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Magnetoencephalography in the study of human somatosensory cortical processing

R. Hari[1,2*] **and N. Forss**[1]

[1]*Brain Research Unit, Low Temperature Laboratory, Helsinki University of Technology, FIN-02015 HUT, Espoo, Finland*
[2]*Department of Clinical Neurosciences, Helsinki University Central Hospital, FIN-00290 Helsinki, Finland*

Magnetoencephalography (MEG) is a totally non-invasive research method which provides information about cortical dynamics on a millisecond time-scale. Whole-scalp magnetic field patterns following stimulation of different peripheral nerves indicate activation of an extensive cortical network. At the SI cortex, the responses reflect mainly the activity of area 3b, with clearly somatotopical representations of different body parts. The SII cortex is activated bilaterally and it also receives, besides tactile input, nociceptive afference. Somatically evoked MEG signals may also be detected from the posterior parietal cortex, central mesial cortex and the frontal lobe. The serial versus parallel processing in the cortical somatosensory network is still under debate.

Keywords: human; somatosensory cortex; SI; SII; magnetoencephalography

1. MAGNETOENCEPHALOGRAPHY

In magnetoencephalographic (MEG) studies, weak magnetic fields generated by cerebral currents are detected outside the head with superconducting sensors (Hämäläinen *et al*. 1993; Hari 1998). The aim is to map the magnetic field pattern accurately and to use it to calculate the most probable source current distribution within the brain. In this way active brain areas and their temporal behaviour can be studied totally non-invasively. MEG is well suited for investigation of various brain regions embedded within cortical sulci and, thus, it complements intracranial recordings which give information mainly from the convexial cortex.

The direction of the external magnetic flux follows, according to the right-hand rule, the net intracellular postsynaptic current in the synchronously activated neuronal population. This relationship was first discovered by comparing polarities of the simultaneously measured magnetic and electric auditory evoked responses (Hari *et al*. 1980) and has been more recently confirmed in slice preparations (Okada *et al*. 1997). According to slice recordings, tissue volumes less than 10 mm^3 can produce clear MEG signals at typical measurement distances outside the head.

The MEG signals are detected first with superconducting pick-up coils and then sensed with SQUIDs (superconducting quantum interference devices), the ultrasensitive detectors of magnetic fields. The present state-of-the-art neuromagnetometers contain 100–300 channels and allow signals to be recorded simultaneously all over the scalp (figure 1).

The skull and scalp, which distort the electric potential distributions, are transparent for magnetic fields. Thus, MEG is able to see neuronal events 'directly through the skull'. With both MEG and electroencephalography (EEG) one can follow the dynamics of brain activation on a (sub)millisecond time-scale. Due to the non-uniqueness of the 'inverse problem' (the deduction of neuronal currents from the measured external electric potential or magnetic field distribution), the generators of MEG signals are typically modelled with one or several current dipoles (figure 1). The spatial resolution of MEG drastically depends on the source configuration but point-like local currents separated by only a few millimetres can be differentiated when their temporal behaviours differ. In studies of the cortical somatosensory network the volume conductor formed by the head can be adequately approximated by a homogeneous sphere.

The main advantages of MEG are, thus, non-invasiveness, which allows repeated recordings as often as desired, excellent temporal resolution, reasonable spatial resolution and robustness of signals so that, when present, they are evident without sophisticated statistical analysis (besides averaging). Furthermore, it is possible to obtain quantitative estimates of neuronal activation (mainly of postsynaptic currents), study the fissural cortex, which has remained largely unexplored even in intracranial recordings and draw conclusions from single-subject data.

However, MEG suffers from the non-uniqueness of the inverse problem, requires a magnetically silent environment for high-quality recordings, is dominated by the activity of the most synchronous neuronal populations and does not provide reliable tools for determining the extent of activation or differentiating temporally co-inciding activations of nearby brain areas.

Despite these pitfalls, MEG has been used successfully for exploration of several cortical processes (for reviews, see for example, Hari *et al*. 1990, 1998; Lounasmaa *et al*. 1996). In this brief review, we focus on applications of MEG to studies of the human somatosensory cortices.

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[*] Author for correspondence (hari@neuro.hut.fi).

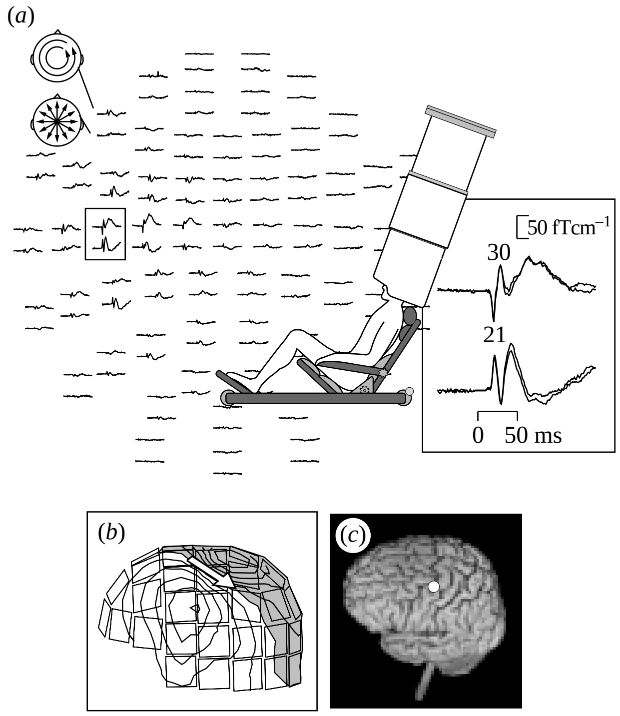

Figure 1. (*a*) Averaged evoked responses to stimulation of the right median nerve, recorded with a whole-scalp neuromagnetometer (middle) which houses 122 SQUIDs on a helmet-like sensor array. Each sensor unit records the changes of the radial magnetic field in two orthogonal directions along the plane of the helmet. The responses are viewed from the top and one pair of the traces is enlarged on the right, with replications superimposed. (*b*) The sensor array viewed from the left, with an example of a field pattern during the 30 ms deflection. The shadowed area indicates magnetic flux out of the head and the white area flux into the head and the arrow indicates the location of the equivalent current dipole which explains the field pattern best at one latency. (*c*) The dipole location is superimposed on the subject's magnetic resonance (MR) image.

2. SOMATOSENSORY-EVOKED FIELDS FROM THE SI CORTEX

(a) *Somatotopical representation at the SI cortex*

The first study of somatosensory-evoked fields (SEFs) reported magnetic signals that were *ca.* 2 cm more lateral for thumb than little finger stimulation (Brenner *et al.* 1978). A similar somatotopical order of generator areas in the SI cortex has since then been repeatedly demonstrated in MEG recordings with small (Hari *et al.* 1984; Okada *et al.* 1984; Narici *et al.* 1991), and large (Hari *et al.* 1993; Yang *et al.* 1993; Shimojo *et al.* 1996; Nakamura *et al.* 1998), sensor arrays. The main features of the somatotopical maps obtained agree with the well-known 'homuncular' organization detected during cortical stimulation (Penfield & Jasper 1954) and by intracranial recordings of somatosensory-evoked potentials (SEPs) (McCarthy *et al.* 1993), with a medial to lateral representation of the foot, trunk, hand, lips and tongue. In the hand area, the most lateral representation is for the thumb and the most medial one for the little finger; the representations of different fingers occupy a 15–20 mm cortical strip along the SI cortex (Baumgartner *et al.* 1991; Hari *et al.* 1993; Tecchio *et al.* 1997). The observed source locations agree well with intracranial recordings (Sutherling *et al.* 1988; Mäkelä *et al.* 1999) and with three-dimensional reconstructions of the somatosensory cortex (Suk *et al.* 1991).

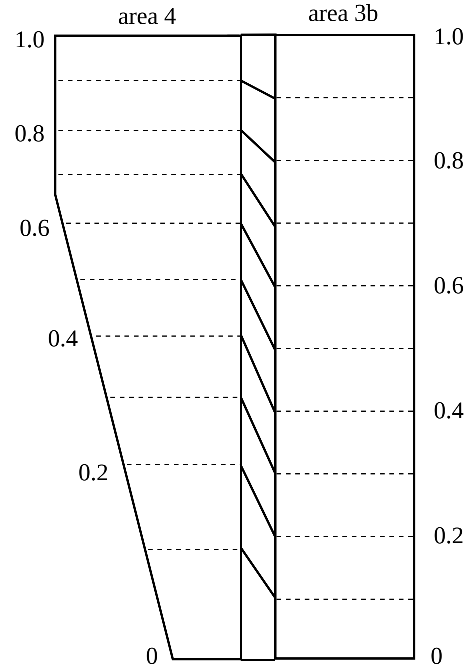

Figure 2. Schematic presentation of the flattened motor and somatosensory cortices. The equal-area borders are connected in 10% steps to illustrate their different heights on the pre-central and post-central sides.

Woolsey *et al.* (1979) noted that the pre-central motor representations were always slightly more medial to the corresponding post-central somatosensory representations; the difference was most prominent at the most lateral part of the central sulcus. We have also observed a similar trend in pre-operative localization of the central sulcus by means of functional landmarks on the post-central and pre-central cortex (Mäkelä *et al.* 1999). According to Woolsey *et al.* (1979), this discrepancy results from the greater need for cortical representation of motor than sensory functions. However, another plausible explanation derives from the different shapes of the pre-central and post-central cortices: whereas the flattened SI cortex (area 3b) is approximately rectangular in shape, the motor cortex (area 4) is triangular in its lateral part, increasing in width towards the more central areas. Figure 2 illustrates that, even if the magnification factors were the same for both areas, these shape differences would result in different heights of the corresponding pre-central and post-central representations and the differences would decrease in the more medial areas, in agreement with the experimental data.

(b) *Neuronal currents underlying SEFs from the SI cortex*

The current direction deduced from the MEG measurements can give useful clues about the neuronal mechanisms underlying the signals. During the earliest cortical response, peaking *ca.* 20 ms after upper-limb and 40 ms after lower-limb stimulation, the direction of the intracellular current is from deep towards superficial

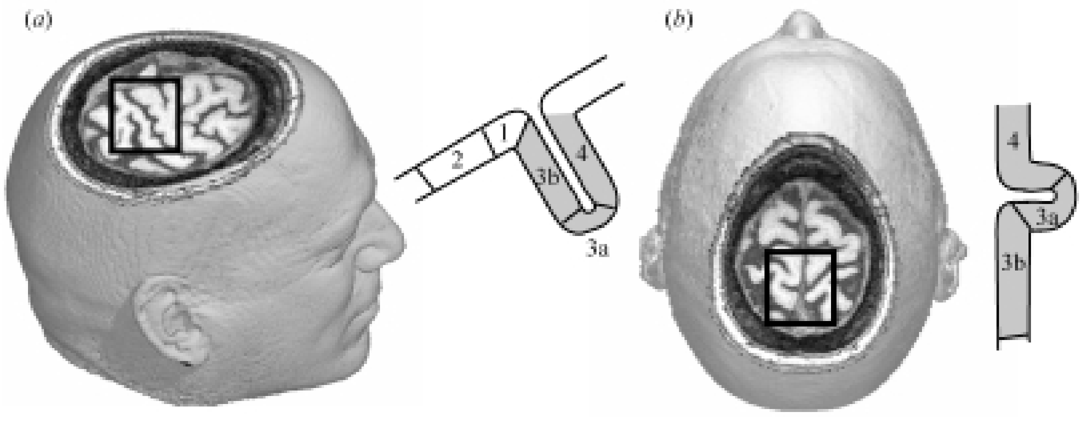

Figure 3. A schematic illustration of the cytoarchitectonic division of (*a*) the hand and (*b*) the foot somatosensory cortices. The shadowed areas indicate areas where currents can generate MEG signals outside the head.

layers of area 3b of the SI cortex, in agreement with excitation in the deep cortical layers, as would also be expected from intracortical recordings in animals (Towe 1966). Such a current would correspond to surface positive potential anterior (frontal) and surface negative potential posterior (parietal) to the central sulcus, in agreement with the polarities of SEPs recorded from the human scalp.

The next deflection has opposite polarity and peaks at 30–35 ms after upper-limb stimulation depending on the interstimulus interval (ISI): the shortest peak latencies are obtained at the shortest ISIs (Wikström *et al.* 1996). This 'P30m'–'P35m' response (the latency notation varies according to the study) thus most probably reflects net intracellular current from surface to depth in the SI cortex.

It is well documented that the N20m and P30m responses to median nerve stimuli behave in different ways during several experimental set-ups. For example, P30m is suppressed significantly more than N20m when the ISI is decreased from 0.5 to 0.2 s (Tiihonen *et al.* 1989). Thus, P30m might reflect polysynaptic input and, thus, be more vulnerable to rate effects. Another possibility is that it reflects the level of cortical inhibition, as suggested by Wikström *et al.* (1996) on the basis of similar recovery cycles of the P35m response and of inhibitory postsynaptic potentials (IPSPs) in cortical cells (Deisz & Prince 1989). Although this is a feasible hypothesis, it waits for confirmation by, for example, pharmacological manipulatons in the monkey cortex. At present it is not known to what extent field potential measurements (as well as MEG) receive contributions from the IPSPs; such a possibility was seriously questioned by Mitzdorf (1985). In addition, the observed fivefold increase in the P30m deflection in patients with myoclonus epilepsy (Karhu *et al.* 1994) is difficult to fit to the idea that increased P30m–P35m amplitudes would reflect increased cortical inhibition. Evidently more studies are needed to clarify this issue.

(c) *Cytoarchitectonic areas activated by upper limb stimulation*

In a sphere, radial currents do not produce any external magnetic field. One would thus expect MEG to be largely blind to the convexial cortex where the net current is radial. Consequently, responses to upper limb stimulation should arise mainly from area 3b, which is situated in the fissural wall (see figure 3), whereas negligible or extremely tiny MEG signals are expected from areas 1 and 2. This agrees well with experimental data (Wood *et al.* 1985; Tiihonen *et al.* 1989; Hari 1991).

Although N20m, the earliest cortical response after median nerve stimulation, is considered to be generated in area 3b, the contribution of the pre-central cortex to P35m is still under dispute because the sources are typically more anterior for P35m than N20m (Tiihonen *et al.* 1989; Kawamura *et al.* 1996). However, Huttunen (1997) proposed that this finding resulted from a modelling error rather than from an additional generator in the pre-central motor cortex. The somatosensory hand and finger representation areas are just posterior to the omega-shaped knob of the pre-central motor cortex (Yousry *et al.* 1997). Thus, any extended activation in this area would result in a curved activation layer, the location of which would be easily mislocated to the pre-central cortex with a single dipole model. Such a mislocation is supported by a recent finding that large-area vibrotactile stimulation of the whole palm results in more anterior source locations than electric stimulation of the median nerve in the same subjects (Jousmäki & Hari 1999). Of course the modelling error could explain the antero-posterior differences between N20m and P35m only if the activated area were significantly wider during P35m than N20m.

Several studies have also found that P35m is generated superior and medial to the generation of N20m. Interestingly, Vanni *et al.* (1996) observed that activation peaking around 40 ms for both ulnar and median nerve stimuli tended to be situated between the 20 ms activations for these nerves, thus probably reflecting convergence towards representations of the other fingers. If these interactions were inhibitory, they would apparently sharpen spatial accuracy when several fingers receive input simultaneously.

The contribution from muscle afferents to cortical somatosensory responses has not yet been completely resolved but is considered to be small (Allison *et al.* 1991). However, in some conditions proprioceptive fibres might play a role. For example, the significantly deeper sources for mixed than sensory median nerve stimulation can be interpreted as a sign that the mixed nerve stimulation

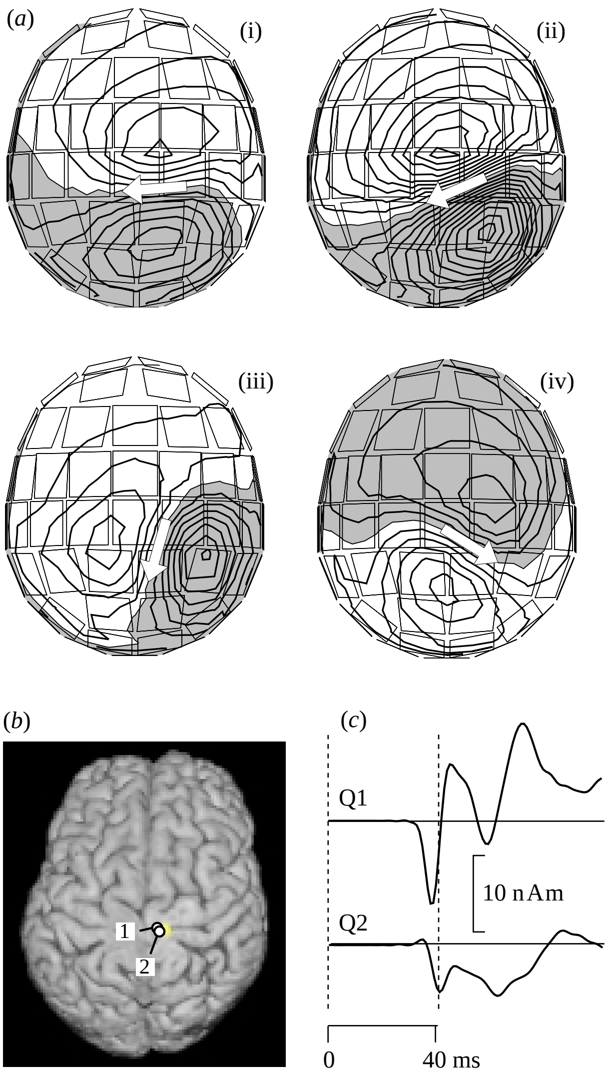

Figure 4. Field patterns (*a*) (i) 36 ms, (ii) 38 ms, (iii) 41 ms, and (iv) 46 ms after stimulation of the left tibial nerve; the sensor array is viewed from the top. (*b*) The two-dipole source model is shown, and (*c*) the strengths of these sources as a function of time. Adapted from Hari *et al.* (1996).

also activated area 3a in the depth of the central sulcus (Kaukoranta *et al.* 1986).

(d) *Cytoarchitectonic areas activated by lower-limb stimulation*

In most subjects, the foot representation is on the mesial wall of the hemisphere where currents perpendicular to the cortical surface are tangential with respect to the skull in all cortical walls, also in those posterior to area 3b in figure 3. Thus, MEG should see all areas in the mesial foot SI cortex and the changes in the relative contributions of the different cytoarchitectonic areas should result in rotating field patterns. This is exactly what happens after tibial, peroneal and sural nerve stimulations (Huttunen *et al.* 1987*b*; Fujita *et al.* 1995; Kakigi *et al.* 1995*b*; Hari *et al.* 1996).

After stimulation of the right tibial nerve, for example, the field patterns rotate counterclockwise (Hari *et al.* 1996) and can be explained by two approximately orthogonal dipoles with fixed locations and orientations but with varying relative strengths as a function of time; the first activation peaks of the two sources differ by 3 ms only (figure 4).

Interestingly, predictions of the sequential activation of different cytoarchitectonic areas, made on the basis of hand area activation, fail in the foot area (Hari *et al.* 1996), implying that the cortical activation sequences differ between the hand and foot somatosensory cortices much more than might be expected on the basis of animal studies. This is conceivable because of the high specialization of the human hand.

(e) *Interaction at the SI cortex*

The fingers evidently have to share some cortical representations since their inputs are highly correlated in space and time. When rare (10%) median nerve stimuli were presented among frequent (90%) ulnar nerve stimuli (ISI 1 s), the 40–70 ms responses from the SI cortex were similar in amplitude and waveform independently of whether the stimulus was rare or frequent in the sequence (Huttunen *et al.* 1987*a*), suggesting strong interaction in the afferent inputs from both nerves to the SI cortex. This is of course somewhat surprising, given that responses to ulnar and median nerve stimuli show somatotopical order.

Similar conclusions, however, also result from recordings of the early responses to median nerve stimuli which were preceded by 20–120 ms by either identical median nerve stimuli or ulnar nerve stimuli applied to the same hand (Huttunen *et al.* 1992). In both conditions N20m was suppressed to the very same extent for delays of up to *ca.* 120 ms, again indicating strong interaction between the median and ulnar nerve inputs at or before the SI cortex.

In agreement with the above studies, stimulation of fingers separately and in pairs has indicated overlap of finger representations in the human SI cortex; the overlap and inhibitory interaction was stonger between anatomically adjacent (II–I) than non-adjacent (II–V) digit pairs (Biermann *et al.* 1998). Inhibition apparently sharpens local representations and, thus, increases discrimination accuracy, which is probably beneficial for differentiating sensations from fingers which are close to each other. The convergence of activity from median and ulnar nerve representations towards representations of the other fingers of the hand (Vanni *et al.* 1996) would agree with this view.

(f) *High-frequency oscillations in the SI cortex*

With a very wide recording passband and a high number of averaged responses, it is possible to pick up *ca.* 600 Hz oscillatory bursts (high-frequency oscillations; HFOs) from the SI cortex after stimulation of different sensory nerves (Curio *et al.* 1994; Hashimoto *et al.* 1996). For upper-limb stimulation, the HFOs are superimposed on the 20 ms response and also generated close to its source; furthermore, both responses show similar somatotopical order (Curio *et al.* 1997). Interestingly, the HFOs are suppressed during sleep whereas the 20 ms response is not (Hashimoto *et al.* 1996). This is a very rare exception to the general rule that, the earlier the response and the higher its frequency content, the more resilient it is to stimulus repetition and changes of vigilance. Consequently, it has been suggested that the 20 ms response and the HFOs reflect different cortical currents: whereas the

20 ms response results from postsynaptic currents, cortical action potential bursts, possibly in cortical inhibitory interneurons, could be the source of the HFOs. If this turns out to be the case, HFOs will provide an interesting new insight into cortical signal processing.

(g) *Activation of the ipsilateral SI cortex*

In human intracranial recordings, ipsilateral responses to median nerve stimuli were observed in areas 4, 1, 2 and 7 (Allison *et al*. 1989). However, no responses were obtained from area 3b, the probable generation site of the MEG signals. Thus, one could doubt the existence of any MEG responses from the ipsilateral SI cortex. Except for the face area, the activation of the SI cortex is in general contralateral (Karhu *et al*. 1991; Hoshiyama *et al*. 1996); positron emission tomography (PET) recordings have confirmed such a bilateral activation (Pardo *et al*. 1997).

Some other findings also suggest bilateral activation of the SI cortex. For example, tactile interference by rubbing of the palm and fingers of one hand enhances P35m to median nerve stimuli in the SI cortex ipsilateral to the rubbed hand (when the responses were elicited by stimulation of the other wrist), probably via transcallosal excitatory pathways (Schnitzler *et al*. 1995); the response of the contralateral cortex was suppressed simultaneously. This result agrees with the suggestion of Iwamura (1998) that the SI cortex is under subthreshold interhemispheric influences. Interactions between inputs from the two hands would evidently be important for integration of somesthetic input during bilateral hand actions.

Furthermore, MEG responses have been reported from the ipsilateral SI cortex, although with high variability in both latency (90–287 ms) and generation site so that the exact sources of the responses remained unsolved (Korvenoja *et al*. 1995). Recently, Nakamura *et al*. (1999) suggested that the appearance of ipsilateral SEFs depends on hand posture, for example tactile stimulation of one index finger of hands in a cross-clasped or oriental praying position resulted in ipsilateral responses that peaked at *ca*. 60 ms, i.e. 15 ms later than the largest contralateral SEF. Thus, one probable explanation is that the ipsilateral response relies on transcallosal transfer modified by hand posture (Nakamura *et al*. 1999), which is not routinely controlled in evoked response studies.

One potential source of confusion is contamination of the recording by accidental stimulation of the other hand: the densely innervated palmar skin is extremely sensitive to tiny vibrations which may produce large 'ipsilateral' responses time-locked to the vibrations. Such a contamination has recently been reported in recordings of movement-related fields (Hari & Imada 1999). Thus, the appearance conditions of ipsilateral MEG responses from the ipsilateral SI cortex still need further evaluation.

3. SEFS FROM THE SECOND SOMATOSENSORY CORTEX SII

Tactile input from the periphery activates several cortical areas. The second somatosensory cortex (SII) is buried deep in the Sylvian fissure. Its neurons have bilateral receptive fields and, therefore, unilateral stimulation elicits bilateral signals. According to cortical stimulation studies, the human SII cortex also has somatotopical order with the face area as the most superficial, the foot area the most medial and the hand area in between (Penfield & Jasper 1954).

On the basis of previous monkey studies, the SII cortex seems to have a role in tactile learning and retention (Garcha & Ettlinger 1978), and it may be an important station in the tactile processing pathway that proceeds from the SI cortex via the SII and insular cortices to the limbic system (Murray & Mishkin 1984). Direct cortical stimulation of the human SII cortex produces percepts such as 'desire to move' and 'incapacity to move' (Penfield & Jasper 1954).

(a) *Characteristics of MEG signals from the SII cortex*

Signals from the human SI and SII cortices were differentiated by means of MEG for the first time 15 years ago (Hari *et al*. 1983*a*, 1984; Teszner *et al*. 1983): clearly distinct activation patterns were observed over the contralateral primary projection cortex and over the SII cortices bilaterally. Since then the location of the human SII cortex has been confirmed with direct cortical recordings (Allison *et al*. 1989) and with other imaging methods (Burton *et al*. 1993).

The MEG responses from the SII cortex are bilateral to unilateral stimuli but typically slightly earlier and stronger to contralateral than ipsilateral stimuli (figure 5). Attention increases response amplitudes (Hari *et al*. 1990; Mauguierère *et al*. 1997*b*; Mima *et al*. 1998*b*). The responses peak around 100 ms to upper-limb stimuli and 10–30 ms later to lower-limb stimuli. The MEG responses are very similar in waveform to responses recorded directly from the cortical surface during neurosurgery (Allison *et al*. 1989).

In MEG recordings the SII cortex hand representation seems to be anterior to the foot area whereas no reliable depth differences have yet been observed; one reason for the failure to demonstrate a consistent somatotopical organization in the SII cortex across subjects might be the rather small size of this area (Hari *et al*. 1993).

Activation patterns of the SII cortex show strong interaction between inputs from the two hands: when left and right median nerve stimuli were presented in pairs once every 2 s, with the stimuli of the pair separated by 300 ms, the responses to the second stimulus of the pair were strongly delayed, independently of whether the preceding stimulus was presented to the same or to the opposite side (Simoes & Hari 1999).

The MEG studies have thus emphasized the role of the SII cortex in integration of input from both body halves. Such fusion might be essential for a unified body image. In fact, one recent suggestion is that the SII cortex is related to the maintenance of body scheme: a patient with an illusory third hand showed smaller responses from the SII cortex when the ghost hand was present (Hari *et al*. 1998), and in patients with limb amputations, the percepts of phantom limbs were associated with decreased EEG activity of the SII cortex (Flor *et al*. 1998).

The SII cortex also seems to integrate somatosensory and motor actions. For example, SII cortex responses to median nerve stimuli are enlarged during simultaneous movements of the fingers and during isometric contraction of the hand muscles (Huttunen *et al*. 1996; Forss &

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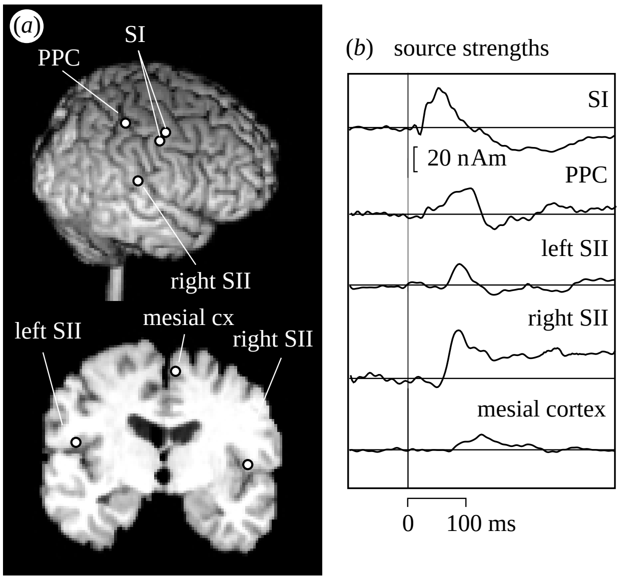

Figure 5. (*a*) Activated areas and their time behaviours as a function of time after stimulation of the left median nerve (mesial cx, mesial cortex); (*b*) a five-dipole model was applied. Adapted from Forss *et al.* (1996).

Jousmäki 1998). Such modification might reflect improved analysis of tactile signals during movements and, thus, increased responsiveness of the SII cortex neurons during behaviourally important input associated with active exploration of the environment. In fact, SII cortex lesions impair texture and shape discriminations (Murray & Mishkin 1984) which require active exploration with fingers. The SII cortex has also been suggested to serve as a cortical loop for cutaneous input to the motor cortex or as a higher-order association centre for tactile learning (Burton 1986).

(b) *Processing of noxious and visceral information*

MEG recordings have provided the first evidence in humans that nociceptive input reaches the SII cortex region: electric stimulation of the dental pulp, CO_2 stimulation of the nasal mucosa and CO_2 laser stimulation of the skin all activated the upper lip of the Sylvian fissure (Hari *et al.* 1983*b*, 1997; Huttunen *et al.* 1986; Kakigi *et al.* 1995*a*). In human intracranial recordings, the very same areas in the operculum have been shown to be activated by painful CO_2 laser stimulation of the skin (Lenz *et al.* 1998). MEG's sensitivity to signals generated in the opercular cortex thus offers promising possibilities for non-invasive studies of human central pain processing.

The pain-related responses elicited by CO_2 stimulation of the nasal mucosa have very long recovery cycles, lasting 20–30 s (Hari *et al.* 1997). Visceral oesophageal stimulation also results in SII cortex responses, peaking at 70–190 ms, with long recovery functions (Schnitzler *et al.* 1998). Interestingly, the distinctiveness of percepts of both modalities decreases rapidly with shortening interstimulus interval, thereby suggesting that the recovery cycle of the SII cortex responses is related to perceptual evaluations. On the basis of the field patterns it seems probable that both noxious and visceral stimuli can activate the SII cortex directly, without sequential processing via the SI cortex.

4. OTHER SOMATOSENSORY CORTICAL AREAS

The posterior parietal cortex (PPC), also known as the parietal association area, is usually considered to integrate sensory and motor processing and to combine tactile and proprioceptive information with other sensory modalities. MEG recordings have revealed activation of the human PPC in the wall of the post-central sulcus (Forss *et al.* 1994*a*), medial and posterior to the SI cortex hand area (figure 5). The source was most active at 70–110 ms, in agreement with the observation of Allison *et al.* (1989) that long-latency SEPs are generated either in one or in both walls of the post-central sulcus.

The human PPC is also activated by more natural airpuff stimuli. In contrast to electric stimuli which always elicit responses in the contralateral PPC, airpuff stimuli activated the PPC constantly in the right hemisphere regardless of the side of stimulation, but with significantly smaller amplitudes for right- than left-sided stimuli. (Forss *et al.* 1994*b*). These results suggest dominance of the right parietal associative cortex in the processing of natural tactile stimuli.

When subjects were asked to detect ulnar or median nerve stimuli by mentally counting them, a novel area of activation was found in the mesial cortex, in the paracentral lobule (Forss *et al.* 1996). This response peaked at *ca.* 110–140 ms (see figure 5) and was significantly reduced or totally vanished if the subjects ignored the stimuli. Mauguierère *et al.* (1997*a*) also found activation of frontal lobes during mental counting of median nerve stimuli, although with great interindividual variability, and suggested that the signals reflect a working memory process.

5. SERIAL VERSUS PARALLEL PROCESSING OF TACTILE INFORMATION

The somatosensory cortical areas form a complex network. The first activation of the SI cortex peaks *ca.* 20 ms after upper-limb stimulation and continues over 100 ms. Activation of the SII cortex typically begins at *ca.* 60–70 ms and continues up to 200 ms (figure 5). Although such timing would be in line with serial processing of somatosensory information via the SI to SII cortex areas (Mauguierère *et al.* 1997*a*), it does not necessarily imply sequential processing because the SII cortex also receives direct thalamic input. However, the importance of the thalamic pathways has remained uncertain and the serial versus parallel processing of somatosensory information between the SI and SII cortices is under continuous debate (Kaas *et al.* 1979; Rowe *et al.* 1996; Zhang *et al.* 1996).

One possibility of resolving this problem would be to study patients with circumscribed lesions in different parts of the parietal lobe. For example, Caselli (1993) proposed, on the basis of patient data, parallel processing in dual somatosensory (ventrolateral and dorsomedial) systems. Furthermore, in one patient with a large ischaemic lesion, extending from the right sylvian fissure to the right central sulcus, no MEG responses were elicited either from the right SI nor the right SII. Nevertheless, the ipsilateral left SII was activated (Forss *et al.* 1999) suggesting that SII cortex can receive input independent of the SI and SII cortices of the other hemisphere. Interestingly, PET studies also suggest parallel rather than serial activation of the SI cortex and other somatosensory cortices (Paulesu *et al.* 1997).

6. PLASTIC CHANGES

Studies of plasticity and functional recovery are important for both basic science and clinical applications. The importance of use-dependent input in modifying the adult central nervous system has been clearly demonstrated in the monkey SI cortex and the temporal coincidence of inputs is of special importance (Wang *et al.* 1995).

(a) *The SI cortex*

Reorganization of cortical maps can occur either after the absence of input, such as limb amputation or due to excess of input such as extensive practice and the accompanying enhanced tactile and proprioceptive input. Some of the plastic changes of the brain's feature maps probably follow rules of self-organization (Kohonen & Hari 1999).

Moligner *et al.* (1993) showed that the representation of fingers in the SI cortex expanded after separation of webbed fingers in two patients with syndactyly. Hari *et al.* (1993) also observed an extended cortical separation of three existing fingers in a subject whose hand had been reconstructed after traumatic amputation of the thumb and middle finger.

Considerable cortical reorganization may take place after limb amputation (Elbert *et al.* 1994; Yang *et al.* 1994). For example, cortical activity elicited by stimulation of the lip extended to the earlier representation of the amputated hand (Elbert *et al.* 1997). Flor *et al.* (1995) observed that plastic changes in the SI cortex are related to the occurrence of phantom-limb pain.

Training can effectively modify cortical representations. For example, the responses to tactile stimulation of the fingering left hand were stronger in string players than in non-musicians and the effect was most prominent in subjects who had started their career at an early age (Elbert *et al.* 1995).

Sterr *et al.* (1998) observed topographically disorganized cortical representation of fingers in blind Braille readers who used three fingers of both hands to read. Whereas in sighted subjects the typical homuncular pattern was observed, in the Braille readers the organization was distorted in one or both hemispheres. Interestingly, this disorganization coincided with behavioural misidentification of which finger was touched, indicating that use-dependent cortical reorganization has clear perceptual correlates.

(b) *Intersensory reorganization*

On some occasions, even more large-scale reorganization can take place. Levänen *et al.* (1998) studied a congenitally deaf 77-year-old man whose auditory cortex did not react to any sounds. Surprisingly, the supratemporal auditory cortex instead reacted to vibrations delivered to the subject's whole palm and fingers. The responses of the auditory cortex were clearly different to frequent 180 Hz bursts and to rare 250 Hz vibratory bursts, indicating that the auditory cortex was able to make a distinction between these two frequencies. Whereas the neuronal basis of this finding is still unclear, it is of interest that a recent intracranial recording study showed that somatosensory input has access to the macaque auditory cortex (Lindsley *et al.* 1998). Thus, the observed tactile activation of the auditory cortex in the deaf subject might reflect an omnipresent tactile input to the auditory cortex which becomes prominent only after unmasking due to missing auditory input.

7. SEFS IN BRAIN DISEASE

SEFs are deformed in various neurological diseases. In myoclonus epilepsy, giant SEFs are typically observed but they are generated at the normal sites in the SI cortex (Karhu *et al.* 1994; Mima *et al.* 1998*a*). In multiple sclerosis, some middle-latency SEFs are enlarged (Karhu *et al.* 1992), and in brain tumours and infarctions various deformations may take place (Mäkelä 1996; Forss *et al.* 1999).

The generation sites of SEFs are useful for preoperative identification of the course of the central sulcus in patients with brain tumours and arteriovenous malformations in whom anatomical landmarks may be unreliable. In subjects who are candidates for epilepsy surgery, the location of the epileptic focus can be determined with respect to the functional areas of the sensorimotor strip.

By comparing clinical symptoms and changes in somatosensory responses the functional role of various somatosensory areas can be studied and recovery from lesions can be followed in successive measurements.

9. CONCLUSIONS

MEG's strength in studies of the somatosensory system is the excellent temporal resolution and the possibility of focusing on activity of the fissural cortex, which has remained poorly explored in intracranial recordings. The present whole-scalp neuromagnetometers also provide an excellent opportunity for studying the brain's spontaneous rhythms and their reactivity besides the evoked responses (Hari & Salmelin 1997; Hari & Salenius 1999). The temporally accurate MEG data nicely complement anatomically accurate PET and functional magnetic resolution imaging recordings, but the MEG community should improve communication of their results, for example by presenting the source locations in Talaraich coordinates. Combination of MEG with EEG will also increase information about the neuronal system under study (Nagamine *et al.* 1998).

The cortical network activated by even simple somatosensory stimuli is complex and widely distributed. Well-selected patients might enlighten the unresolved issue of sequential versus parallel processing between different areas. In the future, interactions between different cortical areas should be studied directly by means of source activations to obtain more specific information.

Until now, most MEG studies of the somatosensory system have applied very unnatural stimuli, probably because natural stimulation is much more difficult in the somatosensory modality than in visual or auditory modalities. To progress further towards unravelling brain functions of active exploration of objects, new 'real-life-like' stimulators should be developed. Better knowledge about the activation of the whole cortical somatosensory network with natural stimuli will also improve the possibilities of MEG for clinical diagnosis and follow-up.

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