Response of Anterior Parietal Cortex to Cutaneous Flutter Versus Vibration

M. Tommerdahl, K. A. Delmos, B. L. Whitsel, O. V. Favorov, and C. B. Metz. Response of anterior parietal cortex to cutaneous flutter versus vibration. J. Neurophysiol. 82: 16–33, 1999. The response of anesthetized squirrel monkey anterior parietal (SI) cortex to 25 or 200 Hz sinusoidal vertical skin displacement stimulation was studied using the method of optical intrinsic signal (OIS) imaging. Twenty-five-Hertz ("flutter") stimulation of a discrete skin site on either the hindlimb or forelimb for 3–30 s evoked a prominent increase in absorbance within cytoarchitectonic areas 3b and 1 in the contralateral hemisphere. This response was confined to those area 3b/1 regions occupied by neurons with a receptive field (RF) that includes the stimulated skin site. In contrast, same-site 200-Hz stimulation ("vibration") for 3–30 s evoked a decrease in absorbance in a much larger territory (most frequently involving areas 3b, 1, and area 3a, but in some subjects area 2 as well) than the region that undergoes an increase in absorbance during 25-Hz flutter stimulation. The increase in absorbance evoked by 25-Hz flutter developed quickly and remained relatively constant for as long as stimulation continued (stimulus duration never exceeded 30 s). At 1–3 s after stimulus onset, the response to 200-Hz stimulation, like the response to 25-Hz flutter, consisted of a localized increase in absorbance limited to the topographically appropriate region of area 3b and/or area 1. With continuing 200-Hz stimulation, however, the early response declined, and by 4–6 s after stimulus onset, it was replaced by a prominent and spatially extensive decrease in absorbance. The spike train responses of single quickly adapting (QA) neurons were recorded extracellularly during microelectrode penetrations that traverse the optically responding regions of areas 3b and 1. Onset of either 25- or 200-Hz stimulation at a site within the cutaneous RF of a QA neuron was accompanied by a substantial increase in mean spike firing rate. With continued 200-Hz stimulation, however, QA neuron mean firing rate declined rapidly (typically within 0.5–1.0 s) to a level below that recorded at the same time after onset of same-site 25-Hz stimulation. For some neurons, the mean firing rate after the initial 0.5–1 s of an exposure to 200-Hz stimulation of the RF decreased to a level below the level of background ("spontaneous") activity. The decline in both the stimulus-evoked increases in absorbance in areas 3b/1 and spike discharge activity of area 3b/1 neurons within only a few seconds of the onset of 200-Hz skin vibration stimulation raised the possibility that the predominant effect of continuous 200-Hz stimulation for >3 s is inhibition of area 3b/1 QA neurons. This possibility was evaluated at the neuronal population level by comparing the intrinsic signal evoked in areas 3b/1 by 25-Hz skin stimulation to the intrinsic signal evoked by a same-site skin stimulus containing both 25- and 200-Hz sinusoidal components (a "complex waveform stimulus"). Such experiments revealed that the increase in absorbance evoked in areas 3b/1 by a stimulus having both 25- and 200-Hz components was substantially smaller (especially at times >3 s after stimulus onset) than the increase in absorbance evoked by "pure" 25-Hz stimulation of the same skin site. It is concluded that within a brief time (within 1–3 s) after stimulus onset, 200-Hz skin stimulation elicits a powerful inhibitory action on area 3b/1 QA neurons. The findings appear generally consistent with the suggestion that the activity of neurons in cortical regions other than areas 3b and 1 play the leading role in the processing of high-frequency (>200 Hz) vibrotactile stimuli.

INTRODUCTION

An extensive literature describes the capacity of humans and nonhuman primates to detect, localize, and discriminate vibrotactile stimuli that differ in frequency and documents the fundamental attributes of the peripheral and central neural mechanisms believed to underlie those perceptual capacities (for review, see Mountcastle 1984; also LaMotte and Mountcastle 1975; Mountcastle et al. 1990). At the same time, there are significant gaps in the present understanding of the relevant neural mechanisms, especially insofar as the global response of anterior parietal cortex (SI) is concerned. For example, no imaging study to date has obtained information about if, and to what extent, the spatial and temporal properties of the SI response modify during continuing vibrotactile stimulation, nor has the relationship between the global SI response and the spike discharge activity of individual SI neurons during temporally extended vibrotactile stimulation been demonstrated. Time-resolved optical intrinsic signal imaging (Bonhoeffer and Grinvald 1996; Villringer and Chance 1997) and extracellular recording of neuronal spike discharge activity were used to characterize both the global response of SI and of individual SI neurons to two frequencies (25 vs. 200 Hz) of vibrotactile stimulation that, at least in humans, evoke very different sensory experiences ("flutter" and "vibration", respectively) (Mountcastle 1984; Mountcastle et al. 1969). The decision to employ the optical intrinsic signal (OIS) imaging method was motivated, in part, by the fact that of the variety of recording methods that are currently available, only optical imaging methods allow one to detect and quantitatively characterize (at relatively good temporal and spatial resolution) the spatially distributed cortical response to natural sensory stimulation. The decision to employ OIS imaging rather than imaging with a voltage-sensitive dye was based on the demonstrations that the former method can be utilized repeatedly and over prolonged time periods without substantial negative impact on cerebral cortical function (Grinvald 1985; Grinvald et al. 1991a,b, 1994; Lieke et al. 1989; Narayan et al. 1994). Compared with the approach the authors used in previous studies to
image the global SI response to natural skin stimuli—the $^{14}$C-2-deoxyglucose (2DG) metabolic mapping method (Juliano and Whitsett 1985; Juliano et al. 1981, 1983, 1989; Tommerdahl et al. 1993)—OIS imaging has two very significant advantages. First, one can obtain multiple images of the response of the same cortical region to the same or different stimuli in the same subject. Second, OIS imaging allows analysis of the temporal characteristics of the response of a cortical region to stimulation. Other important properties of the OIS imaging method are the intrinsic signal detected in the IR range is relatively independent of changes in blood flow (Haglund et al. 1993); the OIS reflects a variety of factors, but most significantly change in the volume of the extracellular fluid compartment attributable to stimulus-evoked changes in extracellular [K$^+$] and/or neurotransmitter release (Cohen 1973; Lieke et al. 1989; MacVicar and Hochman 1991); the OIS is attenuated in a dose-dependent manner by cortical AMPA and N-methyl-D-aspartate (NMDA) receptor blockers (Haglund et al. 1992, 1993; MacVicar and Hochman 1991); the principal source of the signal is the dendrites of cortical pyramidal neurons (Grinvald et al. 1994); and the intrinsic signal is not a direct reflection of either neuronal spike discharge activity or, more generally, the local cortical voltage changes evoked by a sensory stimulus—that is, it has a much slower onset and decay than the neuroelectrical responses of single neurons or neuronal populations and is severely attenuated by drugs (e.g., by NMDA receptor blockers) that do not substantially modify the sensory cortical neuron spike discharge activity evoked by direct, short-latency thalamocortical drive (Armstrong-Jones 1995; Hagiwara et al. 1988; Salt et al. 1995; Tommerdahl and Whitsett 1996; Whitsett et al. 1999).

From the outset, the main objective was to compare the responses of SI to 25- and 200-Hz same-site skin stimulation. Our interest in this comparison derived from the well-known characteristics of the unique sensory experiences elicited in human subjects by low- (1–50 Hz) versus high-frequency (≥200 Hz) sinusoidal vertical displacement skin stimuli (i.e., flutter and vibration, respectively). As has been pointed out by others, although the percept of flutter is referred with great accuracy to the actual locus of low-frequency skin stimulation, as frequency is increased (≥50 Hz) the evoked sensation (vibration) often is referred to tissues deep and remote from the actual site of skin contact (Bolanowski et al. 1988; LaMotte and Mountcastle 1975; Mountcastle 1984; Sherrick et al. 1990). In addition, although a suprathreshold flutter stimulus evokes a percept for as long as it is applied, a vibratory stimulus (e.g., 250 Hz) evokes an intensity percept the magnitude of which increases during the initial 0.5 s, but with continued stimulation declines rapidly and progressively (Berglund and Berglund 1970), and disappears altogether within 1 h of continuous stimulation (Kampik 1930).

The specific rationale for the present experiments was as follows: if the optical response of SI to same-site 25- and 200-Hz stimulation could be recorded and evaluated at sufficient resolution using OIS imaging, it should be possible to use the method not only to look for differences in the time course of SI activation that might underlie the different temporal properties of the percepts evoked by long-duration exposures to flutter or vibratory stimulation, but also to determine if the prominent change in the spatial properties of the sensory experience that accompanies a switch from low- to high-frequency skin stimulation is accompanied by a change in the cortical locus of the stimulus-evoked response. Although a change in the skin locus to which a stimulus-evoked sensory experience is referred is assumed widely to be accompanied by a change in the place of stimulus-evoked activation within primary sensory cortex, for somatosensations this remains to be demonstrated for skin stimuli differing only in frequency. Another characteristic of the different sensory experiences evoked by low- versus high-frequency skin stimulation that remains unexplained in terms of the responsible primary sensory cortical neural events is that the percepts of flutter and vibration can be distinguished on the basis of their sensitivity to the spatial and temporal properties of the evoking stimuli—i.e., the capacity to detect flutter is relatively insensitive to changes in either area of the skin field stimulated or stimulus duration, but the threshold for detection of vibration is exquisitely sensitive to both stimulus area and duration (Verrillo 1965, 1966).

In the experiments described in this paper, continuous 25- and 200-Hz stimuli with durations as long as 30 s were used to evoke SI responses. Published observations led us to employ such long-duration stimuli. First, previous work showed that an increase in the time of exposure to a vibrotactile stimulus leads to an increase in the spatial contrast in the stimulus-evoked SI global activity pattern (Tommerdahl and Whitsett 1996). Second, a recent psychophysical study (Goble and Hollins 1994) showed that human vibrotactile frequency discriminative capacity improves substantially with prior exposure to stimuli similar in frequency to those to be discriminated. And third, a quantitative electroencephalographic (EEG) study of human subjects reported that the contralateral postcentral response to a spatially discrete cutaneous flutter stimulus becomes more spatially localized with increasing duration of stimulation (Kelly et al. 1997; E. F. Kelly and S. E. Folger, unpublished data). These observations led us to anticipate that the global anterior parietal activity pattern evoked by continuous 25- and/or 200-Hz stimulation might change with time after stimulus onset and that differences between the global anterior parietal activity patterns evoked by 25- versus 200-Hz skin stimulation might be greater for long- than for short-duration stimuli.

A previous communication (Mosher et al. 1997) reported some of the findings described in this paper.

**M E T H O D S**

**Subjects and preparation**

Adult squirrel monkeys (Saimiri sciureus; males and females; n = 9) were subjects. General anesthesia was induced, the trachea was intubated with a soft tube, a 1.5-cm-diam opening was made in the skull, a recording chamber was affixed to the skull over the opening with dental acrylic, and the dura overlying anterior parietal cortex was incised and removed. All surgical procedures were carried out under deep general anesthesia (1–4% halothane in a 50/50 mixture of oxygen and nitrous oxide); wound margins were infiltrated with a long-lasting local anesthetic, closed with sutures, and bandaged. Subjects were immobilized with Norcuron (vecuronium bromide) and ventilated with a gas mixture (a 50/50 mix of oxygen and nitrous oxide; supplemented with 0.1–1.0% halothane when necessary) with a positive pressure respirator. Respirator rate and volume were adjusted to maintain end-tidal CO$_2$ between 3.0–4.0%, and EEG and autonomic signs (slow wave content; heart rate, etc.) were monitored.
and titrated by adjustments in the anesthetic gas mixture to maintain values consistent with light general anesthesia. Rectal temperature was monitored and maintained at 37.5°C using a heating pad. A polyethylene cannula inserted in the femoral vein allowed administration of drugs and fluids.

Euthanasia was carried out by intravenous injection of pentobarbitonal (45 mg/kg), followed by intracardial perfusion with saline, followed by fixative (10% formalin). Fiducial marks were placed to guide removal, blocking, and subsequent histological sectioning of the region of cortex studied. All procedures were reviewed and approved in advance by an institutional committee and are in full compliance with current National Institutes of Health policy on animal welfare.

**Stimuli and stimulus protocols**

Sinusoidal vertical displacement (vibrotactile) stimuli were applied using a servocontrolled transducer (Cantek Enterprises, Canonsburg, PA). Stimuli were applied to a circular skin site on the contralateral forelimb or hindlimb via a cylindrical probe. Throughout the data acquisition period the stimulator probe (either 2 or 5 mm diam) remained in continuous contact with the skin. In the absence of vibrotactile stimulation, the probe indented the skin by 500 μm.

In six of the nine subjects, two different stimulus conditions were delivered to the same skin site and were interleaved on a trial by trial basis—i.e., in one trial, a 25-Hz flutter stimulus was applied (between 200 and 400 μm in amplitude), in the next trial a 200-Hz stimulus (amplitude 20–40 μm) was delivered, etc. Stimulus duration was 10 s, and an intertrial interval (ITI) of 60 s was allowed between successive trials. In the other three subjects, images were obtained under two additional conditions (both 10 s in duration)—a “no stimulus” condition and a “complex waveform stimulus” condition—and in the studies of these three subjects, the four trial types were interleaved on a trial-by-trial basis. The complex stimulus was produced by summing the waveforms used for the 25- and the 200-Hz stimulus conditions, analog conversion of the resultant waveform to a DC signal, and provision of that signal to the stimulator controller.

**OIS imaging**

Near-infrared (IR; 833 nm) OIS imaging was carried out using an oil-filled chamber capped with an optical window (Tommerdahl and Whitsett 1996). Images of the exposed anterior parietal and surrounding cortical surface were acquired 200 ms before stimulus onset (“reference images”) and continuously thereafter for 15–30 s after stimulus onset (“poststimulus images”) at a rate of one image every 0.9–1.4 s. Exposure time was 200 ms. Difference images were generated by subtracting each prestimulus image from its corresponding poststimulus image. Averaged difference images typically show regions of both increased light absorption (decreased reflectance) and decreased light absorption (increased reflectance) which are believed widely (e.g., Grinvald 1985; Grinvald et al. 1991a,b) to be accompanied by increases and decreases in neuronal activation, respectively.

The dark (due to increased absorption) regions shown in the difference images in this paper (e.g., Fig. 2) thus are interpreted to be regions of increased neuronal activity, whereas the light (due to decreased absorption) regions correspond to areas of decreased (relative to background) neuronal activity. Difference images of the response to stimulation of the same skin site with 25- and 200-Hz stimulation were obtained in the same experimental run and were alternated on a trial-by-trial basis to control for temporal changes in cortical state unrelated to stimulus conditions which, if unrecognized, might obscure or modify the reflectance patterns associated with particular conditions of skin stimulation.

Figure 1A illustrates the locations (see boxes on drawing of squirrel monkey right hemisphere) of the anterior parietal forelimb and hindlimb fields that were studied and shows (see panels to left and right of the drawing of the hemisphere) the typical arrangement of the boundaries between the different cytoarchitectonic areas in these areas. The digitized low-magnification image of the Nissl-stained section in Fig. 1B shows (by means of the pairs of arrows at the layer I-II junction and the layer VI-white matter junction) the anterior and posterior borders of the highly granular area 3b in the SI forelimb representational area at a level near to the end of the central sulcus. The mediolateral level of this section is indicated by short horizontal arrow along the right margin of the panel on the left (ce, central sulcus; pc, intraparietal sulcus; ML, midline). The image of the Nissl-stained section shown in Fig. 1 was selected to demonstrate that the areal extent of area 3b that can be visualized from the surface decreases progressively as the central sulcus is approached from either a lateral or medial position (note the difference in the horizontal distance between the 2 arrows at the top and bottom of the section) and disappears from view completely at levels where the central sulcus is developed fully.

**Neurophysiological recording**

Extracellular recordings of the spike discharge activity of single SI neurons and local neuron populations were obtained subsequent to the optical imaging phase of the experiments using electrolytically etched, glass-insulated tungsten wires (impedance 300–500 kΩ at a test frequency of 10 kHz). Microelectrode penetrations were carried out under closed-chamber conditions—the recording chamber was filled with artificial cerebrospinal fluid and hydraulically sealed with a glass plate containing an o-ring through which the microelectrode could be advanced under direct visual control. Microelectrode penetrations were inserted at cortical sites distinguished on the basis of the magnitude and direction (increase or decrease) of the optical reflectance change associated with skin stimulation. Conventional approaches and apparatus were used to amplify, filter, display, store, and analyze records (both analog and digital) of neuronal spike trains collected before, during, and after application of the vibrotactile stimuli. The same stimulus conditions and protocols used to obtain optical images were employed to study their effects on the spike discharge activity of cortical neurons. Electrolytic lesions created by passing DC current...
through the recording microelectrode were used to allow postexperimen-
tal identification of the terminal locations of microelectrode tracks
and sites at which neurophysiological recordings of particular interest
had been obtained.

**Histological procedures/identification of cytoarchitectonic boundaries**

Blocks of pericentral region studied were cut, postfixed, cryoprotected, frozen, and sectioned serially in the sagittal plane at 30 μm. Sections were stained with cresyl fast violet and inspected microscopically to distinguish anterior parietal regions on the basis of estab-
lished cytoarchitectonic criteria (Jones and Porter 1980; Powell and Mountcastle 1959; Sur et al. 1982). The boundaries between adjacent cytoarchitectonic areas were identified by scanning individual sagittal sections separated by no more than 300 μm and were plotted at high resolution using a microscope with a drawing tube attachment. The resulting plots then were used to reconstruct a two-dimensional sur-
face map of the cytoarchitectonic boundaries within the region studied with optical and neurophysiological recording methods. The locations of microelectrode tracks and electrolytic lesions evident in the histo-
logical sections were projected radially to the pial surface and trans-
ferrred to the map of cytoarchitectonic boundaries reconstructed from the same sections. As the final step, the cytoarchitectonic boundaries (along with the locations of microelectrode tracks and lesions whenever present) identified in each brain were mapped onto the images of the stimulus-evoked intrinsic signal obtained from the same subject, using fiducial points (made by postmortem applications of india ink or needle stabs) as well as morphological landmarks (e.g., blood vessels and sulci evident both in the optical images and in histological sections). To ensure that determinations of cytoarchitectonic boundaries were uninfluenced by information about the location of intrinsic signal, the experimental identity of the histological sections was concealed from the investigator(s) who identified the locations of cytoarchitectonic boundaries and the relationship between the cytoar-
chitectonic boundaries and the stimulus-evoked IR reflectance patterns for a given anterior parietal region were not evaluated until a final map of cytoarchitectonic boundaries had been generated.

**RESULTS**

**Variability of the stimulus-evoked OIS**

Before attempting a comparison of responses evoked by different frequencies of skin stimulation, it is important to establish both the within-subject and across-subject reproduc-
bility of the stimulus-evoked OIS. To this end, the data in Fig. 2 illustrate the variability of the responses of SI in the same squirrel monkey to a 25-Hz stimulus to the radial interdigital pad of the contralateral hand.

Each of the pair of images (Fig. 2, top right; labeled run 1 and run 2, respectively) shows the average response to 20 presentations of a 25-Hz stimulus. Stimulus duration was 8 s; ITI was 60 s. Note that the locus of the average increase in absorbance (dark region) in the run 1 and run 2 images is similar, even though the two images were generated from data collected at very different times during the experiment—the data used to generate the run 2 image were collected during 20 stimulus trials performed >1 h after delivery of the 20 stimulus trials used to generate the run 1 image. At least for this subject and under this stimulus condition, therefore, the anterior pari-
etal locus and magnitude of the average stimulus-evoked OIS formed from the data obtained during 20 presentations of the same 25-Hz stimulus remained constant over relatively long (>1 h) time intervals.

The surface vascular pattern within the cortical field that yielded the OIS images in Fig. 2 is shown immediately below the run 1 image, and the locus of the upper 2% of the pixels in the run 1 image (accomplished by thresholding the run 1 image) is illustrated on a surface-view reconstruction of the boundaries between anterior parietal cytoarchitectonic fields (shown immediately below the run 2 image). The thresholded image in Fig. 2 clearly reveals that the locus of the reflectance decrease is centered on the area 3b/1 boundary, in good agree-
ment with the topographic map of Sur et al. (1982). Observations similar to those shown in the run 1 and 2 images have been obtained repeatedly in our experiments and are represent?
itative of the reproducibility and temporal stability of the aver-
age anterior parietal optical response to cutaneous flutter stimu-
lation recorded in the same subject.

The images in Fig. 2 (left 2 columns) illustrate, for the same subject, that the anterior parietal locus of the absorbance in-
crease evoked by a 25-Hz skin stimulus is reproducible even when the OIS image is generated from data collected during the delivery of relatively few stimuli (e.g., the images in the column on the extreme left were obtained by averaging the data from 5 successive stimulus presentations—top left image shows the average response to stimuli 1–5, the image next to the top on the left to stimuli 6–10, etc.). Moreover, this good reproducibility of the OIS continues to be evident even when one compares images generated from the data obtained during a single presentation of the 25-Hz stimulus (the images in the column of Fig. 2 labeled Single Trials). Although such “single trial images” reveal an obvious trial-to-trial fluctuation in the intensity of the OIS evoked by a single stimulus application (as expected because there is considerable trial-to-trial variation in the magnitude of SI neuron spike discharge response to a repeated skin stimulus), they also demonstrate that the locus of the OIS remains relatively consistent from one stimulus trial to the next.

Figure 2, bottom, shows for the same subject and stimulus condition how the magnitude of the mean across-trial change in absorbance (by convention, a positive y value indicates an increase in absorbance) varies as a function of distance, as well as the magnitude of the variability in mean absorbance at each sampled locus in the run 1 image (the error bars indicate ±SE). Note that the mean absorbance values at the central focus of the optical response are positive and are unambiguously different (and statistically significantly different) than the mean absorbance values at positions located >350–500 μm lateral or medial to the focus. The presence of negative y values (indicating an absorbance decrease) on both sides of the central focus is also apparent.

The across-subject variability of the OIS evoked by a 25-Hz skin stimulus is illustrated in Fig. 3. Figure 3A shows the average OIS response of three different squirrel monkeys to 25-Hz stimulation of the radial interdigital pad on the contralat-
eral hand; Fig. 3B shows the average response of yet another three squirrel monkey subjects to 25-Hz stimulation, but in these latter three subjects, the stimulus site was on the volar tip of contralateral digit 2 (index finger). Inspection of the images in Fig. 3, A and B, make it evident that although the spatial configuration of the region of absorbance increase (dark region in each image) evoked by the 25-Hz stimulus differs in minor ways from one subject to the next, there is a high consistency in the anterior parietal locus of the OIS from one subject to the
next (it consistently is at the 3b/1 boundary in Fig. 3A and at the 3b/3a boundary in Fig. 3B), even though there were substantial subject-to-subject differences in the development of the central sulcus and in the details of the vascular pattern. The locus of the OIS evoked by radial ID pad stimulation (images in Fig. 3A) and by digit II stimulation (images in Fig. 3B) are in very good agreement with the squirrel monkey anterior parietal region that receptive field mapping studies have shown to receive its principal input from the radial ID pad, and the region that gets its input from the distal tip of digit II (e.g., see Sur et al. 1982).

**Relationship between the reflectance change evoked by skin stimulation and cortical neuron spike discharge activity**

Although a number of published studies have reported substantial evidence indicating that a stimulus-evoked increase in the average absorbance of a cortical region is accompanied by an increase in the spike discharge activity of the neurons in that same region (e.g., Grinvald 1985; Grinvald et al. 1991a,b, 1994; Haglund et al. 1992, 1993; Tommerdahl and Whitel 1996; Tommerdahl et al. 1998), there is much less information that bears on the physiological meaning of a stimulus-evoked decrease in cortical absorbance.

Figure 4 presents data that appear to clarify this issue, at least for squirrel monkey anterior parietal cortex. Shown in Fig. 4A (images in middle and on right) are average difference images (stimulus-prestimulus; each based on the data obtained in 40 trials) obtained at different times after onset of a 25-Hz stimulus to a site on the subject’s contralateral radial interdigital pad. Shown in Fig. 4B are examples of spike train recordings (left) obtained in the course of microelectrode penetrations performed at three different anterior parietal locations (at sites 1–3; the locus of each site in cortex is shown in A, left). Figure 4B, P3, P2, and P1, shows the peristimulus time (PST) histogram computed from the spike trains recorded from a repre-
sentative single neuron recorded in each penetration. The three sites were selected for study with microelectrode recordings on the basis of the average change in absorbance measured at each site earlier in the same experiment: for example, at site 3 the 25-Hz stimulus caused a large increase in average absorbance; at site 2 the same stimulus evoked a decrease in absorbance; and at site 1 there was a modest, but nevertheless significant, increase in absorbance.

The two arrays of average absorbance values plotted in Fig. 4\(B\), bottom right (these arrays were obtained by segmenting the images obtained at 2.2 and 7.0 s after stimulus onset from left to right at a binwidth of 30 \(\mu\)m; bin height 1 mm), reveal that the stimulus-evoked OIS underwent a substantial change between 2.2 and 7.0 s after stimulus onset. Namely, at 2.2 s it was spatially diffuse and unimodal, but at 7.0 s, it consisted of two prominent, nonoverlapping regions of increased absorbance separated and surrounded by regions of decreased absorbance. The sites of the three microelectrode penetrations are indicated in Fig. 4\(B\), bottom (\(\downarrow\) and \(\uparrow\)); note that the y axis indicates changes in absorbance \(\times 10^{-3}\)([reference − stimulus]/reference).

The single neuron recording data shown in Fig. 4\(C\) parallel the OIS imaging results in a number of respects. The pair of spike train rasters shown in Fig. 4\(C\), middle were obtained from two neurons recorded in penetration 2 (the middle left raster was obtained from a layer III neuron, the middle right raster from a layer V neuron); the raster at left was obtained from a layer V neuron recorded in penetration 1; the raster at right was obtained from a layer III/IV neuron in penetration 3.

In general, the spike train data shown in Fig. 4\(C\) reveal a prominent dependency of single neuron spike firing on the prior history of 25-Hz skin stimulation (that is, each of the spike trains modifies progressively during the period of repeated 25-Hz stimulation—the same condition of skin stimulation used to evoke the OIS). Most impressive are the trial-by-trial changes of the layer III neuron studied in penetration 2 (middle left): this neuron’s initially vigorous response to the 25-Hz stimulus declined and disappeared as the stimulus was repeated. In addition, the changes in single neuron spike discharge activity exhibited at each site appear not to be random. Instead the changes in activity take one form when the neuron is located at a site where the stimulus evoked an absorbance decrease (during 25-Hz stimulation the mean firing rate of both the layer III neuron studied in penetration 1 and the layer IV-V neuron studied in penetration 3 remained relatively stable with repetitive stimulation; and at the same time, the mean firing rate observed for each of the same 2 neurons after 25-Hz stimulation, the “background” activity, decreased progressively with repetitive stimulation), and take a distinctly different form for the neuron at the site where repetitive 25-Hz stimulation led to an absorbance decrease. At this site, the layer III neuron progressively lost its initial excitatory response to stimulation, and the background activity exhibited by the layer V neuron, a neuron inhibited by 25-Hz stimulation, increased progressively with repetitive stimulation.

Our tentative interpretation of the spike train data obtained in this (and in similar experiments) is that at each site sampled with a recording microelectrode, the contrast between the mean spike discharge activity level observed during versus after each 25-Hz stimulus changes progressively with stimulus repetition. That is, at each stimulus-activated site in the global response pattern (i.e., at sites where an absorbance increase occurred: penetrations 1 and 3 in Fig. 4), the average rate of spike discharge activity during each presentation of the skin stimulus increased progressively relative to spontaneous activity. Conversely, at the inhibited site (i.e., at the site where an absorbance decrease occurred: penetration 2 in Fig. 4) the tendency was for the mean spike discharge activity evoked after each presentation of the skin stimulus to increase progressively relative to the activity recorded during stimulus application. Activity “difference plots” for the neurons studied at loci where the stimulus evoked an absorbance increase are shown.
in Fig. 4C, bottom left; similar plots for neurons studied at the locus of the absorbance decrease are shown at bottom right. Note that both sets of plots are consistent with the following interpretation: stimulus-evoked change in cortical reflectance is accompanied by change in cortical neuron spike discharge activity, and the sign (increase, decrease) and magnitude of the change in absorbance indicates the sign (excitation, inhibition/suppression, respectively) and magnitude of the change in stimulus-evoked change in cortical neuron spike discharge activity. Although additional study is needed to determine the detailed quantitative relationship between the response recorded with the OIS imaging method and single neuron spike discharge activity, the available data clearly indicate that the OIS imaging method is a powerful method for qualitatively

FIG. 5. Pairs of average prestimulus-poststimulus difference images obtained from SI of 4 subjects. Data were obtained from the hemisphere opposite to the stimulated skin site. All images shown were obtained at 6 s after stimulus onset. Left: images obtained during 20–40 trials during 25-Hz (400 μm) stimulation; middle: images obtained by stimulating the same site with a 200-Hz (40 μm) stimulus; intertrial interval (ITI) was 60 s; stimulus duration was 10 s. Right: surface vascular pattern and cytoarchitectonic boundaries. For subjects 1 and 2 (top 2 rows), stimuli were applied to a site on the volar foot (indicated by filled symbol on figurine at right); for subjects 3 and 4, the stimulus site was on forelimb skin. Although 25-Hz stimulation at each skin site evoked a prominent increase in absorbance in the topographically appropriate region of SI (indicated by dark regions in the images), 200-Hz stimulation of the same sites did not.

FIG. 4. A: images showing surface vascular pattern (top left), thresholded response to 25-Hz skin stimulation at 9.4 s (bottom left), and images of the response acquired at different times after stimulus onset. B: spike trains recordings (left); peristimulus time (PST) histograms (top right); and spatial histograms showing how mean absorbance varies with distance at 2 different times (2.2 and 7.0 s) after stimulus onset. C, top: spike trains obtained from an SI neuron studied during penetration 1 (left), from 2 SI neurons studied during penetration 1 (middle), and from 1 SI neuron studied in penetration 3. Horizontal line at top of each spike train raster indicates time of 25-Hz stimulation; for every neuron the skin site stimulated (contralateral radial interdigital pad) was the same site used to evoke the OIS activity pattern shown in A. Response to 1st stimulus shown at top of each raster; response to 15th stimulus shown at bottom. Graphs show the trial-by-trial difference between each neuron’s mean firing rate during vs. after each stimulus presentation (MFRstim – MFRbackground). Vibrotactile stimulus parameters: 25 Hz, 400 μm peak-to-peak, 7-s duration, 45-s interstimulus interval, stimulator probe contacted 2 mm skin site.
identifying regions in which average neuronal activity is elevated or inhibited/suppressed by natural skin stimulation (also see Tommerdahl et al. 1996a, 1998).

**Comparison of SI responses to 25- and 200-Hz stimulation**

Figure 5 shows the OIS responses of the contralateral SI hindlimb region of two subjects (top 2 rows) and of the contralateral SI forelimb region of two additional subjects (bottom 2 rows) at 6 s after the onset of either a 25- or 200-Hz stimulus to the same skin site. Inspection of Fig. 5 reveals that 25-Hz stimulation (left) evoked a localized increase in absorbance (indicated by dark region) primarily confined to area 3b (a small component of the response to 25-Hz stimulation also occupies a neighboring part of 3a in subject 2, and a neighboring part of area 1 in subject 4). Same-site 200-Hz stimulation, however, yielded quite a different result; in all nine subjects studied (the data for 4 subjects are shown in Fig. 5, middle; each image shows the response at 6 s after onset of stimulation), the region of area 3b that had been maximally activated by 25-Hz stimulation exhibits only background or slightly lower-than-background (decreased) absorbance values.

**Time course of SI response to 25 versus 200 Hz**

While Fig. 5 shows that the response of SI cortex recorded at all times between 6 and 30 s after onset of 200-Hz stimulation of a contralateral skin site consistently is very different from the response recorded 6 s after the onset of same-site 25-Hz stimulation, more detailed consideration of the imaging data obtained at different times after stimulus onset revealed an even more surprising fact: that is, for a brief interval immediately after stimulus onset, the responses to 25- and 200-Hz stimulation are very similar. For example, as is demonstrated by the data (obtained from a single subject) in Fig. 6, there are only minor differences between the responses to 25- and 200-Hz stimulation in the interval between 1.1–2.4 s after stimulus onset (Fig. 6, top 2 rows). Figure 6 also shows that as the duration of the skin stimulus increases, the responses evoked by the different frequencies of stimulation quickly diverge toward the form of those shown in Fig. 5 (it should be recalled that the images in Fig. 5 were obtained at 6 s after stimulus onset).

The temporal evolution of the responses of the subject that provided the data shown in Fig. 6 clearly reveals that whereas the patterned SI response to 25 Hz tends to retain its spatial and intensive characteristics throughout the entire period of stimulation, the response to 200 Hz does not. More specifically, with 200-Hz stimulation, there is an early increase in absorbance (best seen in the response evoked from the digit I site at 2.4 s in Fig. 6) that occupies the same region occupied by the response to 25-Hz stimulation, but unlike the response to 25-Hz stimulation, this component of the response to 200-Hz stimulation weakens rapidly with continued stimulation (in some subjects, it disappeared altogether). By 5.0–6.3 s after stimulus onset, the response consists solely of a spatially extensive region of decreased absorbance (compare the 2 rows of images shown in Fig. 6, bottom). Because the protocol used to obtain time-resolved information interleaved the 25- and 200-Hz stimuli, it is extremely unlikely that nonspecific changes in SI responsivity were responsible for the very different responses to same-site flutter and vibration shown in Figs. 5 and 6.

The time course of the responses of the same subject to same-site 25- versus 200-Hz stimulation was analyzed quantitatively. This was accomplished by determining the 1 × 1 mm SI region (region 1) that underwent the largest increase in absorbance in response to 25-Hz stimulation (region 1 is identified as boxel 1 in Fig. 6, bottom) and the 1 × 1 mm region that underwent the largest decrease in absorbance during the exposure to 200-Hz stimulation (region 2 is identified as boxel 2 in Fig. 6, bottom). While for the 25-Hz condition the same region (region 1 in Fig. 6) underwent the largest absorbance increase each time an image was acquired after stimulus onset, the absolute value of that absorbance increase varied prominently and systematically with time after stimulus onset (shown in Fig. 7). More specifically (see plots for region 1, thin continuous lines in Fig. 7), the magnitude of the absorbance increase associated with 25-Hz stimulation increased rapidly and progressively after stimulus onset, attained a maximum within 4–5 s of stimulus onset, and maintained this level for as long as stimulation continued (stimulus duration was 8 s in the experiment that provided the data shown in Fig. 7). With same-site 200-Hz stimulation, however, the time course of the change in absorbance in region 1 was quite different (see plots with small dashes in Fig. 7). With the initial 2–4 s of stimulus onset, absorbance increased in region 1 in a manner corresponding closely to that seen with 25-Hz stimulation; but with continued 200-Hz stimulation, the magnitude of the increase in absorbance in region 1 declined progressively toward prestimulus levels.

Figure 7 also shows that the changes in absorbance that occurred within region 2 of the same subject varied systematically with time after stimulus onset, and that those changes were different for each frequency of skin stimulation. Specifically, although both 200 and 25 Hz evoked an absorbance decrease within region 2, the magnitude of the decrease was larger and more rapid at the higher stimulus frequency. An additional difference between the behavior of regions 2 and 1 was that the absorbance decrease evoked in region 2 by both frequencies of stimulation (but most prominently by 200 Hz) often did not attain a maximum until 6–8 s or more after stimulus onset (plots with thick continuous and dashed lines in Fig. 7).

**Effects on the OIS of a change in stimulus place**

While a large change in the place of 25-Hz skin stimulation (e.g., Fig. 5) or even a relatively minor change in stimulus location (e.g., Fig. 6) was accompanied by an obvious shift in the location of the pattern of stimulus-evoked absorbance increase within SI, the effect of a change in stimulus place on the locus of the absorbance decrease evoked by 200-Hz stimulation, although evident when the stimulus engaged widely separated body parts (e.g., the foot vs. the hand; Fig. 5), was difficult to detect when stimulus location was shifted to a different site on the same body part. Indeed, comparison of the images obtained at 6.3 s after onset of 200-Hz stimulation of the volar phalanx of digit 1 (2nd image from left in Fig. 6, bottom row) with the image obtained at the same time after onset of 200-Hz stimulation of the volar distal phalanx of digit 3 (image at far right in Fig. 6, bottom row) reveals that the region of maximal absorbance decrease is virtually the same for both placements. An additional tendency was for the
region of maximal absorbance decrease with either 200- or 25-Hz stimulation to be located lateral to the region that responded with an increase in absorbance when a hindlimb skin site was stimulated and to be located medial to the region that responded with an absorbance increase when a forelimb skin site was stimulated.

OIS imaging and neurophysiological recording in the same experiment

Figure 8 shows results obtained in an experiment which employed the two methods to study the response of SI to 25- and 200-Hz same-site skin stimulation. In the initial phase of the experiment, the OIS imaging method was used to monitor and record the responses of contralateral SI to 25 Hz (Fig. 8, left, top and middle) and 200-Hz stimulation (right, top and middle) of the same site on the volar foot. Subsequently extracellular microelectrode recordings of single neuron spike discharge activity were obtained from locations within the same SI region (area 3b and a neighboring sector of area 3a) that in the preceding phase had been observed to respond with an increase in absorbance during 25-Hz skin stimulation.
FIG. 7. Plots of average absorbance values within region 1 (Fig. 6; region of maximal increase in absorbance evoked by 25 Hz) and region 2 (region of maximal decrease in absorbance evoked by 200 Hz) determined for the images shown in Fig. 6. Average absorbance values associated with stimulation of each skin site (sites 1 and 2) are plotted as a function of time after stimulus onset. Top: site 1 (tip of digit 1) stimulation; bottom: site 2 (tip of digit 3) stimulation. Top right: key indicates stimulus frequency (25/200 Hz) used and box/region within which average reflectance value was computed. Note that opposite absorbance changes are evoked in the two regions by 25-Hz stimulation, whereas 200-Hz stimulation leads to only a brief increase in absorbance in region 1 and evokes a larger absorbance decrease than did 25-Hz stimulation in region 2. Region 1 chiefly includes area 3b, whereas region 2 includes area 3a and area 1. Flags indicate ±1 SE.

The results obtained in the OIS imaging phase of these experiments were consistent with the imaging observations described earlier in this paper. That is, 25-Hz stimulation led to a prominent absorbance increase that chiefly occupied area 3b (Fig. 8, bottom right) and remained relatively constant over the full 10-s period of continuous 25-Hz stimulation (Fig. 8, left, top and middle); whereas 200-Hz stimulation of the same skin site evoked an early (at 3 s; top right), weak increase in absorbance that disappeared with continuing 200-Hz stimulation (image at 10 s after onset of 200-Hz stimulation is in Fig. 8, middle right).

In the second phase of the same experiments, radial microelectrode penetrations were performed so that each would traverse one or only a few cell columns within the same region of SI that had responded with an increase in absorbance to 25-Hz stimulation. At each location where the action potentials of a single neuron or a small population of neurons was recorded, the same conditions of 25- and 200-Hz skin stimulation used to obtain optical responses in the initial part of the experiment were re-employed to assess their effects on neuronal spike discharge activity. The superimposed PST histogram pairs shown in Fig. 9 were constructed from the spike train data obtained at four different depths of the same radially oriented microelectrode penetration (spike discharge activity was recorded from a small neuron population at sites 1–3; the activity of a single unit was recorded at site 4). This penetration was performed at the site labeled “P1” in Fig. 8, bottom right.

The neural activity patterns shown by the PST histogram pairs in Fig. 9 are representative of the observations obtained in other microelectrode penetrations obtained in a study of the time course of SI single neuron responses to long duration stimuli (K. A. Delemos, E. Roy, M. Hollins, and M. Tommerdahl, unpublished results). Inspection of each of the histogram pairs shown in Fig. 9 (●, spike trains evoked during 25-Hz stimulation; □, spike trains evoked by 200-Hz stimulation; each superimposed pair of PST histograms was obtained at a different area 3b recording site) makes evident the strong parallels between the spike train activity and optical signals evoked from area 3b by the different frequencies of same-site stimulation. Specifically, during most of the 15-s stimulation period, the 25-Hz stimulus evokes a substantially higher mean rate of spike firing than did 200-Hz stimulation; after <1 s of 200-Hz stimulation, mean firing rate declines to a level near or below the mean rate of spike discharge recorded from the same neuron in the absence of stimulation (‘‘spontaneous’’ activity); and the mean rate of spike discharge attained by a neuron within the initial 100–300 ms of stimulation is virtually the same for the 25- and 200-Hz stimulation (insets in Fig. 9 show an expansion of each PST pair over the time window 0–2 s). The observations illustrated in Fig. 9, therefore, appear fully consistent with our interpretation of the OIS imaging observations: although 25-Hz stimulation of a skin site elevates the spike discharge activity of neurons within a sector of area 3b throughout the entire period of skin stimulation, same-site 200-Hz stimulation evokes a much more transient elevation of the spike discharge activity of the same area 3b neurons.

Does 200-Hz skin stimulation inhibit SI?

Because a stimulus-evoked increase in absorbance conventionally is interpreted to imply stimulus-evoked neuronal excitation and a decrease in absorbance as suppression/inhibition of sensory cortical activity (e.g., Tommerdahl and Whitsett 1996), the prominent decrease in absorbance we observed consistently with 200-Hz skin stimulation raised the possibility that a high-frequency stimulus evokes a suppressive/inhibitory effect on a spatially extensive SI region, including the regions of areas 3b and 1 that respond with an increase in absorbance to same-site cutaneous flutter. Our expectation was that if this was true, simultaneous delivery to the same skin site of both 25- and 200-Hz stimuli should evoke opposing influences on areas 3b/1, leading to a reduction in the magnitude of the absorbance increase evoked by “pure” 25-Hz stimulation of the same skin site.
Figure 10 shows representative findings obtained in an experiment (3 experiments of this kind were carried out) designed to evaluate the prediction that if the predominant effect of 25-Hz stimulation on the contralateral areas 3b and 1 is excitatory and if a major component of the effect of 200-Hz stimulation is inhibitory, then simultaneous application of both frequencies to the same skin site should suppress/inhibit the OIS attributable to pure 25-Hz stimulation. Four different conditions were interleaved in such experiments: one condition each for the two frequencies (25 vs. 200 Hz) of same-site skin stimulation, a third condition in which no stimulus was presented (a no-stimulus trial), and a fourth condition in which the complex waveform (25 Hz + 200 Hz) stimulus was applied. For the experiment shown in Fig. 10, the complex waveform stimulus was a 400-μm peak-to-peak amplitude, 25-Hz sinusoid on which a 20-μm peak-to-peak amplitude, 200-Hz sinusoid was superimposed, and the other two conditions in which a stimulus was delivered involved either 400-μm, 25-Hz or 20-μm, 200-Hz stimulation. All stimuli (the complex waveform and the 25- and 200-Hz stimuli) were delivered to the same site on the contralateral thenar eminence—see black region on figure at bottom left. The image showing the surface vascular pattern near the bottom of Fig. 10 also shows the locations of the cytoarchitectonic boundaries in this subject. Figure 10, bottom right, shows for each trial type under which imaging data were acquired (that is, for the 25- and 200-Hz stimulation conditions, and in the absence of stimulation) the time course of the average change in absorbance that occurred within a 2.0 × 4.0 mm area 3b boxel (flags indicate ±SE). The area 3b boxel used to obtain the plots in Fig. 10 is shown in the thresholded image of the 25-Hz response at the bottom left. At a time shortly (2.3 s) after onset of the complex waveform stimulus, the SI response (Fig. 10, top, 3rd from left; also see plots) is very similar to that evoked by the 25-Hz stimulus (Fig. 10, top left). As stimulation with the complex waveform stimulus continued, however, the magnitude of the absorbance increase declines substantially and progressively (Fig. 10, see images in 3rd column from left at 5.1, 7.9, and 10.7 s after stimulus onset; also see plots). In contrast, the optical response evoked by the pure 25-Hz stimulus (Fig. 10, left) remained relatively constant during the full period (8 s) of stimulation. Because the same 25-Hz stimulus component was present in both conditions, the most parsimonious explanation for the very different time courses of the OIS responses to 25 and to 25 + 200 Hz (complex waveform) skin stimulation evident in Fig. 10 is as follows: the 200-Hz component of the complex waveform stimulus evoked a suppressive/inhibitory effect on SI which became evident at 3–5 s of continuous stimulation, and with continuing stimulation, this suppressive/inhibitory effect increased in magnitude (the suppression/inhibition exhibits prominent temporal summation). Similar results were obtained in all three experiments in which the SI responses to
the complex waveform (25 + 200 Hz) and to 25-Hz same-site stimulation were recorded and evaluated.

DISCUSSION

Stimulus-evoked SI suppression/inhibition

A number of published cortical imaging studies have reported outcomes indicating that, in addition to evoking neuronal excitation, natural sensory stimuli evoke highly structured spatial patterns of both cortical neuronal suppression and inhibition. For example, spatially ordered areas of decreased blood flow (Cox et al. 1993; Moskalenko et al. 1996), spatially patterned regions of decreased voltage-sensitive dye fluorescence (Kleinfeld and Delaney 1996), and spatially patterned populations of stimulus-activated glutamate decarboxylase containing neurons (presumably GABAergic inhibitory neurons) have been identified in rodent barrel cortex during controlled whisker stimulation and spatially structured patterns of both local increases and decreases in 2DG uptake—the former interpreted to indicate an increase in average local neuroelectrical activity, the latter as a decrease to below-background levels of local average neuroelectrical activity—have been reported as a consistent feature of the response of both monkey and cat SI and SII cortex to controlled skin stimulation, as well as to joint rotation (Juliano et al. 1981, 1983, 1989; Tommerdahl et al. 1993, 1996a; Whitsel and Juliano 1984; Whitsel et al. 1989, 1991). Similarly, the evidence obtained in recent functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) human brain imaging studies (Apkarian 1995a,b, 1996; Apkarian et al. 1994; Derbyshire et al. 1996; Coghill et al. 1994) and in optical imaging studies of the somatosensory cortex in anesthetized monkey subjects (Tommerdahl et al. 1996a, 1998) indicate that a noxious skin heating stimulus normally evokes activation of the topographically appropriate region in one cortical territory (area 3a, SII and/or anterior cingulate cortex) and simultaneously suppresses the
FIG. 10. Comparison of the time course of the responses of the contralateral SI forelimb region to 25- (left), 200- (2nd column from left), and combined 25 Hz + 200 Hz stimulation of a skin site on the thenar eminence (3rd column from left). Right: pattern of absorbance change (no organized pattern is apparent) in the absence of skin stimulation. Protocol (use of interleaved stimuli in the same run) used to obtain these OIS imaging results was identical to that used to obtain the data shown in Fig. 6. Note that response to 25-Hz stimulation is well maintained over the total period of skin stimulation. In contrast, the increase in absorbance evoked by the combined 25 Hz + 200 Hz stimulus to the same skin site approximates that obtained with the 25-Hz stimulus only during the 1st 1–3 s of stimulation—with continuing complex waveform stimulation the increase in absorbance becomes increasingly weaker—and by 10.7 s after stimulus onset, much of the SI forelimb region exhibits only a decrease in average reflectance. Plot at bottom right shows average absorbance vs. time after stimulus onset. Flags indicate ±1 SE.
activity in the corresponding region in other functionally related territories (areas 3b and 1). Also relevant to the idea that stimulus-evoked mechanoreceptive afferent activity can evoke SI suppression/inhibition is an observation reported in a study of SI neurons in conscious behaving monkeys: Lebedev et al. (1994) found that the mean firing rate (MFR) of SI neurons stimulated on the contralateral palm of the hand at 127 Hz was significantly lower than the rates obtained at 27 and 57 Hz, leading those authors to conclude that the “decrease in MFR of neurons with cutaneous receptive fields (RFs) at 127 Hz may be due to inhibitory mechanisms dependent on stimulus frequency.” Unfortunately, however, the study of Lebedev et al. (1994) provided no information about the locus in SI of the neurons that exhibited this behavior other than indicating that the neurons with cutaneous receptive fields that were studied were in areas 3b, 1, and 2 (the majority were in area 1).

The evidence provided by the imaging experiments of this study indicate that within only a brief interval (1–2 s) of the onset of a 200-Hz skin stimulus, the effect on the optical properties of the region of contralateral SI cortex that receives short-latency input from the stimulated skin site reverses sign and also changes its spatial characteristics: that is, the optical response switches from an initial, highly localized increase in absorbance (centered on one anterior parietal location: area 3b) to a spatially widespread decrease in absorbance (centered on area 3a, but also involving areas 3b and 1). On the basis of the results obtained in our combined OIS imaging and single-unit recording experiments, and on the findings obtained in the OIS imaging experiments that used a complex waveform stimulus consisting of 25- and 200-Hz components (it should be recalled that the latter demonstrated that the response of SI attributable to 25-Hz stimulation is weakened or eliminated by concurrent 200-Hz stimulation; Fig. 10), this switch in SI optical properties that occurs within 1–2 s after the onset of 200-Hz skin stimulation apparently reflects a conversion of the effect on area 3b/1 neurons from an initial excitation to a profound and spatially widespread suppression/inhibition.

Possible contributions to perception of the SI suppression/inhibition evoked by 200-Hz stimulation

Although there is an extensive human psychophysical literature on the perceptual consequences of 200-Hz skin stimulation, much remains to be learned because, with only rare exceptions (e.g., Berglund and Berglund 1970; Kampik 1930), human studies have not emphasized the perceptual effects of high-frequency (>200 Hz) skin stimuli lasting >1 s. The results of this study suggest that the population of QA-type neurons in the areas 3b/1 representational zone for a stimulated skin site (the QA neurons in areas 3b and 1 are widely assumed to underlie the capacity to detect cutaneous flutter and discriminate vertical skin displacement over the frequency range 10–50 Hz) (see LaMotte and Mountcastle 1975; Mountcastle et al. 1984) is exposed to a potent suppressive/inhibitory process within 1–2 s after the onset of high-frequency (e.g., 200 Hz) stimulation of that same skin site.

The well-known observation by LaMotte and Mountcastle (1975, 1978, 1979) that destruction of contralateral postcentral cortex does not eliminate the capacity of monkeys to detect cutaneous flutter stimulation, but permanently destroys subjects’ capacity to discriminate between and identify frequencies of 10–50 Hz, suggests an interpretation of the perceptual meaning of the OIS imaging and neurophysiological data presented in this paper that we think merits consideration. Specifically, if our proposal that 200-Hz stimulation exerts a prominent inhibitory influence on the anterior parietal regions (areas 3b and 1) required for cutaneous frequency discrimination is correct, then the demonstration that areas 3b and 1 in monkey are required for vibratotactile frequency discrimination but not for detection (LaMotte and Mountcastle 1975, 1978, 1979), raises the following possibility: the inhibition of areas 3b and 1 elicited by 200-Hz stimulation should be expected to degrade subjects’ capacity to discriminate and identify frequencies of 10–50 Hz but, because areas 3b and 1 apparently are not required for the detection of frequencies of 10–50 Hz, should leave the capacity for detection of cutaneous flutter relatively unimpaired. A recently completed study has provided human psychophysical evidence consistent with this suggestion: it was demonstrated that a suprathreshold 200-Hz adapting stimulus adversely affects discriminative capacity at frequencies near to 25 Hz (Delemos et al. 1999).

Although an impairment of sensitivity to flutter subsequent to even a brief exposure to a suprathreshold 200-Hz stimulus might be attributed to adaptation occurring at some point along the projection pathway between RA-type skin mechanoreceptors and the QA neurons of areas 3b and 1 (referred to as “adaptation within the RA channel,” a possibility that cannot be rejected with certainty on the basis of the available evidence), such an interpretation appears difficult to reconcile with this study’s finding that ≤30 s of continuous suprathreshold 25-Hz skin stimulation produces relatively little suppression/inhibition of the intrinsic signal in areas 3b/1 (Figs. 2–6; also Fig. 10). Also, the fact that 2DG metabolic mapping experiments in both monkey and cat have demonstrated that a high-amplitude (0.5–1.0 mm peak-to-peak) 25-Hz sinusoidal skin stimulation evokes a prominent, columnar pattern of above-background 2DG uptake in the topographically appropriate sector of areas 3b and 1 even after preexposure to such stimulation for a prolonged period (for 15 min to >1 h) before administration of the 2DG tracer (Juliano and WhitSEL 1981, 1983, 1989; Tommerdahl et al. 1996a), makes it seem very unlikely that a central process caused by an elevated level of activity in RA afferents is responsible for the prominent suppression/inhibition of area 3b/1 and its QA neurons observed in the present study. The point deserving emphasis is that although our previous 2DG experiments used grossly suprathreshold conditions of 25-Hz skin stimulation that undoubtedly evoked continuous, near-maximal or maximal RA afferent drive from the stimulated skin site for ≥1 h immediately before the attempt to label the responding regions of SI cortex, 25-Hz flutter stimulation still elicited prominent above-background 2DG uptake in areas 3b and 1 (it is presumed, therefore, that the prolonged conditioning period of maximal or near-maximal RA afferent drive used in those 2DG experiments did not interfere with the ability of flutter stimulation to evoke substantial area 3b and 1 neuronal spike discharge activity during the period after the tracer was injected).

On the basis of these and similar observations, our view is that the relatively modest level of activity evoked in RA afferents by the 20- to 50-μm peak-to-peak amplitude 200-Hz stimulus condition used in the experiments of the present study should be regarded as unlikely to have trig-
These published findings lead us to propose that the discovery of nearby site (Ekblom and Hansson 1982; Pertovaara 1979) of a stimulatory effect when the vibratory stimulus is applied to the same site as the stimulus that evokes the pain experience or to a nearby site (Ekblom and Hansson 1982; Pertovaara 1979). These published findings lead us to propose that the discov-

er that 200-Hz stimulation, but not 25-Hz stimulation of the same skin site, suppresses area 3a (for example, see Fig. 6) and the finding that noxious skin heating selectively activates area 3a (Tommerdahl et al. 1996a, 1998) are both consistent with the proposal that it is area 3a, and not areas 3b and 1, which plays the leading role in the perception of noxious skin heating stimuli (Tommerdahl et al. 1996a, 1998).

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