Simultaneous Early Processing of Sensory Input in Human Primary (SI) and Secondary (SII) Somatosensory Cortices

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Karhu, J. and C. D. Tesche. Simultaneous early processing of sensory input in human primary (SI) and secondary (SII) somatosensory cortices. J. Neurophysiol. 81: 2017–2025, 1999. The anatomic connectivity of the somatosensory system supports the simultaneous participation of widely separated cortical areas in the early processing of sensory input. We recorded evoked neuromagnetic responses non-invasively from human primary (SI) and secondary (SII) somatosensory cortices to unilateral median nerve stimulation. Brief current pulses were applied repetitively to the median nerve at the wrist at 2 Hz for 800–1,500 trials. A single pulse was omitted from the train at random intervals (15% of omissions). We observed synchronized neuronal population activity in contralateral SII area 20–30 ms after stimulation, coincident in time with the first responses generated in SI. Both contralateral and ipsilateral SII areas showed prominent activity at 50–60 ms with an average delay of 13 ms for ipsilateral compared with contralateral responses. The refractory behavior of the early SII responses to the omissions differed from those observed at ~100 ms, indicative of distinct neuronal assemblies responding at each latency. These results indicate that SII and/or associated cortices in parietal operculum, often viewed as higher-order processing areas for somatosensory perception, are coactivated with SI during the early processing of intermittent somatosensory input.

INTRODUCTION

A widely held view of cortical somatosensory organization is that the sensory scene is completed by serial, hierarchical processing of gradually more complex stimulus features. Anatomically, this view is supported by the presence of large, somatotopically organized primary receiving cortices with converging projections to smaller association areas. Primary somatosensory cortex SI contains, from anterior to posterior, four cytoarchitectonic areas 3a, 3b, 1, and 2 (Brodman 1909; Economo 1929). In monkey, each area is occupied by a complete body map (Nelson et al. 1980; Pons et al. 1985, 1987b) with the largest cortical representations of peripheral sites like fingers or face corresponding to the largest somatosensory receptor density. The somatosensory association areas of posterior parietal cortex (PPC) are located posterior to primary somatosensory cortex (SI) (Powell and Mountcastle 1959). Areas 3a and 3b receive the densest thalamocortical afferentation and project to areas 1 and 2. Only the latter are connected anteriorly to the motor areas and to posterior association areas (Jones 1986). The anatomically hierarchical corticocortical projections between the subdivisions of SI and association cortices are taken to advocate functional hierarchy in somatosensory processing.

In addition to PPC, further processing of tactile information occurs in second somatosensory cortex (SII) and neighboring cortical areas that are located in the parietal operculum posterior to the face representation in SI and medial to the primary auditory areas (for a review, see Burton 1986). Originally, Woolsey and Fairman (1946) demonstrated that this “second” somatosensory area exists in a variety of animals and has separate representations for different parts of the body. The activation of this area to somatosensory stimulation first was observed in man by intraoperative cortical recordings in epileptic patients (Penfield and Jasper 1954) and noninvasively with magnetoencephalographic (MEG) recordings (Hari et al. 1984, 1993) and with positron-emission tomography (Burton et al. 1993, 1997a; Ledberg et al. 1995). Recent anatomic and physiological studies in monkeys have clarified the borders of the region that traditionally was designated as SII, the neighboring parietal ventral area (PV) (Krubitzer et al. 1995) and insular cortex, which includes retrosinsular area (Ri) and granular insula (Ig) (Burton et al. 1995). Interestingly, at least two of these opercular regions seem to have relatively complete body maps with enlarged representation of the hand area similar to that observed in SI (Burton et al. 1995; Krubitzer et al. 1995). The more anterior region is connected more strongly with the area 3b in SI and is possibly more responsive to cutaneous stimulation than the posterior one (Burton et al. 1995; Robinson and Burton 1980b).

Extensive anatomic and physiological studies have confirmed that SII obtains bilateral input (Robinson and Burton 1980a; Whitssel et al. 1969; for a review, see Burton 1986). All cytoarchitectonic areas of SI are connected reciprocally with the ipsilateral SII; however, the main source of reciprocal callosal fibers between SI and contralateral SII may be in area 2 (Manzoni et al. 1986). Area 3b has callosal connections also with PV, and SII is interconnected densely with both ipsi- and contralateral PV (Krubitzer and Kaas 1990). The callosal connections between SI and SII are organized somatotopically (Manzoni et al. 1986), and this topographic organization appears to duplicate that of the association connections between SI and SII in the ipsilateral hemisphere (Jones and Powell 1969). The cortico-cortical association input from SI may have a significant role in defining the response properties of neurons in SII and neighboring areas to peripheral stimuli, and, subsequently, SII may contribute via corticocortical pathways to tactile learning and memory (Friedman et al. 1986; Mishkin 1979; Murray and Mishkin 1984; Suzuki and Amaral 1994).
The cortico-cortical and thalamocortical connectivity of SII and adjacent cortices provides a substrate for both early participation in the initial processing of somatosensory input and in higher-order processing, which includes input from SI. Functionally, SII has been associated with processing of the temporal features of somatic sensation (Burton and Sinclair 1991; Ferrington and Rowe 1980), with sensorimotor integration (Huttunen et al. 1996), with tactile attention (Mima 1998), and with tactile learning and intermanual transfer (Ridley and Ettlinger 1976). SII, together with other parietal regions (Iwamura et al. 1994), may integrate somatosensory information from both sides of the body (Manzoni et al. 1986; Ridley and Ettlinger 1976). These observations indicate that SII has the capacity to perform several functions depending on the overall demands of somatosensory processing. However, the timing of neuronal activity in SII and parietal operculum with respect to the other somatosensory areas has remained somewhat evasive. In this study, we used intermittent median nerve stimulation and whole-scalp magnetoencephalography to obtain functional evidence for timing of initial activation of neuronal assemblies in human primary and secondary somatosensory cortical areas.

METHODS

Subjects and stimuli

We report results from six healthy volunteers (age 25–50 yr). Informed consent was obtained from all subjects. Unilateral median nerve stimulation was delivered through transcutaneous electrodes at the wrist in the form of a train of brief constant current pulses (rectangular shape, 0.3-ms duration) at 2 Hz (interstimulus intervals of 0.5 s). Individual pulses in the train were omitted randomly (15% omissions) to investigate possible responses to a brief interruption of the temporal pattern of the stimuli (Fig. 1C). The pulse amplitudes (4–6 mA) were adjusted individually to be completely painless but strong enough to cause a muscle twitch in the hand muscles innervated by the median nerve. Between 800 and 1,500 pulses were delivered to each stimulated nerve.

Data acquisition

Neurophysiologic responses to median nerve stimulation were recorded with a magnetoencephalographic (MEG) array. Subjects were seated underneath a cryogenic dewar containing a helmet-shaped array of 122 superconducting quantum interference detectors (SQUIDs) (Ahonen et al. 1993). The SQUID sensors were mounted in pairs on planar substrates at 61 sites over the scalp. Each sensor was configured to sample the temporal variation of the local magnetic field gradient created by changes in current flow in the brain. Figure 1, A and B, shows the distribution of the sensors across the array and results of a simulation of MEG signals corresponding to idealized sources of current in SI and in SII.

Measurements were performed inside a magnetically shielded room. Three small coils were located on the subject’s scalp before entering the room. A 3-D digitizer (Polhemus Navigation Science, Colchester, VT) was used to record the locations of the coils with respect to nasion and left and right preauricular points. During the measurement session, each coil was energized individually with current immediately before recording a block of data. The position of the head with respect to the array was determined from measurements of the magnetic field patterns generated by these test currents. This allowed the alignment of a coordinate system for the MEG data with magnetic resonance images for each subject (1-T Siemens Magnetom system with a MPR3D sequence).

FIG. 1. A and B: magnetoencephalographic (MEG) signal detection illustrated with simulated data. Magnetic resonance (MR) images of the subject NI show the locations (−) of dipolar current sources in primary (SI; A) and secondary (SII; B) somatosensory cortices. Tails indicate the directions of the current flow at each location. Corresponding MEG signals are shown on the right. Each of the 61 squares in the array contain 2 superconducting sensors that measure, respectively, the gradients dBz/dx and dBy/dy of the magnetic field component Bn perpendicular to the x-y plane determined by the detector substrates. →, amplitudes and orientations of the local magnetic field gradients. MEG signals are strongest in those sensors that are located directly over the dipolar sources. C: experimental design showing the temporal pattern of the stimuli. Repetitive electrical stimulation of the median nerve at the wrist at 2 Hz was interrupted by infrequent omissions of single stimuli. Sequence of occurrence of the expected but omitted stimuli (O), the 1st stimuli after an omission (F), and all the subsequent stimuli (S) was randomized.

Data recorded by the array were band-pass filtered at 0.03–330 Hz and sampled at 1 kHz. Average evoked MEG responses were calculated on-line time-locked to the presentation of stimuli S and of stimuli F over 600-ms epochs (c.f. Fig. 1C). In a separate calculation, responses were averaged over 1,100-ms time-locked to the anticipated but omitted stimuli (an omission is indicated by the letter O in Fig. 1C). These epochs also included responses to the subsequent first stimulus after an omission (stimuli F in Fig. 1C). Averaged evoked MEG responses for epochs containing all stimuli except those following immediately after an omitted stimulus (stimuli S in Fig. 1C) were calculated subsequently off-line. A vertical electrooculogram was used to reject trials contaminated by eye movements and blinks (rejection limits ±150 μV).

Signal analysis

An equivalent current dipole (ECD) model was used to characterize neuronal population activity in superficial fissural cortex. An ECD is a short segment of current flow used to approximate a fairly well-localized (~cm) region of activity (Williamson and Kaufman 1981; for a review, see Hämäläinen et al. 1993). MEG responses for these sources were computed using a spherical head model with parameters fixed by an approximation of the local curvature of the sphere to the configuration of the skull directly over the presumed source location. Individual ECD locations and orientations were determined for sources in SI, SII, and associated cortical areas from a least-squares fit of the predicted signals to the data. Signals were used for subsets of 34 channels located over central (SI and parietal sources) and temporal (SII and parietal opercular sources) areas, respectively. SQUID
sensors detect relative changes in the signal strength as a function of time, necessitating a choice of baseline for the measured responses. The baseline for the epochs containing responses to the omitted stimuli and to the first stimuli after omission was the average of the sensor readings from 100 to 5 ms preceding the omission. The baseline for the evoked responses to the subsequent stimuli was the average of the sensor readings from 100 to 5 ms before the corresponding stimulation.

A quantitative measure of the overlap of two patterns of MEG signal strengths and orientations, such as those shown in Fig. 1, A and B, can be determined directly from the data (Ilmoniemi and Williamson 1987; Uusitalo and Ilmoniemi 1997). The degree of overlap is characterized by a single parameter, the signal-space (SSP) angle. Current distributions in the brain that generate identical patterns of signals in the MEG array are not distinguishable: the corresponding SSP angle is 0°. Signal patterns that are completely orthogonal determine an SSP angle of 90°. All ECDs used in the present analysis, including those of SI and SII, had pairwise SSP angles in excess of 30° and consequently could be adequately distinguished by the 122-channel MEG array.

The random omissions of individual stimuli elicited responses that appeared as more complex and widespread patterns of activity across the array. Characterization of these responses by ECD sources was not attempted. The complex omission responses were characterized at specific latencies directly as the patterns of signals recorded in the MEG array. Waveforms were determined simultaneously for all of the ECD sources and the omission-related responses from a multicomponent analysis of the MEG data (Tesche et al. 1995). These waveforms are referred to in the text as SSP waveforms.

The measured data contained contributions from neuronal population activity within the human brain and also contributions from various external noise sources. These noise sources, referred to collectively as ‘system noise,’ were uncorrelated with the brain signals. The effective system noise for each SSP component was determined from data recorded for the same number of trials and sampling frequency/filter settings with no subject under the array (Tesche et al. 1995). Only features such as repeatable peaks in evoked response waveforms that had amplitudes exceeding the corresponding system noise by ≥2.5 SD were accepted for further analysis. The statistical significance of source strength differences between all the averaged responses except the first ones after omissions (responses to the S stimuli in Fig. 1C) and the responses to the first stimuli after omissions (responses to the F stimuli in Fig. 1C) was tested by Student’s paired two-tailed t-test.

RESULTS

Figure 2 shows the locations and orientations for sources in SI and SII (subject N1). The averaged SSP waveforms indicate time-locked neuronal population activity in contralateral SI and in bilateral SII cortices to right median nerve stimulation. During the first 200 ms after the omitted stimuli, the waveforms for SI and SII are on the order of system noise. In contrast, the activation of SI to the first and subsequent median nerve stimulations after omissions begins with brisk, prominent responses at ~20 ms after the stimulation. In general, SI waveforms display a characteristic, well-known pattern of neuromagnetic responses at 35, 45, 60–80, and ~100 ms (Hari et al. 1984, 1993; Mauguie`re et al. 1997a,b).

Surprisingly, SII contralateral to stimulation also shows initial activity at ~20 ms after the stimulus with prominent bilateral responses occurring first at 40–60 ms. Because the SSP angles between SI and SII for all recordings were on average 66 ± 13°, (complete dissimilarity 90°), disentanglement of their respective signals in the present analysis is highly likely. In contrast, activation of separate neuronal populations within SII would correspond to almost identical patterns of signals in the MEG array. Thus the SII SSP waveforms shown here may contain at each latency contributions from slightly different locations and orientations of the underlying sources within SII and immediately adjacent areas in parietal operculum.

Figure 3 shows SSP waveforms for contralateral SI and bilateral SII sources for both hemispheres in all subjects. The responses to the first stimuli after omissions and the responses to all the other stimuli are depicted separately. In SI, the initial 20-ms responses were evident in all studied hemispheres. In contralateral SII, the 20-ms activity was detected in 7 of 12 studied hemispheres (subjects N1, N2, N3, N5, and N6) and the 40–60-ms activity in 9 of 12 studied hemispheres (subjects N1, N2, N3, N4, and N5). The first response of SII preceded the first
response of SI in four hemispheres (subjects N1, N3, and N5). The 100-ms responses were observed in all studied hemispheres. In SII ipsilateral to stimulation, SII responses could be recognized at around 50 ms in 8 of 12 studied hemispheres and at 100 ms in all studied hemispheres. Ipsilateral 50- and 100-ms SII activity peaked significantly later than the corresponding activity of contralateral SII (cf. Table 1).

Figure 4 shows the SII responses to contralateral median nerve stimulation in all subjects with a larger amplification than in Fig. 3. The identification of the latencies of the P1, P2, and P3 peaks are indicated on the figure. The amplitudes of these early SII responses for each subject and hemisphere are shown in Table 2. The earliest P1 response in SII (mean latency 20.9 ± 2.9 ms) coincides in time with N20 response in SI (20.8 ± 1.4 ms). P1 was followed by an opposite deflection (N1; 29.2 ± 4.4 ms) in seven hemispheres and subsequent activation (P2; 40.7 ± 4.0 ms) was followed by an opposite deflection (N2; 54.3 ± 7.3 ms) in six hemispheres. The most prominent SII activity started at ~80 ms (mean latency 83.8 ± 10.3 ms).

Preceding omissions did not have any significant effects on SI responses, whereas they clearly enhanced the 100-ms, but not earlier, responses in SII. The enhanced responses to omissions during the 100-ms response are shown in Fig. 4 as the difference area between the SSP waveforms for the first responses after omissions and the SSP waveforms for responses to subsequent stimuli. The group-averaged difference area to stimuli immediately after an omission is 7.1 ± 5.5 nAm, whereas the difference area to all the other stimuli is 2.1 ± 1.2 nAm (P < 0.01).

Figure 5 displays the relationship between the latency of the earliest SI response and the body length, between the earliest SII response and the body length, and between the earliest SI and SII responses. There is a clear dependence between the latencies of early SI and SII responses and the body length. All correlations are linear with the explained proportions of variance 84% (SI vs. body length), 78% (SII vs. body length), and 89% (SII vs. SI).

DISCUSSION

Early neuronal population activity in SII

In this study, noninvasively recorded evoked neuromagnetic responses revealed early synchronized neuronal population activity in human SI and in parietal operculum, most likely in SII or adjacent somatosensory cortex. This activity started 20–30 ms after intermittent median nerve stimulation in contralateral SII and coincided in time with the first neuromagnetic activity in the primary receiving cortex SI (representing the initial thalamocortical volley to area 3b). In four hemispheres, the peak activity in SII areas preceded the activity in SI. There was also a clear dependence between the latencies of initial SI and SII responses and the body length. Body length is not a direct measure of the distance from the stimulation site to cortex along the peripheral conducting nerve fibers. However, it is very closely correlated with the latency of the initial somatosensory evoked responses in SI as shown by normative studies for intersubject comparisons of somatosensory evoked potentials (for example, Chiappa 1990). The similar dependence between the latency of early SII responses and the body length strongly suggests a quite direct anatomic route to SII areas.

The initial activity in contralateral SII areas was followed by an ~40-ms evoked responses. Corresponding responses emerged in ipsilateral SII areas slightly later, at 50–60 ms.

| TABLE 1. SII responses to contra- and ipsilateral median nerve stimulation |
|---------------------------------|-----|-----|-----|
| Contralateral | n | Ipsilateral | n |
| SII SEFs, ms | | |
| P1 | 20.9 ± 2.9 | 7 | |
| P2 | 40.7 ± 4.0 | 9 | 53.6* ± 4.2 | 8 |
| P3 | 83.8 ± 10.3 | 12 | 106.4* ± 27.6 | 12 |
| SI SEFs, ms | | |
| N20 | 20.8 ± 1.4 | 12 | |

Latencies (±SD) have been calculated from averaged responses excluding the first responses after omissions. n, number of hemispheres showing each response. The significance of differences between contra- and ipsilateral latencies, *P < 0.01 (t-test). SI and SII, primary and secondary somatosensory cortices; SEF, somatosensory evoked field.
This 10- to 20-ms delay suggests callosal transmission of input from the contralateral hemisphere (cf. Burton 1986; Manzoni et al. 1986). The 40- to 60-ms time frame is significantly shorter than that determined previously by the 100–180 ms bilateral SII responses to regular stimuli (Hari et al. 1984, 1993; Hämaäinen et al. 1990). This first sign of bilateral activity is an indicator of the time required for the initiation of interhemispheric somatosensory processing of intermittent stimuli in parietal operculum.

To our knowledge, early evoked responses in the 40-ms latency range have been observed twice before in contralateral human SII by intracranial recordings. In these two series of epileptic patients, small SII responses were observed in 1 of 20 (Woolsey et al. 1979) and in 1 of 25 studied subjects (Lüders et al. 1985). These sparse observations are consistent with the primary findings by Penfield and Rasmussen (1954), who could define an SII area in only 8 of 350 cases of stimulation of the sensorimotor cortex during brain surgery. The much higher prevalence of SII responses in this study may be in part due to the different sensitivity of used methods to neuronal currents. Human SII resides in the depth of sylvian fissure, which is not reached by intracranial grid electrodes but which is readily accessible to MEG recordings (Hari et al. 1984).

**Parallel anatomic routes to SI and SII**

Simultaneous 20-ms neuronal population activity of primary receiving cortex SI and SII clearly requires an anatomic substrate for the conduction of peripheral input to receiving neurons. The thalamocortical connectivity of SII and neighboring areas in parietal operculum obey, in primates, a general principle that is different from the connectivity of SI. SI receives the great majority of input via a single (caudal ventral posterior lateral; VPLc) relay nucleus, whereas the somatic cortical fields of parietal operculum each receive inputs from an assembly of thalamic nuclei and the individual thalamic somatosensory nuclei each project to more than one cortical field (Burton 1984; Burton et al. 1990; Friedman and Murray 1986; Krubitzer and Kaas 1992; Manzoni et al. 1986; Stevens et al. 1993). The anatomic routes that mediate touch, pressure, and position from peripheral nerve endings to SI via VPL of...
thalamus are characterized by a strict organization according to the submodalities of somatic sensation. Separate sets of thalamic relay cells project to specific areas in SI. Signals from muscle afferents project to area 3a (Phillips et al. 1971) and from slowly and rapidly adapting mechanoreceptors project mainly to areas 3b and 1, correspondingly (Kaas et al. 1979). Signals from joints, muscles, and other “deep” structures project to area 2 (Burchfield and Duffy 1972; Iwamura et al. 1993; Pons et al. 1985).

The ventroposterior inferior thalamic nucleus (VPI) appears to be the main source of afferentation to the area traditionally designated as SII (Burton et al. 1990; Friedman and Murray 1986; Krubitzer and Kaas 1992; Stevens et al. 1993). It is distinct from VPLc even if some thalamic relay cells in VPLc may convey information to both SI and SII. VPI includes also finger-like protrusions of neuron groups that extend to the region of ventroposterior nucleus (VP). Neurons in all parts of VPI project preferentially to SII rather than to SI, and PV in parietal operculum receives the majority of its thalamic input via VPI (Krubitzer and Kaas 1992). Another substantial source of afferentation resides in dorsal part of posterior nucleus (Po) (Burton et al. 1990; Friedman and Murray 1986), centrolateral nucleus (CL) (Stevens et al. 1993), and possibly also in anterior pulvinar (Burton et al. 1990). The insular and retrolimbic regions receive their input from a variety of nuclei (including VPI) located at the posteroventral border of thalamus (Friedman and Murray 1986). A number of subcortical somatosensory afferent pathways to SII and neighboring cortices are dissociated from those to SI.

Functional interaction between SI and SII

Neuronal activity in SII may depend on the integrity of processing in SI or may even receive the majority of the low-frequency sensory input via SI in primates (Garraghty et al. 1990; Mountcastle et al. 1969; Pons et al. 1987b). The functional consequences of ablations or inactivations of SI cortical areas in monkeys originally supported the view of hierarchical processing of somatosensory input. Removal of SI or even area 3a or 3b alone seriously impaired further processing of tactile information (Garraghty et al. 1990; Pons et al. 1987a). Furthermore, total removal of the hand representation in SI left the corresponding area in SII initially unresponsive, but after 6–8 wk this area was occupied by foot representation (Pons et al. 1988). This observation contradicted the notion of any functionally significant direct thalamic input from hand nerve endings to SII. However, deactivation of SI in cats and prosimians did not have a clear effect on the responsiveness of SII to cutaneous stimuli (Burton and Robinson 1987; Garraghty et al. 1991; Turman et al. 1992) and recent investigations in marmosets using reversible inactivations of SI (Rowe et al. 1996; Turman et al. 1995; Zhang et al. 1996) suggest that SI and SII receive independent input in these species. One possible hypothesis to account for the results of lesion studies would be an ability of the somatosensory system to provoke subthreshold excitatory postsynaptic effects on SII via callosal and/or ipsilateral reciprocal connections between SI and SII (Manzoni et al. 1986). This kind of functional network could modulate the reactivity of different cortical regions and be also responsive to the overall attentional or anticipatory state of the somatosensory system. A recent study in marmosets provided evidence that reduction in SII responsiveness in association with cooling of SI was attributable to the loss of background facilitatory influence rather than a blockage of peripheral input via a putative serial pathway from SI (Zhang et al. 1996). In another study, trained monkeys lost the ability to discriminate somatosensory frequencies after lesions restricted to SI but could relearn the tasks at higher thresholds with SII intact (LaMotte and Mountcastle 1979).

SII activation depends on stimulus intervals and attention

SII is capable of responding to temporal information over a wide variety of time scales from milliseconds to several seconds. In addition to high-frequency input, “vibration,” (>100 Hz) (Burton and Sinclair 1991; Hämmäläinen et al. 1990), low-frequency “flutter” (1–50 Hz) activates SII neurons strongly in primates. Indeed, in some recent studies the majority of activated SII neurons produce high-fidelity responses to very low-frequency input at 1–10 Hz (Burton and Sinclair 1991). At
the level of neuronal assemblies, similar responsiveness to the slow temporal features of input is supported by previous neuromagnetic studies, which have revealed very consistently the sensitivity of the 100-ms SII response to regular interstimulus intervals (ISIs) \( \leq 10-20 \) s (Hari et al. 1984, 1993; Mauguìère et al. 1997a,b). In contrast, early SI neuronal population responses are suppressed due to repetitive stimulation only at ISIs \( < 150-120 \) ms (Huttunen et al. 1992).

The early coactivation of contralateral SI and parietal operculum during regularly presented stimuli interspersed with omissions has not been reported in the earlier studies in man which used uninterrupted trains of stimuli (Forss et al. 1996; Hari et al. 1984, 1993). Quite recently intermittent stimulation studies with random omissions and slightly longer ISIs of 1.2 s also failed to evoke 20–60 ms activity in SII and surrounding areas (Mauguìère et al. 1997b). Because many aspects of the measurement techniques were roughly comparable for the previous and present MEG studies, we conclude that the neuronal populations in parietal operculum that respond at short latencies to intermittent somatosensory input may not have been effectively activated by the regular stimulation or by intermittent stimulation with 1.2-s ISI to the level of detection in the previous studies. The large number of averaged responses used in the present study (800–1,500) served to enhance the signal-to-noise ratio and thus the detectability of fairly low-amplitude responses in parietal operculum.

Random omissions of robust somatosensory stimuli may draw attention involuntarily to the stimulation and modulate the neuronal response of cortical areas. Poranen and Hyvärinen (1982) suggested that activity of individual neurons in SII can be altered by attentional effects. Neurophysiological studies in monkeys have revealed increased firing rates in SI and both increased and decreased firing in SII during a selective spatial attention task (Hsiao et al. 1993). Very recently, a selective attention study using vibrotactile stimuli showed predominantly suppressed firing rates in SII during the anticipation of a stimulus and relatively enhanced activity during and after the attended stimulus (Burton et al. 1997b). In two studies of somatosensory attention, directed attention increased the magnitude of neuromagnetic 100-ms SII activity to some extent (Mauguìère et al. 1997a,b; Mima et al. 1998), but there were no signs of attentional enhancement of SII activity at 20–60 ms.

We may use the previous results to suggest a consistent interpretation of the data presented here. In the present study, the early SII responses at 20 and 40–60 ms showed no enhancement to the stimuli immediately after the omission, whereas the responses at \( \approx 100 \) ms enhanced significantly. We did not experiment directly on the ISIs in this study. However, given the lack of change of the amplitude of the shortest latency responses in SII to a preceding stimulus omission, which in effect doubles the ISI from 0.5 to 1 s, one might not expect to see any major ISI dependence for this response.

In contrast, the enhancement of 100-ms responses agrees nicely with the previously reported long recovery cycle \( \leq 10-20 \) s for SII responses at this latency range to both median nerve (Hari et al. 1984, 1993) and cutaneous (Hari et al. 1990) hand stimulation. The contrasting refractory behavior between the early and late SII responses reported here suggests activation of separate underlying neuronal assemblies during intermittent stimulation. Interestingly, similar stimulus dependence and slow recovery of population responses are taken in the auditory modality to represent the duration of sensory memory traces (Lü et al. 1992). The interpretation of 100 ms responses in SII as an indicator of sensory memory would be consistent with the observed impairments in frequency discrimination and tactile learning after lesions of SII cortex (LaMotte and Mountcastle 1979; Ridley and Ettlinger 1976).

Conclusions

The data reported here are indicative of separate somatosensory pathways contributing to early contralateral SI and SII responses. In addition, the data support activation of two functionally separate neuronal assemblies in SII or adjacent cortical areas underlying the early and late SII responses. Results from anatomic and PET studies are consistent with the contribution of multiple neuronal populations to simultaneous synchronous activity in SII and surrounding areas (Burton et al. 1995, 1997a; Krubitzer et al. 1995). In the present study, some of the early contralateral SII responses appear to emerge even before those in SI. However, even very short delays of responses, on the order of 2–3 ms, would allow for a synapse in SI and subsequent signal transmission via SI to SII. Thus on the basis of the present evoked response data, it cannot be concluded that the early SII activity was mediated exclusively by separate thalamocortical connections or by additional cortical afferents from SI. However, the data do demonstrate the coactivation of SII and/or associated cortices in parietal operculum with SII during the early processing of the intermittent somatosensory input.

The timing of somatosensory input appears to be crucial for the activation of neuronal populations in SII and/or adjacent cortical areas. Interestingly, recent MEG results showed very early (16–20 ms) neuronal responses to an identical median nerve stimulation in human cerebellum (Tesche and Karhu 1997). This result, together with that of the present study, suggests that early coactivation may span both cerebral and cerebellar neuronal assemblies in somatosensory networks during intermittent somatosensory stimuli. The main factor separating these studies from earlier ones is the relatively rapid somatosensory stimulation interspersed by randomly timed omissions with a predictable duration. In a recent PET study, anticipated somatosensory stimuli produced a substantial suppression of blood flow in SII (Drevets et al. 1995). We may speculate that if SII areas are deeply involved in the detection of temporal features of somatosensory input, the early responses may reflect an enhancement of the fast, direct processing of anticipated stimuli in SII. In this case, somatosensory networks which are associated with the analysis of the timing of stimuli may modulate the function of pathways to SII or of the receiving SII neurons.

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