The Representation of the Human Oral Area in the Somatosensory Cortex: a Functional MRI Study

The tactile sensation of the teeth is involved in various oral functions, such as mastication and speech. Using functional magnetic resonance imaging, we investigated the cortical sensory representation of the oral area, including the teeth. First, we identified the somatotopic representation of the lips, teeth and tongue in the postcentral gyrus (GpOC). Tactile stimuli were applied to the lower lip, tongue and teeth. The foci activated by each stimulus were characterized by the center of gravity (COG) of activated areas. Secondly, we examined the rostro-caudal changes in the somatotopic organization in the GpOC in terms of the overlap between each sensory representation. In the rostral portion of the GpOC, the COG of the representation of teeth was located significantly superior to that of the tongue and inferior to that of the lip, consistent with the classical 'sensory homunculus' proposed by Penfield; however, this somatotopic representation became unclear in the middle and caudal portions of the GpOC. The overlap between each representation in the middle and caudal portions of the GpOC was significantly greater than that in the rostral portion of the GpOC. These findings support the theory that the input from oral structures converges hierarchically across the primary somatosensory cortex.

Keywords: fMRI, oral area, postcentral gyrus, somatosensory cortex, teeth representation

Introduction

When one bites into a fresh apple, one can control the optimal force of the movement of the jaws and perceive its crispy texture through the sensory information arising from the teeth. Such information, especially from periodontal mechanoreceptors, is important in controlling biting behavior. Moreover, it provides feedback information during the initial contact with food in the chewing cycle and other manipulations involving the teeth; for example, while food is positioned and held prior to biting (Trulsson and Johansson, 1996). Periodontal afferents play an important role not only in the discrimination of interdental size or thickness (Morimoto, 1990; Jacobs and van Steenbergh, 1994) but also in the reflexes of the masticatory muscles, bite-force sensation (van Steenbergh, 1979; Linden, 1990) and oral stereognosis (Jacobs et al., 1997). Although there are several human studies of peripheral tooth sensation (Trulsson et al., 1992; Trulsson and Johansson, 1994, 1996, 2002), few have investigated tactile tooth sensation at the cortical level. Penfield and Rasmussen (1950) investigated human sensory somatotopy intraoperatively. In their study, the representation of the teeth, gingiva and jaws was located below that of the lips and above that of the tongue, and could not be subdivided. Since then, several non-invasive studies of human sensory somatotopy of oral structures have focused on the postcentral gyrus (Yamashita et al., 1999; Lotze et al., 2000b; Nakahara et al., 2004). In these studies, however, the representation of the teeth was not investigated. Human studies using functional neuroimaging are few and their results are inconsistent. Using magnetoencephalography (MEG) with electrical stimulation of the gingiva but not teeth, Nakahara et al. (2004) revealed that the dipole evoked by gingival stimulation was in the primary somatosensory cortex, located inferior to that of the lips and close to that of the tongue. Using functional magnetic resonance imaging (fMRI) and painless vibrotactile dental stimulation, Ettlin et al. (2004) found activation in bilateral insular cortex and the supplementary motor area; however, they found no activation in the primary somatosensory area. Hence, the representation of the teeth in the primary somatosensory cortex remains to be clarified.

Recently, a hierarchical structure of tactile information processing in the primary somatosensory cortex has been proposed (Iwamura., 1998). While the majority of neurons in area 3b have a receptive field confined to one finger, neurons with receptive fields covering multiple fingers increased towards the caudal portion of the postcentral gyrus (Iwamura et al., 1980, 1983, 1993). This finding suggests that somatosensory information from different body parts can be integrated as they are conveyed caudally in the primary somatosensory cortex.

The purpose of the present study was to clarify the somatotopic organization of the oral area, including the teeth, in the primary somatosensory cortex in humans using fMRI. We studied the cortical organization along two orthogonal directions: ventro-dorsal (inferior-superior) and rostro-caudal. First, we characterized the somatotopic representation in the rostral portion of the postcentral gyrus (GpOC) along the ventro-dorsal axis using the centers of gravity (COGs) of the activated areas induced by the tactile stimuli of teeth, lips and tongue. Secondly, we investigated how this somatotopic organization changes along the rostro-caudal axis in the GpOC by locating the COGs and the overlap of activated areas of cortex. To address how this overlap changes, we classified the activated voxels in the GpOC into two types: simple receptive field (SRF) voxels, which were activated by only one stimulus, and composite receptive field (CRF) voxels, which were activated by more than one stimulus. We then examined how the proportion of SRF and CRF voxels changed with caudal progression in the GpOC.

Materials and Methods

Subjects

Fourteen healthy volunteers (eight males and six females, mean age = 32.6 years, range 24-56 years) participated in this study. Thirteen...
subjects were right-handed and one was left-handed according to the Edinburgh handedness inventory (Oldfield, 1971). None of the subjects had a history of neurological or psychiatric illness. The protocol was approved by the ethical committee of the National Institute for Physiological Sciences, Japan. Before the experiment, the subjects were informed in detail about the nature of the experiment, and gave their written informed consent for the study.

Sensory Stimulation
Subjects were stimulated at three areas on the right side of the oral area: the lower lip, the tongue and the upper central incisor tooth. Tight, but comfortable, foam padding was placed around each subject’s head to minimize any movement. The subjects wore a cheek retractor throughout the scanning period, so that the experimenter could stimulate the specific targeted intra-oral region without touching the surrounding structures.

For lower-lip stimulation, the tactile stimuli consisted of rubbing the lip using a stick with a piece of Velcro at its tip. The contact zone between the lip and the Velcro was ~5 mm wide. The lower lip was stimulated 1 cm to the right of the midline. The stick used for stimulation was fixed on a table that was set on both edges of the scanner bed to avoid it touching the subject’s body. The stick was allowed to rotate around its long axis to minimize the possibility of touching the surrounding structures. The oscillating movement of the stick provided oscillating strokes of ~5 mm at the contact zone. The rotation was acoustically cued at a constant frequency of 1 Hz. Using the same settings, the anterior part of the tongue, 1 cm to the right of the midline, was stimulated. The right upper incisor tooth was also stimulated using the stick with a grooved rubber tip which held the tooth (Fig. 1). Oscillating movement of the stick provided torque force to the incisor at a constant frequency of 1 Hz.

Stimulation was provided by the same well-trained experimenter (J.J.M.) to minimize the variability of stimuli across the subjects. The subjects were instructed to remain still and to close their eyes in the scanner during the acquisition of functional scans. Before the experiment, each stimulus was tested in the scanner to confirm that the stimulation was clear and constant, and that the stick was touching only each target area specifically.

Data Acquisition
The subjects underwent two scanning runs for each target area. Each run consisted of an alternating pattern of three stimulation and four rest periods, each of which was 20 s in duration. In each scanning run, 38 volumes were acquired using T2*-weighted gradient echo-planar imaging (EPI) sequences using a 3.0 Tesla scanner (Allegra, Siemens, Volksdorf, Germany). Each volume consisted of 32 oblique slices, each 3.0 mm in thickness without a gap, which were taken parallel to the central sulcus so that the cortical representation of the oral area along the central sulcus could be observed in a single slice. The time interval between two successive acquisitions of the same slice was 4000 ms, with a flip angle (FA) of 90° and 52 ms of echo time. The field of view (FOV) was 192 mm and the in-plane matrix size was 128 \times 128 pixels. For anatomical reference, T1-weighted magnetization-prepared rapid-gradient echo (MPRAGE) images (TR = 1400 ms, TE = 4.38 ms, FA = 8°, FOV = 192 mm, matrix size = 256 \times 256 pixels, slice thickness = 3 mm) for each subject with the identical location parameters of EPI.

In addition, high-resolution 3D T1-weighted MPRAGE (TR = 2500 ms, TE = 4.38 ms, FA = 8°, FOV = 230 mm, matrix size = 256 \times 256 pixels, slice thickness = 1 mm) images were obtained for each subject.

Data Analysis
The first three volumes of each scanning run of functional images were discarded due to unsteady magnetization, and the remaining 35 volumes per run (210 volumes per subject) were used for the analysis. The data were analyzed using statistical parametric mapping (SPM99; Wellcome Department of Cognitive Neurology, London, UK) (Friston et al., 1994, 1995a) implemented in Matlab (Mathworks, Sherborn, MA).

Head motion was corrected with the SPM99 realignment program (Friston et al., 1995a). Following realignment, the high-resolution 3D T1-weighted MRIs were co-registered to EPI images with reference to the anatomical T1-weighted MRI with the identical location parameters of the functional images. This is because EPIs are T2*-weighted images with lower resolution, and hence are difficult to coregister with high-resolution 3D T1-weighted images directly. The parameters for affine and nonlinear transformation into a template of T1-weighted images already fitted to standard stereotaxic space (MNI template) (Evans et al., 1994) were estimated with the co-registered high-resolution 3D T1-weighted images by the least-square means (Friston et al., 1995a,b). The parameters were applied to the functional images. No spatial smoothing was applied because the analysis was performed primarily on a single-subject basis. A general linear model was used to identify voxels with stimulus-related signal changes. The stimulation period was modeled using a boxcar function convolved with a hemodynamic response function, and significant correlations between the observed response and the modeled response were estimated, yielding t value maps.

Region of Interest (ROI) Definition
The ROI of the oral representation was defined in the GPoC contralateral to the stimulated side. The ROI was defined in each axial slice of the normalized high-resolution anatomical image of each individual, which were 1 mm thick (Fig. 2). First, the superior and inferior margins were defined in the axial slices as z = +25 mm and +55 mm, respectively. The superior margin corresponds to the anatomically defined motor hand areas identified by the anatomical landmark of the inverted-omega sign (Yousry et al., 1997; Ferretti et al., 2003). The motor hand area was used to locate the sensory hand area, which is immediately caudal to it (Jasper et al., 1960; Stohr and Goldring, 1969; Broughton et al., 1981; Allison et al., 1989; Woolsey et al., 1979; Ibanez et al., 1995). Here we assume that the representation of the oral area of the primary somatosensory cortex is located inferior to that of the hand (Penfield and Rasmussen, 1950). The inferior margin (z = +25 mm) was set based on previous studies to exclude activity in the second somatosensory cortex (Ruben et al., 2001; Ferretti et al., 2003). Individual analysis confirmed segregated activation clusters dorsal and ventral to the arbitrary border, corresponding to SI and S2 respectively.

Secondly, the central and postcentral sulci were identified on the high-resolution anatomical images using standard procedures (Steinmetz et al., 1990) for every slice between z = 25 and 55 mm. Finally, the quadrilateral ROI was defined as follows. The GPoC was defined as the antero-postero-medial vertices of the ROI were defined as the fundus of the central and the postcentral sulci, respectively. The antero-lateral and postero-lateral vertices were defined as the points of intersection of the extension of the two sulci with the tangent to the arc drawn by the lateral margin of the GPoC. The quadrilateral ROI in each axial slice was defined as the enclosed region made by connecting these four points. Moreover, to delineate the changes in somatotopagic organization from

Figure 1. Device for tooth stimulation. The subject wore a cheek retractor. The stimulation device consisted of a stick with a grooved rubber at its tip that held the right central incisor. The stick was fixed on a table (not shown).
define three sub-ROIs. The quadrilateral were trisected, and the points marking 1/3 and 2/3 were connected to three sub-ROIs (rostral, middle and caudal). The lateral and medial sides of the region made by connecting four vertices: the antero-medial (AM), postero-medial (PM), antero-lateral (AL) and postero-lateral (PL). Moreover, the ROI was divided into the rostral to the caudal portion of the GPoC, the ROI was divided into three sub-ROIs (rostral, middle and caudal); the lateral and medial sides of the quadrilateral were trisected, and the points marking 1/3 and 2/3 were connected to define three sub-ROIs.

**Figure 2.** Region of interest (ROI) defined at the postcentral gyrus. The axial slices from z = 25 mm to 55 mm of the anatomically normalized high-resolution T1-weighted image of one subject are displayed in the upper row. The lower row shows the image of one subject are displayed in the upper row. The lower row shows the location of the sensory representation.

Using the threshold of SPM99, the activated voxels in each stimulus condition within each sub-ROI were defined using SPM99, with a threshold of $t = 2.5$ to $t = 5.0$, $P < 0.05$ without correction for multiple comparisons. In addition, our analysis was based on the hypothesis proposed by Penfield and Rasmussen (1950) that the representation of the teeth is located significantly superior to that of the tongue and inferior to that of the lip. Linear contrasts were used to compare the COGs of the tongue and lip representations against the representation of the tooth.

**Evaluation of the Overlap of Sensory Representations**

To evaluate the overlap of the cortical activations elicited by the three stimulated oral areas, SRF and CRF voxels were defined as the voxels activated by only one stimulus condition and by two or three stimulus conditions, respectively.

The proportion of the number of the CRF voxels to the number of total voxels activated by at least one stimulus condition was calculated in each sub-ROI and subjected to an RM-ANOVA with sub-ROI (rostral, middle and caudal) as the within-subject factor. Pairwise comparisons using linear contrasts were also performed to contrast rostral versus middle, and middle versus caudal. This was based on the idea that neurons in the GPoC with multiple receptive fields increased with a caudal progression, as shown in a previous animal study (Iwamura, 1998). In addition, to investigate whether this tendency was observed consistently for each different representation, we calculated separately the proportion of the number of CRF voxels activated by a particular stimulus condition to the number of total voxels activated by this particular stimulus condition; this was then subjected to an RM-ANOVA with two within-subject factors [sub-ROIs (rostral, middle and caudal) and stimulus site (tongue, tooth and lip)]. Pairwise comparisons using linear contrasts were also performed between the rostral and middle, and the middle and caudal, sub-regions.

**Results**

Typical individual data are shown in Figure 3. The activated foci during tooth stimulation were located between those for the tongue and lip, and were separated in the rostral portion of the GPoC, whereas they merged together in the caudal portion.

**Location of Sensory Representation**

In the rostral portion of the GPoC, the COG of the tooth representation was located between those for the lip and tongue, consistent with the 'sensory homunculus' (Penfield and Rasmussen, 1950). In the middle and caudal regions, however, this arrangement of COGs was less clear (Fig. 4). The RM-ANOVA for the entire data set of COG locations revealed significant main effects of stimulus site $F(2,26) = 7.059, P < 0.001$, middle $F(2,26) = 6.654$, $P = 0.005$, and their interaction $F(2,26) = 7.059, P < 0.001$. Separate RM-ANOVAs in each sub-ROI revealed significant main effects of stimulus site in the rostral $F(2,26) = 14.449, P < 0.001$, middle $F(2,26) = 5.099, P = 0.014$ and caudal $F(2,26) = 6.654, P = 0.005$ regions. In the rostral portion of the GPoC, the comparison of the tongue and lip locations compared with the tooth location using the

**Table 1**

<table>
<thead>
<tr>
<th>Sub-region of interest</th>
<th>Stimulation</th>
<th>Averaged Talairach’s coordinates, mm (SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>x</td>
<td>y</td>
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<tr>
<td>Rostral</td>
<td>Lip</td>
<td>$-55.5 (0.68)$</td>
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<tr>
<td></td>
<td>Tooth</td>
<td>$-58.8 (0.69)$</td>
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<tr>
<td></td>
<td>Tongue</td>
<td>$-57.1 (0.52)$</td>
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<tr>
<td>Middle</td>
<td>Lip</td>
<td>$-58.3 (0.62)$</td>
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<td></td>
<td>Tooth</td>
<td>$-57.6 (0.77)$</td>
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<tr>
<td></td>
<td>Tongue</td>
<td>$-58.1 (0.73)$</td>
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<tr>
<td>Caudal</td>
<td>Lip</td>
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<tr>
<td></td>
<td>Tooth</td>
<td>$-56.7 (0.50)$</td>
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<tr>
<td></td>
<td>Tongue</td>
<td>$-57.9 (0.49)$</td>
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The averaged coordinates of the centers of gravity of the cortical activations

In the rostral portion of the GPoC, the comparison of the tongue and lip, and were separated in the rostral portion of the GPoC, whereas they merged together in the caudal portion.

1. **Evaluation of the Location of the Sensory Representation**

Using the t-values of all the significantly activated voxels in each sub-ROI, the Talairach’s coordinates of the COGs (Lotze et al., 2000a,b) were calculated to evaluate the location of the somatotopic representation of each stimulated site (Table 1). The evaluation of the location was performed in terms of the $z$ coordinates of the COGs. The location of the COGs was subjected to a repeated-measures analysis of variance (RM-ANOVA), with the two within-subject factors of stimulated site (tongue, tooth and lip) and sub-ROIs (rostral, middle and caudal). Moreover, a separate RM-ANOVA was performed in each sub-ROI with stimulated site (tongue, tooth and lip) as the within-subject factor. In addition, our analysis was based on the hypothesis proposed by Penfield and Rasmussen (1950) that the representation of the teeth is located significantly superior to that of the tongue and inferior to that of the lip. Linear contrasts were used to compare the COGs of the tongue and lip representations against the representation of the tooth.
the COG of the tongue was located significantly inferior to that of the tooth \[ F(1,13) = 7.335, P = 0.018 \] but was not different from that of the lip \[ F(1,13) = 0.003, P = 0.954 \]. In the caudal portion, the COG of the tooth was significantly superior to that of the tongue \[ F(1,13) = 11.628, P = 0.005 \] and lip \[ F(1,13) = 8.819, P = 0.011 \].

**Overlap of the Sensory Representations**

The proportion of the CRF voxels increased gradually in the rostral-to-caudal direction (Fig. 5). The RM-ANOVA revealed significant main effects of sub-ROIs \[ F(2,26) = 6.154, P = 0.006 \], and the pairwise comparison using linear contrasts revealed a significant increase from the rostral to middle portion \[ F(2,26) = 7.629, P = 0.016 \], although no significant increase was observed from the middle to the caudal regions \[ F(2,26) = 1.733, P = 0.211 \]. The proportion of CRF voxels in each stimulus condition also increased gradually in the rostral-to-caudal direction (Fig. 6); the RM-ANOVA revealed main effects of sub-ROIs \[ F(2,26) = 7.134, P = 0.003 \], but neither a significant main effect of stimulus site nor an interaction between sub-ROIs and stimulus site. Pairwise comparisons using linear contrasts revealed a significant increase from the rostral to middle regions for the tooth \[ F(1,13) = 6.286, P = 0.026 \], the lip \[ F(1,13) = 8.378, P = 0.013 \] and the tongue \[ F(1,13) = 7.663, P = 0.016 \] conditions. However, no significant increase was found from the middle to caudal regions for the tooth \[ F(1,13) = 0.652, P = 0.431 \], the lip \[ F(1,13) = 1.858, P = 0.196 \] and the tongue \[ F(1,13) = 1.344, P = 0.267 \] conditions.

**Discussion**

Using tactile stimulation to the oral regions, we showed that the cortical somatosensory representation of the tooth was located superior to that of the tongue and inferior to that of the lip in the rostral portion of the GPOc. This somatotopic organization was less clear in the middle and caudal portions of the GPOc. In addition, the proportion of CRF voxels increased in the rostral-to-caudal direction in all stimulus conditions, suggesting that the sensory representations of different oral regions showed more overlap in the middle and caudal regions than in the rostral portion of the GPOc.

**Somatotopic Representation**

We used COGs to evaluate the somatotopic representations of the oral regions. COGs have previously been used for somatotopic mapping of the somatosensory or motor cortex, although the details of the experiments differed (Lotze et al., 2000a,b; Hlustik et al., 2001; Dechent and Frahm, 2003). This is partly because split representations, in which multiple regions were activated by one stimulus, were often observed in somatotopic mapping in non-human primates (Manger et al., 1996). In the present study, we also observed split representations with multiple activated clusters induced by one stimulus (Fig. 3). COGs are useful in such cases to specify the location of the representation.

Brodman’s areas 3a, 3b, 1 and 2 correspond roughly to the fundus of the central sulcus, its posterior bank, the crown of the postcentral gyrus and the anterior bank of the postcentral sulcus, respectively (Geyer et al., 1999, 2000; Greifkes et al., 2001). Thus antero-posterior differences in somatotopic precision revealed by ROI analysis may be partly explained by the differences in underlying cytoarchitectonic structures.
The somatotopic organization of the teeth in the rostral portion of GPoC was similar to that reported in non-human primate studies in area 3b contralateral to the stimulated side (Manger et al., 1996; Jain et al., 2001). The present finding is concordant with the ‘sensory homunculus’ (Penfield and Rasmussen, 1950). In Penfield’s study, the subjects verbalized the subjective sensation induced by the electrical stimulation of the cortical surface. By contrast, in the present study, the subjects were given tactile stimuli peripherally and the brain responses were identified objectively using functional images. Although these two studies adopted different approaches, the converging results indicate that the sensory representation of the oral area in the primary somatosensory cortex is organized such that the tongue, teeth and lips are located in the ventral-to-dorsal direction.

The Overlap of the Cortical Activations
We found that the proportion of CRF voxels increased in the middle and the caudal regions compared with the rostral portion of the GPoC. These results are consistent with previous non-human primate studies regarding the sensory representation of the digits (Iwamura et al., 1980, 1983, 1993) and the oral area (Toda and Taoka, 2001, 2002, 2004). In humans, a non-invasive study of finger representation suggests that a greater number of adjacent activated foci showed greater overlap in areas 1 and 2 than in area 3b, and there was a partial reversal of digit order (Kurth et al., 2000). The present study indicates a similar organization for the representation of oral areas in the primary sensory cortex.

Because of this representational change, a hierarchical scheme for sensory information processing has been proposed such that the somatosensory information from different parts of the body are integrated as they are conveyed from the primary sensory-receiving stage to the more associative stage. For example, areas 3a and 3b receive dense projections from the thalamus and connect to areas 1 and 2 in the GPoC, while areas 1 and 2 receive far fewer projections directly from the thalamus than does area 3 (Jones and Powell, 1970; Jones, 1975; Jones and Burton, 1976). In addition, the latency of the neuronal responses to vibration stimuli was longer in area 2 than in areas 3 or 1 (Lebedev and Nelson, 1996). These results, and those of other human studies (Urbano et al., 1997; Eskenasy and Clarke, 2000), suggest that the larger part of sensory information is conveyed serially via cortico-cortical connections between these areas.

The caudal portion of the GPoC might play an important role in integrating sensory information from various areas and sending it to other cortical regions. Anatomically, area 2 projects to the primary motor cortex (Burton and Sinclair,
1996). Functionally, inactivation of the digit region of area 2 is known to impair hand behavior (Hikosaka et al., 1985), whereas inactivation of area 3b and area 1 did not. Mastication and articulation require multiple oral structures to work cooperatively and mastication is significantly affected by the loss of function of a single oral structure (Trulsson and Johansson, 1996). Hence, we suggest that the rostral-to-caudal progression of the overlap of sensory representations might indicate converging input from oral structures, including the teeth. This hierarchical representation might aid the complex coordinated control of the oral structures.

Conclusion
To investigate the cortical organization of sensory information processing in humans of the oral region, including the teeth, we used fMRI to observe the activations induced in the primary somatosensory cortex following tactile stimulation of the lip, the incisor tooth and the tongue. The tooth representation, as used fMRI to observe the activations induced in the primary processing in humans of the oral region, including the teeth, we used fMRI to observe the activations induced in the primary somatosensory area. The somatotopic organization of the oral structures was expressed by the COGs, was located superior to that of the incisor tooth and the tongue. The tooth representation, as used fMRI to observe the activations induced in the primary processing in humans of the oral region, including the teeth, we used fMRI to observe the activations induced in the primary somatosensory cortex of the first somatosensory cortex of the conscious monkey. Brain Res 325: 375-380.


References


