Attention Modulates Both Primary and Second Somatosensory Cortical Activities in Humans: A Magnetoencephalographic Study

TATSUYA MIMA, TAKASHI NAGAMINE, KAORI NAKAMURA, AND HIROSHI SHIBASAKI
Department of Brain Pathophysiology, Kyoto University School of Medicine, Shogoin, Sakyo-ku, Kyoto 606–8507, Japan

Mima, Tatsuya, Takashi Nagamine, Kaori Nakamura, and Hiroshi Shibasaki. Attention modulates both primary and second somatosensory cortical activities in humans: a magnetoencephalographic study. J. Neurophysiol. 80: 2215–2221, 1998. To clarify the role of primary and second somatosensory cortex (SI and SII) in somatosensory discrimination, we recorded somatosensory evoked magnetic fields during a stimulus strength discrimination task. The temporal pattern of cortical activation was analyzed by dipole source model coregistered with magnetic resonance imaging. Stimulus intensity was represented in SI as early as 20 ms after the stimulus presentation. The later components of SI response (latency 37.7 and 67.9 ms) were enhanced by rarely presented stimuli (stimulus deviancy) during passive and active attention. This supports an early haptic memory mechanism in human primary sensory cortex. Contra- and ipsilateral SII responses followed the SI responses (latency 124.6 and 138.3 ms, respectively) and were enhanced by attention more prominently than the SI responses. Active attention increased SII but not SI activity. These results are consistent with the concept of ventral somatosensory pathway that SI and SII are hierarchically organized for passive and active detection of discrete stimuli.

INTRODUCTION

Somatosensory information is represented in multiple areas of human brain. Among them, the primary and second somatosensory cortices (SI and SII) are the principal regions for tactile perception. Activation studies with positron emission tomography in human reported that somatosensory stimulation increases regional blood flow in SI and the parietal opercular cortex (including SII) (Bonda et al. 1996; Burton et al. 1997; Fox et al. 1987; Seitz and Roland 1992). However, there is only a limited information on the temporal pattern of the activation and function in these areas (Allison et al. 1992, 1989; Hari et al. 1983, 1993; Lüders et al. 1985; Mima et al. 1997). On the basis of the lesion studies, SI is believed to be indispensable for somatosensory perception (Carlson 1980; Randolph and Semmes 1974), and SII is proposed to be involved in the higher order somatosensory perception including tactile discrimination and memory (Caselli 1993; Murray and Mishkin 1984; Ridley and Ettlinger 1976, 1978). This functional hierarchy does not imply unidirectional or serial anatomic connections because somatosensory signals from the ventroposterior thalamus are processed serially from SI to SII as well as in parallel (Garraghty et al. 1991; Pons et al. 1987, 1992; Zhang et al. 1996). Studies in monkeys (Burton and Sinclair 1990, 1991; Sinclair and Burton 1993) showed that neuronal activity in SII shows spatial as well as modality convergence and greater stimulus specificity dependent on SI activity. This is in accord with the hypothesis that SII serves as a higher order region for somatosensory information processing. These observations also support the concept of a ventral somatosensory pathway from SI via SII to the insula, which finally projects to limbic structures related to long-term memory (Friedman et al. 1986; Mishkin 1979). This study addresses the question about the time course of SI and SII activation as well as the responsiveness of these regions to passive versus active attention to stimulus change, with a whole head magnetoencephalography (for review see Hämäläinen et al. 1993). Previous human studies on somatosensory recognition mainly utilized a spatial attention task stimulating different fingers (Desmedt and Tomberg 1989; Garcia-Larrea et al. 1995; Hari et al. 1990; Kekoni et al. 1996; Mauguie é et al. 1997; Yamaguchi and Knight 1991). In these tasks, however, cortical receptive areas are different for attended and nonattended stimuli because of somatotopic organization. Accordingly, the rate of impulse arrival at the somatosensory cortex is different for stimuli delivered to different digits. Thus it is difficult to disentangle the effect of attention from that of stimulus presentation rate or stimulus deviancy (Hari et al. 1990; Nagamine et al. 1998). To address this problem, we employed a stimulus intensity detection task (Michie 1984; Michie et al. 1987) in which the activated brain areas shared somatotopy. We examined the effects of both passive and active attentions on neural activity in SI and SII.

METHODS

Ten right-handed volunteers were the subjects for the present study [age 26.3 ± 4.6 yr (mean ± SD), 4 females and 6 males]. All subjects gave the informed consent before the experiments according to the approval by the Committee of Medical Ethics, Graduate School of Medicine and Faculty of Medicine, Kyoto University.

Stimulus and task

An oddball paradigm was employed in which two kinds of electric pulse of 0.2-ms duration were given to the right median nerve at the wrist at the fixed repetition rate of 2 Hz. One stimulus was strong (10% above the motor threshold) and the other was weak (10% above the sensory threshold). In experiment 1, strong stimuli occurred 90% of the time, and an infrequently (10%) and randomly occurring weak stimulus served as the deviant rare stimuli. In experiment 2, the probabilities of the strong and weak stimuli were
reversed (strong 10%; weak 90%). During the recording period, the subjects were asked to look at the screen placed 1 m in front of them. For each of the two experiments, two different tasks were examined in separate sessions. In the active attention task, subjects were instructed to mentally count the deviant (rare) stimuli. In contrast, during the passive attention (ignore) task, subjects watched a self-chosen video shown on the screen without any requirement to pay attention to any stimulus.

Data acquisition

During the recording, the subjects were quietly seated in the magnetically shielded room (NKK, Yokohama, Japan) with their head fixed in a helmet-shaped magnetometer array, which has 122 first-order planar SQUID gradiometers (Neuromag 122, Neuromag, Helsinki, Finland). The planar gradiometer detects the largest signal just above the local electric generator source. Cortical electromagnetic activities and simultaneously recorded electrooculogram (EOG) were averaged with respect to the stimulus onset for the time window of 350 ms including the prestimulus baseline of 50 ms (pass band 0.03–320 Hz, sampling rate 920 Hz). Any signals with amplitude exceeding either 150 μV for EOG or 3,000 fT/cm for MEG were rejected from the average. At least 50 sweeps for infrequent stimuli and ~400–500 for frequent stimuli were averaged during each recording session. Sequential order of the experiments and task was randomized and counterbalanced among subjects. At least two recording sessions were performed for each task, and the grouped average, thus obtained, was used for further analysis.

The Cartesian coordinate system for each head was defined by measuring three anatomic landmarks (nasion, left and right preauricular points) with Isotrack three-dimensional digitizer (Polhemus Navigation Sciences, Colchester, VT). The x-axis passed the preauricular points from the left to the right. The y-axis ran through the nasion and perpendicular to the x-axis. The cross point between these two lines was used as the coordinate origin (anterior positive). The positive z-axis was upward. Three-dimensional magnetic resonance images were acquired by Siemens 1.0-T Magnetom system and were used for the anatomic coregistration. The location and orientation of the head relative to the dewar were measured with three head position indicator coils fixed on the scalp.

Data analysis

To identify the generator source for the response, equivalent current dipole (ECD) was computed by using a least-squares search (Hämäläinen et al. 1993). ECDs explaining >80% of the field variance (goodness-of-fit value) were utilized for further analysis. The magnitude of the cortical activation was expressed as a strength of the generator source (dipole moment). Multidipole model was constructed based on the assumption that the sources were fixed in location and orientation, but their strength and directions changed as a function of time (Scherg and von Cramon 1986). The ECD at SII was searched by a projection method (Uusitalo and Ilmoniemi 1997). If the MEG responses over SII were overlapped with the simultaneously occurring SI signals, the predicted SI activity was subtracted before the fitting of ECD. For the statistical evaluation, either analysis of variance (ANOVA) or multivariate ANOVA was utilized. Three factors, intensity (strong vs. weak stimuli), deviance (frequent vs. rare stimuli), and task (mental counting vs. ignoring) were assessed.

Results

Mean stimulus intensity for strong and weak stimuli was 5.0 ± 1.5 and 2.1 ± 0.5 mA, respectively (mean ± SD). All subjects could easily discern the stimulus difference. The mean error rate during mental counting task was 7.2 ± 7.9% for experiment 1 and 6.3 ± 5.6% for experiment 2, which were not significantly different.

The early components of somatosensory evoked magnetic fields (SEFs) were maximal over the left central area (Fig. 1). Magnetic activities with longer peak latencies (100–200 ms) were recognized at bilateral temporal-parietal areas in the SEFs after the rare stimuli.

At the left central area, three successive peaks were identified with the peak latency of 20.1 ± 1.0, 37.3 ± 12.5, and 67.9 ± 12.6 ms, which were designated as N20m, P40m, and P60m, respectively. Source localization of each of the three components and the bilateral temporal–parietal responses revealed that N20m, P40m, and P60m components were localized at the hand area of SI and that bilateral temporal–parietal peaks were at the ipsilateral and contralateral SII (SIIc and SIIi, respectively, Fig. 2). The locations of the sources were not affected by any conditions. The direction of the ECD for N20m pointed anteriorly, and that for both P40m and P60m pointed posteriorly. Generator sources for SII responses pointed superior–anteriorly. Multidipole analysis applied to these three generators explained >80% of the field variance of the acquired signals up to ~150 ms, and no other sources were required. Parameters of three components generated from SI (component N20m, P40m, and P60m), and those of bilateral SII responses (side SIIi and SIIc) are shown in Table 1.

SI responses in general were significantly affected by intensity and deviance but not by task (P = 0.0001, 0.0001, and 0.5145, respectively). However, because significant interactions between component and intensity or deviance were observed, the effects of intensity and deviance were evaluated for each SI component. Intensity yielded significant effects on all three components, and deviance had significant effect on P40m and P60m but not on N20m (Fig. 3A). SIIc and SIIi responses after rare stimuli (either strong or weak) were recognized in 22 and 14 of 40 data sets, respectively. SII response after frequent stimuli was rarely identified (4/40). Therefore, the effects of side, intensity, and task were tested in the SEFs after rare stimuli. The magnitude of SII response was significantly larger for the contralateral side (Table 1, P = 0.02). Irrespective of side, SIIc and SIIi responses were significantly affected by both intensity and task (P = 0.0001 and 0.0001, Fig. 3B). Active attention to either weak or strong stimuli increased SI activity.

Discussion

This study focusing on the sequential processing of somatosensory inputs demonstrated that in humans passive and
FIG. 1. Typical example of somatosensory evoked magnetic fields (SEFs) after the right median nerve stimulation at wrist in experiment 1 during the attention task (mental counting of rare stimuli). The head is viewed from the top. In each pair of signals, the derivatives of the magnetic fields along the latitude and longitude are shown separately as the top and bottom traces, respectively. Two different blocks of averages for each of the 2 kinds of stimuli (strong frequent stimuli: gray line; weak rare stimuli: black line) are superimposed. Vertical line at each channel indicates the stimulus onset. Representative channels showing the responses at primary, and contra- and ipsilateral second somatosensory cortices (SI, SIIc, and SIIi, respectively) are magnified, and each recognizable peak is designated (N20m, P40m, and P60m at SI, SIIc, and SIIi responses).
active attention modulates neural activity in both SI and SII, but in a different manner.

The physiological characteristics of stimuli (i.e., intensity) strongly affect the magnitude of SI and SII activation. Stimulus intensity was represented in SI in the earliest stage at 20-ms poststimulation (N20m). Even in the ignoring condition, passive or automatic attention to stimulus deviance modulated both SI response at a little later stage (P40m and P60m) and bilateral SII responses. A simple explanation such as the interstimulus interval effect (Hari et al. 1990) is unlikely the cause for these findings because, in this study, the same cortical receptive areas were activated by both rare and frequent stimuli, and both weak and strong stimuli resulted in a deviancy effect. It is possible that the SEF changes in experiment 2 were partially associated with sensory factors because median nerve receptive neurons with higher threshold are expected to be activated only by the strong infrequent stimuli. However the observation that both rarely delivered weak and strong stimuli induced the stronger activation in SI and SII than the frequent ones suggests that stimulus deviancy accounts for the results. This attention capture (passive attention) hypothesis is supported by similar observation of a deviancy-related neuronal activity in the auditory modality (mismatch negativity, MMN) (Hari et al. 1993; Javitt et al. 1994; Näätänen et al. 1978, 1993; Winkler et al. 1993). The MMN is attributable to the activity in sensory-specific areas (primary and secondary auditory cortex) and is proposed to be a neural marker of an early echoic memory system (Csépe et al. 1992; Hari et al. 1984). The SI passive attention activity may reflect an early haptic memory mechanism analogous to the auditory MMN. This hypothesis can be supported by the result that task has no effect on SI activity. In contrast to the earliest stage of SI response (20 ms) reflecting a direct thalamocortical projection, the later components (P40m and P60m) are associated with the GABAergic interneurons in SI (Wilkström et al. 1996). Recent studies in cortical plasticity revealed an important role of GABAergic system in control of afferent activity-dependent
TABLE 1.  Parameters of ECDs for each identifiable component of SEFs

<table>
<thead>
<tr>
<th>Source</th>
<th>Mean Latency, ms</th>
<th>x-axis, mm</th>
<th>y-axis, mm</th>
<th>z-axis, mm</th>
<th>Dipole Moment, nAm</th>
</tr>
</thead>
<tbody>
<tr>
<td>SI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>N20m</td>
<td>20.1 ± 1.0</td>
<td>-47.5 ± 6.9</td>
<td>14.6 ± 9.0</td>
<td>95.1 ± 6.7</td>
<td>12.7 ± 6.2 (n = 52)</td>
</tr>
<tr>
<td>P40m</td>
<td>37.3 ± 12.5</td>
<td>-42.1 ± 8.6</td>
<td>15.2 ± 9.4</td>
<td>96.0 ± 8.5</td>
<td>16.4 ± 9.6 (n = 48)</td>
</tr>
<tr>
<td>P60m</td>
<td>67.9 ± 12.6</td>
<td>-45.4 ± 7.8</td>
<td>12.8 ± 7.6</td>
<td>94.8 ± 7.5</td>
<td>20.1 ± 13.5 (n = 74)</td>
</tr>
<tr>
<td>SIIc</td>
<td>124.6 ± 31.7</td>
<td>-49.8 ± 5.4</td>
<td>18.8 ± 11.6</td>
<td>66.8 ± 10.8</td>
<td>20.4 ± 11.3 (n = 22)</td>
</tr>
<tr>
<td>SIIi</td>
<td>138.3 ± 24.3</td>
<td>45.4 ± 9.3</td>
<td>15.5 ± 9.4</td>
<td>75.1 ± 12.2</td>
<td>18.4 ± 7.9  (n = 14)</td>
</tr>
</tbody>
</table>

Values are means ± SD with number of data sets in parentheses. ECD, equivalent current dipole; SEFs, somatosensory evoked magnetic fields; SI, primary somatosensory cortex; SIIc and SIIi, contra- and ipsilateral second somatosensory cortex, respectively. * Mean locations of N20m, P40m, and P60m are not significantly different among each other (multivariate analysis of variance, primary somatosensory cortex, SIIc and SIIi, contra- and ipsilateral second somatosensory cortex, respectively. * Mean locations of N20m, P40m, and P60m are not significantly different among each other (multivariate analysis of variance, P > 0.05).

changes of the neuronal excitability (for review see Jones 1993). It is conceivable that this GABAergic system might be involved in detection of the unfamiliar deviant stimuli.

In texture discrimination tasks, the discharge of SI neurons correlated with the gratings of the surface, whereas that of SII neurons reflected the change in grating (Jiang et al. 1997; Sinclair and Burton 1993). In agreement with these single neuron recordings, SII responses in this study were almost exclusively elicited by the rare (deviant) stimuli. This result suggests that the effect of attention is stronger in SII than in SI and that SII does not represent a somatotopic copy but rather the selected version of the external world. Moreover, an attention-related enhancement of the response was observed in SII but not in SI, supporting the involvement of SII in higher order processing for somatosensory perception. The association between SII and active attention is supported by previous animal studies in which SII responses were characterized by labile and inconsistent responses to nontask passive testing (Burton and Sinclair 1990, 1991; Jiang et al. 1997; Sinclair and Burton 1993) and were enhanced by a tactile discrimination task (Hsiao et al. 1993). However, the effect of attention on SII responses was not clear in the previous human studies with spatial attention task (Hari et al. 1990; Mauguire et al. 1997). This divergence in the effect of attention is most likely explained by the difference in the attributes of the target. In the auditory attentional system, MMN was affected by a sharp focused attention developed by an intensity discrimination task but not by a frequency discrimination task (Woldorff and Hillyard 1991). This difference in the attentional effect is reasonable because the attentional modulation would be more prominent when discriminations are made within populations of neurons than when the discriminations are made between the somatotopically/totopically organized populations of neurons.

Sequential activation of SI and SII and the systematic transformation of somatosensory information suggest that the analysis of stimulus intensity is not only spatially but also temporally distributed across the hierarchically organized somatosensory system including SI and SII. The behavior of SI and SII components is partly similar to cognitive components reported in previous event-related potential studies (Desmedt and Tomberg 1989; Garcia-Larrea et al. 1995; Michie 1984; Michie et al. 1987). However, these findings cannot be directly compared with those previous studies because scalp-recorded potentials tend to reflect the summation of brain activities generated from multiple areas, whereas the current MEG study focused on the local activities arising from SI [especially area 3b or SI-proper (Kaas 1983) ] and bilateral SII. Although subdivision of the somatosensory areas within the parietal operculum was recently proposed (Burton et al. 1995, 1997; Krubitzer et al. 1995; Mima et
al. 1997), we used the term SII response for denoting the largest activity in the human parietal operculum. In this experiment, the location of the generator sources in SII and their direction were not affected by the task, suggesting that sensory cortex.

We thank Drs. Robert T. Knight and Naohito Fujiwara for useful comments and discussions. This study was partly supported by the Japan Ministry of Education, Science, Sports, and Culture Grants-in-Aid for Scientific Research (A)09308031, (A)08558083, (C)09670655, Priority Areas Grant 08279106, and International Scientific Research Grant 10044269 and also by Japan Society for the Promotion of Science Research for the Future Program Grant RTFTF97L00201.

Received 13 May 1998; accepted in final form 1 July 1998.

REFERENCES


Pons, T. P., Garraghy, P. E., Friedman, D. P., and Mishkin, M. Physio-


