (white circles) after stimulation of the ipsilateral MN, which was not the result of lateralized scalp voltage projection of SIII sources (N100 and N130, middle row) but was due to a higher positive projection of the contralateral N110 source after rMN than lMN stimulation on ipsilateral temporal electrode positions (lower row).

**Figure 4.** (A) Drawing of the precentral (yellow line), central (CS, orange line), postcentral (red line), posterior subcentral (PSS, blue line) sulci and sylvian fissure (SF, green line) on brain surface. In the first step for morphometric analysis of the
anterior (aPO) and the posterior (pPO) portion of the parietal opercula, the anterior boundary of aPO was defined as the y level of the lateral end of the CS (orange asterisk) and the posterior boundary as the junction of PSS with SF (yellow asterisk), pPO ranged from PSS to the posterior limit of SF (white asterisk). (B) Illustration of the second step of morphometric analysis. Medial and lateral PO borders (white asterisks) were determined on coronal MRI slices, and the length of the intrasulcal contours of the upper wall of the SF was measured between these mediolateral borders. (C) Projection of aPO and pPO areas on an axial MRI slice (section is on a level with the intersection point of PSS and SF) in one representative subject. (D) Top view of the brain with projection of the area depicted in E (black frame). (E) Axial projection of aPO and pPO borders and source locations of the N110 component (mean ± 1 SD). Medial and lateral borders of aPO and pPO are indicated by small dots, large dots indicate N110 dipole source locations (left, red colour). Colour coding shows the number of subjects whose aPO and pPO borders were within the range of measured y coordinates. Horizontal solid and dotted grey lines mark the transition between aPO and pPO (mean ± 1 SD). The aPO size did not differ between hemispheres, whereas the pPO was larger in the left than right hemisphere (p < 0.005) due to its further posterior limit on the left side. SII sources were located within the pPO in both hemispheres, consistent with their presumed generation in the cytoarchitectonic area OP1 (Eickhoff et al. 2006b) and the functional area SII (Disbrow et al. 2000) of the parietal operculum.

Figure 5. Laterality indices of N110 source activities in the contralateral SII cortex (SIIc) and the size of the posterior parietal operculum (pPO). Black dots mark the two left-handers. N110 and PO asymmetries were strongly correlated (ρ = 0.69, p < 0.005), indicating a close structural-functional link between these measures.
# Table 1

Side comparison of late latency MN SEP scalp potentials

<table>
<thead>
<tr>
<th></th>
<th>rMN</th>
<th>IMN</th>
<th>p values&lt;sup&gt;a&lt;/sup&gt;</th>
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<tr>
<td><strong>Contralateral potentials</strong></td>
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<tr>
<td>N80 latency (ms)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>80.0 ± 1.9</td>
<td>77.5 ± 1.6</td>
<td>n.s.</td>
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<tr>
<td>N80 amplitude (µV)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>-3.1 ± 0.9</td>
<td>-2.4 ± 0.8</td>
<td>n.s.</td>
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<tr>
<td>N110 latency (ms)</td>
<td>109.1 ± 2.0</td>
<td>115.0 ± 2.9</td>
<td>n.s.</td>
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<tr>
<td>N110 amplitude (µV)</td>
<td>-4.0 ± 0.4</td>
<td>-2.1 ± 0.4</td>
<td>p &lt; 0.002</td>
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</tbody>
</table>

| **Ipsilateral potentials** |           |           |
| N100 latency (ms)         | 93.4 ± 2.7 | 98.1 ± 3.4 | n.s. |
| N100 amplitude (µV)       | -1.4 ± 0.2 | -2.8 ± 0.3 | p < 0.001 |
| N130 latency (ms)<sup>c</sup> | n/a       | n/a       | n/a |
| N130 amplitude (µV)<sup>c</sup> | n/a       | n/a       | n/a |

Values are indicated as mean ± s.e.m. at electrode channels T3/4 against average reference. rMN, right median nerve stimulation; IMN, left median nerve stimulation; <sup>a</sup> Student’s paired t test, <sup>b</sup> N80 scalp potentials were only delimitable from N110 deflections in 7/16 subjects, <sup>c</sup> N130 scalp potentials were not definitely detectable due to their superimposition with the N140 cognitive component (vertex negativity)
Table 2

Side comparison of SII source latencies and strengths

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<th>rMN</th>
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<tr>
<td><strong>Contralateral SII sources</strong></td>
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<tr>
<td>N80 latency (ms)</td>
<td>82.6 ± 1.9</td>
<td>85.9 ± 1.9</td>
<td>n.s.</td>
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<tr>
<td>N80 strength (nAm)</td>
<td>33.3 ± 5.3</td>
<td>32.4 ± 5.0</td>
<td>n.s.</td>
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<tr>
<td>N110 latency (ms)</td>
<td>109.5 ± 2.5</td>
<td>114.9 ± 2.6</td>
<td>n.s.</td>
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<tr>
<td>N110 strength (nAm)</td>
<td>57.6 ± 6.7</td>
<td>39.3 ± 4.9</td>
<td>p &lt; 0.005</td>
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<tr>
<td><strong>Ipsilateral SII sources</strong></td>
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<td></td>
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<tr>
<td>N100 latency (ms)</td>
<td>98.5 ± 3.2</td>
<td>97.6 ± 3.2</td>
<td>n.s.</td>
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<tr>
<td>N100 strength (nAm)</td>
<td>25.3 ± 2.9</td>
<td>28.7 ± 4.1</td>
<td>n.s.</td>
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<tr>
<td>N130 latency (ms)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>127.2 ± 3.5</td>
<td>127.8 ± 3.1</td>
<td>n.s.</td>
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<tr>
<td>N130 strength (nAm)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>30.1 ± 3.3</td>
<td>32.7 ± 3.5</td>
<td>n.s.</td>
</tr>
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</table>

Values are indicated as mean ± s.e.m. rMN, right median nerve stimulation; IMN, left median nerve stimulation; <sup>a</sup> Student’s paired t test