Preserved Responsiveness of Secondary Somatosensory Cortex in Patients with Thalamic Stroke

Cortical representations may change when somatosensory input is altered. Here, we investigated the functional consequences of partial “central” deafferentation of the somatosensory cortex due to a lesion of the ventroposterior lateral nucleus (VPL) in patients at a chronic stage after solitary infarction of the thalamus. Event-related functional magnetic resonance imaging during electrical index finger stimulation of the affected and nonaffected side was performed in 6 patients exhibiting contralesional sensory deficits (mainly hypesthesia). Involvement of the VPL and additional nuclei was determined by high-resolution magnetic resonance imaging (MRI) and subsequent MRI-to-atlas coregistration. For the group, statistical parametric maps showed a reduced activation of contralateral primary somatosensory cortex (SI) in response to stimulation of the affected side. However, no significant difference in the activation of contralateral secondary somatosensory cortex (SII) compared with stimulation of the nonaffected side was detected. Correspondingly, the ratio of SII-to-SI activation for the ipsilesional hemisphere was markedly elevated as compared with the contralesional hemisphere. For preserved responsiveness of SII in thalamic stroke comparable with that of the contralesional hemisphere, possible explanations are a direct thalamocortical input to SII mediating parallel information processing, nonlinear response behavior of SII in serial processing, or reorganizational processes that evolved over time.

Keywords: fMRI, reorganization, SI, SII, thalamus, VPL

Introduction

In the somatosensory system, cortical information processing takes place in spatially distributed and reciprocally interconnected regions. The thalamus holds a decisive position within this network: signal flow from the body periphery is relayed in the ventroposterior lateral nucleus (VPL) and from the face in the ventroposterior medial nucleus (VPM) to the primary somatosensory cortex (SI) (Jones and Powell 1969; Krubitzer and Kaas 1987). Secondary somatosensory cortex (SII) receives projections from SI and in turn sends feedback projections (Manzoni and others 1986; Burton and others 1995). This pattern of anatomical connectivity between primary and secondary somatosensory areas on one side and sequential electrical activity on the other side (Mauguiere and others 1997; Della Penna and others 2004) has formed the basis for the notion of serial information processing in the primate somatosensory system (Pons and others 1987; Graftagh and others 1990; Kaas and Garraghty 1991). The principle of hierarchical transmission appears to be realized also within the cytoarchitectonically defined subdivisions of SI itself (areas 3b, 1, and 2; Iwamura 1998), so it was suggested that only area 3b should be regarded as the primary somatosensory area, and it was referred to as “SI proper” (Kaas 1983). On the other hand, despite strong evidence for serial processing, it is also established for non-human primates that SII receives afferents mainly from ventroposterior inferior nucleus (VPI) and via collateral projections also from VPL (Friedman and Murray 1986; Krubitzer and Kaas 1992; Qi and others 2002), but the density of the latter is reported to be comparatively small. Together with several electrophysiological studies, direct thalamocortical input to SII supports the hypothesis of physiologically relevant parallel information processing. For instance, microelectrode recordings in primates revealed virtually simultaneous stimulus-induced neuronal activity in SI (areas 3b and 2) and SII (Nicollels and others 1998), and in humans, early SII dipole activity (~20 ms after stimulation) was observed in magnetoencephalography (MEG) being nearly coincident with the initial dipole activity in SI (Karhu and Tesche 1999).

Peripheral deafferentation of somatosensory cortex is known to induce reorganization of representational maps in SI with invasion of the neighboring cortical representational fields into the initially silent one. This was shown in primates with experimental nerve lesions (Pons and others 1991) as well as in patients after limb amputation (Elbert and others 1994; Yang and others 1994; Flor and others 1995). Less is known about functional consequences of reduced sensory input at a central level, though similar processes were observed following experimental “incomplete” thalamic lesions in primates (Jones and others 2002). Here, thalamic infarctions can serve as a lesion model of partial “central” deafferentation of somatosensory cortex in humans. In patients exhibiting hypesthesia due to posteriorlateral thalamic lesions, early components of somatosensory evoked potentials (SEPs) are consistently reduced (Kudo and Yamadori 1985; Chu 1986). However, it is controversial how this apparent reduction of neural activity translates into neurovascular signals in the “sensorimotor cortex” (Remy and others 1999; Staines and others 2002).

From the perspective of systems physiology, we addressed the question to what extent the relation between responsiveness of primary and secondary cortical areas of the ipsilesional hemisphere is altered as compared with the contralesional hemisphere when thalamic relay function is impaired. For this purpose, we performed event-related functional magnetic resonance imaging (fMRI) during electrical index finger stimulation in patients with partial lesions of the VPL due to thalamic infarction at a chronic stage.

Subjects and Methods

Subjects and Neurological Examination

Patients registered at our hospital with the diagnosis of thalamic infarction were recruited for this study. The study was approved by
the local ethics committee, and participating patients gave written informed consent prior to experimental procedures. All patients underwent history taking and neurological examination comprising detailed testing of somatosensory functions and motor performance. For quantification of hypesthesia, tactile thresholds (for dynamic touch) were regionally measured by brief indentations of Frey filaments at increasing forces (Johannsen and others 1980).

### Morphological Magnetic Resonance Imaging and Localization of Thalamic Lesions

Morphological imaging was performed on a clinical whole-body scanner (1.5 T. Magnetom Vision, Siemens, Erlangen, Germany) using a standard head coil. To screen for potential extrathalamic and intrathalamic lesions, transversal $T_1$- and $T_2$-weighted images of the entire brain as well as images of the diencephalon using a turbo inversion recovery magnitude sequence, respectively, were made. Finally, a three-dimensional data set at high resolution using a magnetization prepared rapid acquisition gradient-echo (MPRAGE) imaging sequence (TR, 941 ms; TE, 4 ms; flip angle, 12°; voxel size, $1 \times 1 \times 1 \text{mm}^3$) was acquired.

The three-dimensional MPRAGE image data set comprising the thalamus was coregistered with the superimposed coronal section outlines of a digitized version of an anatomical atlas of the human brain (Ma and others 2004) by means of a self-written software: first, the “interhemispheric” midsagittal plane and then the orthogonal plane through the bicommissural line between the anterior and posterior commissure were determined as reference planes; in the next steps, the images were repetitively transformed (translation, rotation, linear scaling) by the examiner with respect to visually identified structural landmarks (such as caudate nucleus, wall of the third ventricle, putamen). With this approach, the thalamic nuclei affected by the infarction could be specified on each thalamic section. Lesion sizes were determined on the MPRAGE images in individual space in terms of maximal diameters in the medial-to-lateral, anterior-to-posterior, and superior-to-inferior directions (Table 1).

#### fMRI Protocol

Functional imaging was performed partly in a separate session on the same scanner. Prior to scanning, somatosensory thresholds for index finger stimulation were determined in each subject; electrical current pulse trains (7 Hz) at increasing intensities of 0.2-mA steps were delivered subsequently to the index finger of the nonaffected and affected side via bipolar ring electrodes (using a constant current stimulator; Neurorack 2, Nihon-Kohden, Tokyo, Japan), and the subject was asked to report any sensation on the respective finger (methods of limits and others 2004). The “interhemispheric” midsagittal plane and then the orthogonal plane through the bicomissural line between the anterior and posterior commissure were determined as reference planes; in the next steps, the images were repetitively transformed (translation, rotation, linear scaling) by the examiner with respect to visually identified structural landmarks (such as caudate nucleus, wall of the third ventricle, putamen). With this approach, the thalamic nuclei affected by the infarction could be specified on each thalamic section. Lesion sizes were determined on the MPRAGE images in individual space in terms of maximal diameters in the medial-to-lateral, anterior-to-posterior, and superior-to-inferior directions (Table 1).

#### fMRI Analysis

Functional images were analyzed with the software SPM99 (Statistical Parametric Mapping; Wellcome Department for Cognitive Neurology, University College London, UK) running on Matlab (version 5.3; MathWorks, Natick, MA, USA). The initial 3 images were discarded due to $T_1$-saturation effects. Image preprocessing comprised realignment to the first image, correction for slice time acquisition, spatial normalization to a symmetrytized EPI template (obtained by averaging the EPI template and its sagittally mirrored copy) in Montreal Neurological Institute (MRI), standard space, and spatial filtering (Gaussian kernel, full width at half-maximum, $8 \times 8 \times 10 \text{mm}^3$). Voxel fMRI signal time series were temporally filtered (low cutoff time constant $~100$ s, high cutoff time constant $3 \text{ s}$). Statistical $T$ maps were calculated by regression analysis based on the general linear model (Friston and others 1995) using the stimulus onset function of each stimulation condition convolved with the canonical hemodynamic response function as regressor. The protocol consisted of 4 conditions: stimuli of low and high intensities were presented to the affected and nonaffected side (60 trials each). Trials occurred scan-triggered by a digital interface controlled by a custom-written program in Labview (National Instruments, Austin, TX, USA) in a randomized order at variable interstimulus intervals (mean, $~6$ s; range, $3--9$ s; jitter, $1 \text{ s}$). Each somatosensory stimulus was represented by a train of 4 single pulses of 7 Hz. In several prior fMRI experiments, a frequency of 7 Hz for electrical finger stimulation reliably led to robust fMRI responses in the somatosensory cortex (Krause and others 2001, Ruben and others 2001, Deuchert and others 2002, Blankenburg and others 2003). To allow for comparability in interhemispheric analysis of fMRI responses, stimulus intensities were identical for either body side; these were determined individually according to the following constraints due to partly marked threshold differences: 1) The high stimulation amplitude was adjusted at least 0.4 mA (range 0.4--1.0 mA) below the threshold for uncomfortable sensation (i.e., consistently below painful stimulation) of the nonaffected side. 2) The low amplitude was at least 0.4 mA (range 0.4--1.2 mA) above the sensory threshold as determined for the nonaffected side. The mean stimulus intensities were $3.9 \pm 0.3 \text{ mA}$ and $6.9 \pm 0.4 \text{ mA}$, thus, on average, $0.73 \pm 0.27 \text{ mA}$ above sensory threshold of the nonaffected side and $0.63 \pm 0.29 \text{ mA}$ below the threshold for nontolerated sensation on the respective side. Functional imaging was performed using a blood oxygenation level-dependent signal contrast (BOLD; Bandettini and others 1992; Frahm and others 1992; Kwong and others 1992; Ogawa and others 1992)-sensitive $T_2$*-weighted gradient echo planar imaging (EPI) sequence (TE, 60 ms; flip angle, 90°; TR, 2 s; 16 slices at a voxel size of $4 \times 4 \times 5 \text{ mm}^3$). Including baseline acquisition, the fMRI protocol spanned 750 scans. This approach with a brief stimulus duration, randomly alternating stimulus conditions at randomly varying interstimulus intervals (Dale 1999), was used to minimize potential time-dependent fluctuations in signal behavior due to, for example, adaptation or habituation and allowed for a duration of the fMRI experiment tolerable for the patients (25 min).

### Table 1

Overview on patients selected for the group analysis

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (years)</th>
<th>Gender</th>
<th>History (days)</th>
<th>Type of stroke</th>
<th>Site of lesion</th>
<th>Maximal diameters (mm)</th>
<th>Somatosensory symptoms</th>
<th>Additional symptoms</th>
<th>Affected nuclei (Fig. 2)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>68</td>
<td>M</td>
<td>748</td>
<td>Isch</td>
<td>Left</td>
<td>5</td>
<td>Hyp, The</td>
<td>Min</td>
<td>VPL, VPM, VPI, VLP, Pul</td>
</tr>
<tr>
<td>2</td>
<td>66</td>
<td>M</td>
<td>702</td>
<td>Hem</td>
<td>Left</td>
<td>10</td>
<td>Hyp</td>
<td>Min, Mot, Spa</td>
<td>VPL, VLP, VLA, VA, CM, MD</td>
</tr>
<tr>
<td>3</td>
<td>61</td>
<td>M</td>
<td>136</td>
<td>Isch</td>
<td>Left</td>
<td>9</td>
<td>Hyp, The</td>
<td>Me, Mot</td>
<td>VPL, VLP</td>
</tr>
<tr>
<td>4</td>
<td>62</td>
<td>M</td>
<td>709</td>
<td>Isch</td>
<td>Left</td>
<td>6</td>
<td>Hyp, Par, The</td>
<td>Min</td>
<td>VLP</td>
</tr>
<tr>
<td>5</td>
<td>63</td>
<td>M</td>
<td>218</td>
<td>Isch</td>
<td>Left</td>
<td>8</td>
<td>Hyp, Dys, Gra</td>
<td>Min, Atx, Mot</td>
<td>VPL, VLP, Pul</td>
</tr>
<tr>
<td>6</td>
<td>60</td>
<td>M</td>
<td>59</td>
<td>Isch</td>
<td>Left</td>
<td>13</td>
<td>Hyp, Dys</td>
<td>Min</td>
<td>VPL, Pul</td>
</tr>
</tbody>
</table>

| Mean    | 63.3        | 428.7  |

Note: Med-lat, medial-to-lateral; Ant-post, anterior-to-posterior; Sup-inf, superior-to-inferior; M, male; Isch, ischemic; Hem, hemorrhagic. History was defined as presenting in hospital and performing the fMRI experiment; maximal lesion diameters in anterior-to-posterior, medial-to-lateral, superior-to-inferior direction are given in individual space. In all subjects, VPL was affected and sensory deficits of the hand were present (Dys, dysesthesia; Hyp, hypesthesia; Par, paresthesia; The, thermohypesthesia; Gra, graphdysesthesia; Mot, paresis; Min, minute motor activity disturbance; Spa, spasticity; Atx, ataxia). Beyond VPL, in some cases, further somatosensory nuclei were involved by thalamic infarction (VA, ventral anterior nucleus; VLA, ventrolateral anterior nucleus; VLP, ventrolateral posterior nucleus; Pul, Pulvinar; CM, central medial nucleus; MD, mediodorsal nucleus).

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realign. Because thalamic lesions were lateralized (Table 1), preprocessed functional images of each subject were transversally mirrored prior to normalization. In order to allow for inferences on interhemispheric differences, nonmirrored as well as mirrored images of the selected subjects were included together as separate sessions (n = 12) into a fixed-effects analysis (Friston and others 1999). Consequently, T contrasts between the stimulation conditions of the nonaffected and affected side (“contralateral vs. ipsilateral hemisphere”) and vice versa could be specified. For the 4 main effects (stimulation of affected and nonaffected side at low and high intensity, respectively), T contrasts were defined together on the lateralyzed sessions (n = 6), and the respective T maps were thresholded at significance levels corrected for multiple comparisons (Table 2; Fig. 3, at corrected P < 0.05). Due to a strong anatomical a priori hypothesis, the significance level for T maps for interhemispheric contrasts was set to an uncorrected P value of 0.001. Finally, activation volumes of separable clusters were determined in number of voxels on the basis of T maps for different corrected significance levels (P < 0.01, P < 0.025, P < 0.05; Table 2); consequently, ratios between activation volumes of contralateral SII and contralateral SI (“SII-to-SI activation ratios”) were calculated for the contralateral and ipsilateral hemisphere in order to provide a rough estimate for the interhemispheric difference in the extent of activation in primary and secondary somatosensory areas.

Results

In total, 6 subjects (mean age, 63.3 years; range, 60–68 years; all male and right handed) were selected for the group analysis according to the following criteria: 1) exclusively thalamic infarction within a chronic stage (>60 days) and lack of additional cerebral disorders, 2) a unilateral intrathalamic lesion with involvement of the VPL, and 3) report of contralateral hypesthesia or other sensory deficits such as paresthesia or dysesthesia (Table 1). No exclusion criteria were defined regarding the type or number of additionally affected nuclei.

Clinical Symptoms

All patients reported reduced regional tactile sensitivity of hand or forelimb area for clinical testing of light touch; pallesthesia and joint position sense were in normal ranges in all cases. Five patients showed slight deficits in minute motor activity. As compared with the nonaffected side, patients showed a mean elevation of somatosensory thresholds for electrical index finger stimulation (7 Hz) of 1.0 ± 0.44 mA (35.5%; Fig. 1) and mean tactile thresholds in a range of 8–17% for the hand and forearm region as determined by Frey filaments. Thresholds for uncomfortable (i.e., nonpainful but not tolerated) sensation as determined by electrical stimulation were 7.53 ± 0.60 mA for the nonaffected and 8.73 ± 1.47 mA for the affected (hypesthetic) side.

Localization of Thalamic Lesions

In all subjects, lesions were located in the posterior portion of the thalamus; in 1 patient (subject 2), thalamic stroke was of hemorrhagic origin and in 5 patients of ischemic origin (most probably due to an infarction of the thalamogeniculate artery; Bogousslavsky and others 1988). In all patients, the VPL was markedly affected (Fig. 2); in 1 case, the VPM and VPI were involved in the lesion to a minor extent (Table 1).

fMRI Main Effects

At a significance level of P < 0.05 (corrected for multiple comparisons), the statistical T map (fixed-effects analysis, n = 6) for stimulation of the nonaffected index finger at high intensity showed robust activation clusters in contralateral SI, in contralateral primary motor cortex (M1), and bilaterally in SII (Fig. 3D). Stimulation at low intensity was associated with mere activation of the contralateral sensorimotor cortex (SI and M1; Fig. 3C). For stimulation at high intensity, BOLD signal increases were significantly higher in contralateral SI and SII than for stimulation at low intensity (T contrast “high-intensity stimulation vs. low-intensity stimulation of nonaffected side”; uncorrected P < 0.001, not shown). Stimulation at low intensity of the affected side did not elicit any significant activation of SI but
a small activation in SII (Fig. 3A). Stimulation of the affected side at high intensity was associated with activations in contralateral (i.e., ipsilesional) SI and SII (Fig. 3B), whereas no activation in ipsilateral SII was detectable (Table 2).

**Interhemispheric Differences in Elicited BOLD Responses**

At high stimulation intensity, activations of contralateral SI and contralateral posterior parietal cortex were higher for stimulation of the nonaffected side compared with the affected side as revealed by the interhemispheric contrast "contralesional vs. ipsilesional hemisphere" (i.e., "high-intensity stimulation of nonaffected side vs. high-intensity stimulation of affected side"); uncorrected \( P < 0.001 \); Fig. 4B, Table 3). For this contrast as well as for the inverse one ("high-intensity stimulation of affected side vs. high-intensity stimulation of nonaffected side," not shown), no significant difference in BOLD signal change was detectable in contralateral SII. The \( T \) map for the interhemispheric contrast further reveals a difference in activation of small extent within ipsilateral SII for stimulation of the nonaffected side at high intensity (Fig. 4B) that had led to bilateral SII activation (Fig. 3D). Correspondingly, activation volumes of contralateral SII were rather similar (Table 2), and as a consequence, the relation between SII and SI activation is higher for the ipsilesional than for the contralesional hemisphere. As a rough estimate of the extent of difference, this is quantified also by the ratios of activation volumes SII/SI in response to high-intensity stimulation (Table 2), for example, 67.7 for the contralesional and 0.64 for the ipsilesional hemisphere as determined at a corrected \( P < 0.025 \).

**Figure 1.** Somatosensory thresholds of the subjects \( n = 6 \) as determined for stimulation with current pulse trains (7 Hz) of the index finger of the affected and nonaffected side (prior to fMRI experiment). The mean threshold difference between the affected and nonaffected side was 35.5%.

**Figure 2.** MRI-to-atlas coregistration: Transformed coronal slices of the diencephalon (MPRAGE images) of each patient superimposed with an atlas of the human thalamus (Mai and others 2004; reproduced with kind permission); only the section with the largest in-plane extent is shown.
Discussion
We performed fMRI during electrical index finger stimulation in patients with solitary thalamic infarction at a chronic stage in order to characterize the altered spatial activation patterns within the somatosensory network due to partial central deafferentation of the cerebral cortex at the level of the VPL. In summary, stimulation of the affected side in this patient group was associated with 1) a reduced activation of contralateral SI, 2) a diminished activation of contralateral M1, and 3) a preserved activation of contralateral SII comparable with the response of contralateral SII for stimulation of the nonaffected side; as a consequence, the ratio of activation volumes between contralateral SII and contralateral SI for stimulation of the affected side (i.e., the ipsilesional SII-to-SI activation ratio) is larger than that of the contralesional hemisphere.

Sensory Deficits and Localization of Thalamic Lesions
All patients showed sensory deficits (hypesthesia, paresthesia, or dysesthesia) of the hand and distal upper extremity, so that an affection of the respective receptive fields within the VPL could be assumed. Stimulation of the index finger was used because the digits of the hand have comparably large representations within the cortex as well as the thalamus (Kaas and others 1984). The localization of thalamic lesions on the basis of the magnetic resonance imaging (MRI)-to-atlas coregistration was a prerequisite for delineation of affected thalamic nuclei and characterization of the lesional extent. Thus, an assumed affection of the VPL was confirmed, and an involvement of further somatosensory nuclei, such as the VPM and VPI, was qualitatively assessed. However, this approach of MRI-to-atlas coregistration potentially bears errors due to individual anatomical variability or the assumption of linearity for the coregistration procedure.

Activation of the Somatosensory Network of the Contralesional Hemisphere
Stimulation of the index finger of the nonaffected side led to physiological cortical activation patterns as previously demonstrated in several fMRI studies (Ruben and others 2001; Deuchert
difference was specified (not shown). Note that 'stimulation of affected side vs. stimulation of nonaffected side,' no significant standard single-subject and posterior parietal cortex for low intensity ('contralesional vs. ipsilesional hemisphere') reveal higher activations in contralateral SI contrasts 'stimulation of nonaffected side vs. stimulation of affected side' (i.e., due to strong a priori hypothesis) obtained from the fixed-effects analysis (Fig. 3). The activation was stronger, and robust activations of contralateral SI was observed. At high stimulus intensity, SI activation was observed despite a lack of significant SI activity. As compared with stimulation of the nonaffected side, stimulation of the affected side was associated with a marked reduction of contralateral SI activation. For stimulation at low intensity, which was below sensory threshold in 5 out of the 6 patients, no cortical fMRI signal change was observed. There are various evidences that the extent of SI activation is related to the perception of somatosensory stimulus strength or neural activity (Hashimoto and others 1988; Arthur and Boniface 2003). The decrease in fMRI activation of SI corresponds to a lowered level of excitation that is most probably caused by a reduced number of functionally intact thalamocortical projections and is the correlate of elevated somatosensory perception threshold of the affected body side. Similarly, early SEP components that are generated in SI subregions were found to be markedly attenuated or abolished in patients with infarctions of the posterior thalamus and the internal capsule (Nakanishi and others 1978; Kudo and Yamadori 1985; Chu 1986).  

**Reduced Activation in Ipsilesional SI**

As compared with stimulation of the nonaffected side, stimulation of the affected side was associated with a marked reduction of contralateral SI activation. For stimulation at low intensity, which was below sensory threshold in 5 out of the 6 patients, no cortical fMRI signal change was observed. There are various evidences that the extent of SI activation is related to the perception of somatosensory stimulus strength or neural activity (Hashimoto and others 1988; Arthur and Boniface 2003). The decrease in fMRI activation of SI corresponds to a lowered level of excitation that is most probably caused by a reduced number of functionally intact thalamocortical projections and is the correlate of elevated somatosensory perception threshold of the affected body side. Similarly, early SEP components that are generated in SI subregions were found to be markedly attenuated or abolished in patients with infarctions of the posterior thalamus and the internal capsule (Nakanishi and others 1978; Kudo and Yamadori 1985; Chu 1986).

**Physiological Basis of Maintained Contralateral SII Activity at Reduced Contralateral SI Activity: Circuitry or Plasticity?**

Stimulation at high intensity of the affected side was followed by contralateral SII activation comparable with that in response to stimulation of the nonaffected side as revealed both by similar cluster sizes and respective interhemispheric T contrast (Table 2; Fig. 4). In addition, at low stimulus intensity, a small SII activation was observed despite a lack of significant SI activity. On the basis of the model of serial information processing with SII activity depending on excitatory drive from SI, a reduced activation of SII could have been expected as well. In principle, there are 3 possible interpretations for a preserved contralateral SII responsiveness or—in other terms—increased SII-to-SI activation ratio associated with the deafferentation at the level of the VPL: 1) parallel information processing in SII mediated by a direct thalamocortical input to SII, 2) nonlinearly SI-dependent serial processing in SII as discussed above, and 3) time-dependent plastic change of SI processing induced by altered input from SI.
The concept of serial information processing in primates has been weakened in favor of the model of parallel SI and SII operation. Beyond lesion studies showing the maintained SI activity despite inactivation of SI (Zhang and others 1996, 2001), strong evidence is provided by multielectrode recordings in monkeys, demonstrating that neurons in SII virtually spike simultaneously with those in SI (Nicolelis and others 1998). Similarly, it was shown in MEG recordings in humans that the initial dipole activity in SII was coincident or partly preceding that of SI (Karhu and Tesche 1999) and SEPs from chronically implanted electrodes in the SII region exhibited small components with a latency of ~20 ms (Barba and others 2002).

After all, coincidence or slight delays in onsets between SI and SII activity do not exclude monosynaptically mediated feed-forward excitation of SI by SI activity, which lasts only a couple of milliseconds, and, vice versa, longer latency differences do not exclude functionally relevant parallel input to SII. Nevertheless, parallel processing appears to be physiologically relevant in higher primates and humans. Besides collateral projections originating from VPL, the VPI nucleus is a possible candidate mediating afferent input to SII (Krubitzer and Kaas 1992). In this study, the VPI was apparently unaffected in 5 out of the 6 patients. Furthermore, stimulation of the affected side at high intensity did not elicit a significant activation of ipsilateral SII (Table 2), and the interhemispheric contrast revealed a significant difference between signal changes in ipsilateral SII in response to stimulation of the affected and nonaffected side (Fig. 4). Ipsilateral SII activation in response to somatosensory stimulation is assumed to be driven by contralateral SII via transcallosal fibers (Frot and Mauguire 1999). One might speculate that the lack of contralesional SII activation despite a robust ipsilesional SII activation is a consequence of disturbed thalamic relay function as also a direct thalamocortical input to ipsilateral SII is discussed in the literature; for instance, in patients with right-hemispheric stroke affecting SII, a maintained SEF activity of ipsilateral SII was observed, so the authors proposed a functionally relevant direct thalamocortical afference to SII (Forss and others 1999). However, this question on thalamocortical versus intracortical connections is beyond the scope of our study.

Finally, an increased responsiveness of SII might have evolved over time and resemble reorganizational changes. For peripheral deafferentation, the capability for reorganizational processes, that is, changes in receptive field representation of adjacent body areas in consecutive relay sites such as the dorsal column nuclei, the VPL, and finally SI, is well established (Jones and Pons 1998; Jones 2000). For instance, the receptive field organization within the thalamus can be reshaped by altered corticothalamic feedback as has been shown for primates (Engzenger and others 1998). It might be possible that lesions induced altered receptive field organization both in the VPL and consequently in SI. This was demonstrated in primates with targeted lesions of the VPL (Jones and others 2002) and is suggested by stereotactically electrode recordings in a single patient after thalamic stroke (Ohara and Lenz 2001). This could be an explanation for the fact that despite irreversible destruction of considerably large portions of the VPL, the clinical symptoms of hypesthesia or dysesthesia are comparatively weak. In clinics, recovery of sensory functions following stroke is a well-known phenomenon. For example, a case study on thalamic infarction reported on the recovery of tactile perception thresholds within a time period of about 6 months (Staines and others 2002). Following this line of interpretation, SI responsiveness observed here may have developed over time. One approach to address the issue of plastic reorganization within the somatosensory network is a follow-up study with fMRI examination of patients in an acute and at a chronic stage of thalamic infarction. One might expect for an early phase of thalamic infarction that SI activity is rather decreased and later at a chronic stage coupled stronger to SI activity.

### Notes

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