Published in final edited form as:

Exp Brain Res. 2008 May ; 187(3): 349–358. doi:10.1007/s00221-008-1307-y.

Monkey primary somatosensory cortical activity during the early reaction time period differs with cues that guide movements

Yu Liu, John M. Denton, and Randall J. Nelson

Department of Anatomy and Neurobiology, University of Tennessee Health Science Center, 855 Monroe Avenue, Memphis, TN 38163, USA

Abstract

Vibration-related neurons in monkey primary somatosensory cortex (SI) discharge rhythmically when vibratory stimuli are presented. It remains unclear how functional information carried by vibratory inputs is coded in rhythmic neuronal activity. In the present study, we compared neuronal activity during wrist movements in response to two sets of cues. In the first, movements were guided by vibratory cue only (VIB trials). In the second, movements were guided by simultaneous presentation of both vibratory and visual cues (COM trials). SI neurons were recorded extracellularly during both wrist extensions and flexions. Neuronal activity during the instructed delay period (IDP) and the early reaction time period (RTP) were analyzed. A total of 96 cases from 48 neurons (each neuron contributed two cases, one each for extension and flexion) showed significant vibration entrainment during the early RTPs, as determined by circular statistics (Rayleigh test). Of these, 50 cases had cutaneous (CUTA) and 46 had deep (DEEP) receptive fields. The CUTA neurons showed lower firing rates during the IDPs and greater firing rate changes during the early RTPs when compared with the DEEP neurons. The CUTA neurons also demonstrated decreases in activity entrainment during VIB trials when compared with COM trials. For the DEEP neurons, the difference of entrainment between VIB and COM trials was not statistically significant. The results suggest that somatic vibratory input is coded by both the firing rate and the activity entrainment of the CUTA neurons in SI. The results also suggest that when vibratory inputs are required for successful task completion, the activity of the CUTA neurons increases but the entrainment degrades. The DEEP neurons may be tuned before movement initiation for processing information encoded by proprioceptive afferents.

Keywords

Neuronal activity; Primary somatosensory cortex; Vibration; Wrist movement; Monkey

Introduction

Primary somatosensory cortex (SI) is largely a sensory-specific area. The patterns of neuronal activity evoked in SI vary depending on the modality of sensory stimulation. One characteristic discharge pattern is the rhythmic neuronal activity in response to somatic vibratory stimuli (Mountcastle et al. 1969; Nelson et al. 1991, 2002; Lebedev et al. 1994; Lebedev and Nelson 1995; Salinas et al. 2000; Romo and Salinas 2003). To some extent, vibration-entrained activity reflects the frequency of vibratory inputs, although some SI neurons may be sensitive to lower frequencies while others are sensitive to higher frequencies. Within certain perceptive ranges, neuronal firing rates (FR) are related to the magnitude of vibration (Mountcastle et al. 1969).

It remains unclear if the degree of vibration entrainment changes when vibratory information is required for performing a task as compared with conditions during which the same vibratory input presents but is not a crucial element for a successful task performance.

Our studies have shown similarities in the characteristics of wrist movements that are triggered by vibratory go-cues only (VIB) compared with movements triggered by vibratory and visual go-cues in combination (COM). In both conditions, however, the reaction times are significantly shorter than during movements initiated by visual go-cues only (Nelson et al. 1990; Liu et al. 2007). We wondered if the activity of vibration-sensitive SI neurons differs during the two conditions (i.e., VIB and COM trials). These trials have similar reaction times and both have vibratory stimuli, but in COM trials, visual go-cues were presented simultaneously with the vibration. We hypothesized that when visual go-cues are present, they may take precedence in movement initiation. As a result, SI neuronal responses to vibratory stimuli may be different when visual cues are present. Such differences, if present, may imply that neuronal activity in SI varies depending on whether or not the somatosensory input is required during a movement.

In the present study, we examined SI neuronal activity during the early reaction time period (RTP), i.e., the first 10 vibratory cycles (57 Hz). This period begins immediately after go-cue onset and is the time during which preparation of wrist movements occurs. We wanted to establish that changes in FRs and/or activity entrainment occur when wrist movements are guided by vibratory inputs only or in combination with visual signals. The present results show that the FRs of some SI neurons with cutaneous receptive fields increase to some extent, but are significantly less entrained, during tasks in which somatosensory input is the only cueing signal available to guide wrist movements as compared to when both vibratory and visual cues are available.

Methods

Behavioral paradigm

Animals used in the present study were cared for in accordance with the Guide for the Care and Use of Laboratory Animals (1996). The experimental protocols were approved by the Institutional Animal Care and Use Committee of The University of Tennessee Health Science Center. Two adult male rhesus monkeys (*Macaca mulatta*, 9.5–10.5 kg) were trained to make wrist flexion and extension movements. The experimental apparatus and behavioral paradigm have been described previously (Liu et al. 2005). Briefly, each monkey sat in an acrylic monkey chair with his right forearm on an armrest. His right palm rested on a plate (manipulandum) attached, at the end nearest his wrist, to the axle of a brushless DC torque motor. A load of 0.07 Nm was applied to the manipulandum that assisted wrist extensions and opposed flexions. The load ensured that the monkey actively maintained constant wrist position during the instructed delay period (IDP) of the task and good contact with the manipulandum during task performance (Fig. 1).

Each monkey viewed a visual display located 35 cm in front of him at eye level. The display had a light-emitting diode (LED) that indicated the direction for each upcoming wrist movement (direction LED). This red LED, when lit, signaled extension; when unlit, it signaled flexion. Extensions and flexions were executed in alternating 10-trial blocks. A modality LED, also on the display, signaled the type of movement guidance stimuli that would be presented in each trial. This green LED, when lit, signaled vibratory cues would be presented either with or without visual stimuli to trigger and guide movements. Thus, if the green LED was unlit, only visual guidance stimuli were presented. The display also had 31 vertically arranged position LEDs. The center LED was larger and of a different color than the 15 LEDs above

and the 15 LEDs below the center LED. These LEDs, when illuminated, indicated current wrist position. That position was sampled and displayed at a frequency of 100 Hz.

Three task periods were considered: the IDP, the RTP, and the movement period. Trials began when the monkey centered the plate. At this time, the direction and modality LEDs were either illuminated or left unlit (see above), and the IDP began. The task required the monkey to hold steadily during the IDP at the center position for 0.5, 1.0, 1.5, or 2.0 s (pseudorandomized). If the monkey failed to hold still within $\pm 0.5^\circ$ of center for the allotted time, the trial was cancelled. A new trial could begin once the plate was re-centered. If that monkey held steadily for the appropriate time, sensory stimuli were presented that initially served as go-cues for movements and subsequently guided movements to their endpoints either 5° or 10° from center. For the visual stimulus-only (VIS) trials, movements were made in response to the appearance of a visual target that indicated the movement endpoint. The monkey's task was to superimpose the wrist position cursor over the target LED. For vibratory stimulus-only (i.e., VIB trials) trials, movements were triggered by vibration to the monkey's palm. Vibration was delivered by feeding a constant amplitude sine wave into the torque motor controller, causing the axle to oscillate. The angular deflection of the plate that resulted during the vibration was less than 0.06° (Lebedev and Nelson 1995). The movement endpoint was specified by a linear increase in the vibratory frequency from 57 Hz, when the plate was centered, to 97 Hz as the distance from the animal's current wrist position to the target decreased to zero. When the wrist position was superimposed with the target, the vibratory frequency was abruptly changed to 127 Hz. In the combined-cue paradigm (i.e., COM trials), trials were initiated by the simultaneous occurrence of both visual and vibratory stimuli, and the movement endpoints were specified by the combination of VIS and VIB targets. The animal was required to hold the plate within $\pm 0.5^\circ$ of the target position for at least 0.5 s to receive a fruit juice reward. Target locations (5° or 10°) were pseudorandomly presented within large blocks of approximately 180 trials for each paradigm. If the animal moved in the wrong direction or failed to hold at the target, the trial was canceled. As before, a new trial began when the monkey once again centered the plate and held a steady position (Fig. 1).

Electrophysiological recording and histology

Once each animal reached a steady daily performance level, a DelrinTM recording chamber was surgically implanted under sterile conditions. For several months following the implantation, extracellular recordings were made of cortical neurons using tungsten microelectrodes (2–3 Mega Ohms; Micro Probe, Potomac, MD, USA) and conventional filtering and amplification. Transdural penetrations were made daily into postcentral somatosensory areas, as well as precentral motor cortices. Neuronal activity was discriminated by a template-matching Multispike Detector (Alpha Omega Engineering, Nazareth, Israel), was time-stamped relative to the animal's behavior, and was stored in a computer (Nelson 1988; Nelson et al. 1991; Lebedev et al. 1994). Wrist position was digitized at 100 Hz and stored along with the digital records of neuronal activity. After each recording, peripheral receptive fields were determined. Neuronal responses to passive hand/wrist movements, indentation of punctuate skin surfaces, and gentle touch and palpation of the hand/arm muscles were noted, as well as responses to visual stimuli that were tested with a flashlight (Lebedev and Nelson 1995). These responses to stimuli defined the neuron's passive receptive field.

In one of the final recording sessions, electrolytic lesions were made at six cortical locations by passing 10 mA of current for 10 s. Five days after the lesions were made, the animal was deeply anesthetized with pentobarbital sodium and transcardially perfused with 10% buffered formol-saline. Histological sections of the cortex were prepared, and electrode tracks were reconstructed based on the depth of each recording site from the point where the cortical activity was first encountered and the location of the marking lesions (Nelson 1988; Nelson et al.

1991). The location of each recording site was subsequently transferred to a photograph of the surface of the recording areas after appropriate scaling. Alignment of brain sections was based on the location of the central and intraparietal sulci. Recording sites were further characterized according to reconstructed electrode tracks and the cortical cytoarchitecture (Jones and Wise 1977). The precise laminar location of recordings could not be determined with this technique. Special attention was paid, however, to confirming that the recorded neurons presented in this study were located in SI.

Data analyses

The SI neurons described in this study showed significant vibratory entrainment of their activity during the early RTPs for VIB and COM trials. VIS trials were analyzed but used simply for kinematic and timing comparisons with VIB and COM trials. To identify these neurons, single unit activity during correctly performed 10° trials was analyzed for both extension and flexion movements. The activity of each neuron during the period coinciding with the first 10 vibratory (57 Hz) cycles, and thus for the 175.4 ms immediately after go-cue onset, was examined. The length of this period was chosen because it ends about 100 ms before movement onset, at a time when activity related to impending movements begins. The vibration entrainment was illustrated in polar plots of the distribution of spikes as a function of vibratory phase (phase plots). The degree of entrainment was determined by circular statistics (Rayleigh test; Batschelet 1981) and demonstrated by the mean vector length (r):

$$r = (1/n) \left[\left(\sum \sin (2\pi f t_i) \right)^2 + \left(\sum \cos (2\pi f t_i) \right)^2 \right]^{1/2}$$

where f is the frequency of vibration, t_i represents the time of spike occurrences, and n is the number of spikes (see Nelson et al. 2002, for details about implementation). Greater r indicated better activity entrainment during the period analyzed. Moreover, the angular position of the mean vector in phase plots indicated the preferred phase for activity and was related to the vibratory phase at which the most activity was distributed.

The selected neurons were classified according to their receptive fields tested immediately after each recording. There were basically three classes: most of them demonstrated either cutaneous (CUTA) or deep (DEEP) receptive fields; a few showed no detectable receptive field. Only the CUTA and DEEP neurons were included in the present study.

The changes in FRs during the early RTPs were determined based on the analyses of activity during the late IDPs (the last 300 ms; Fig. 1). Unpaired and paired t -tests, as appropriate, were used to examine whether the differences in FRs and mean vector lengths were statistically significant. Data were expressed as mean $\pm$ standard error unless specified otherwise.

Results

Animal behavior and recording locations

The monkeys performed correctly in over 85% of the trials. For correctly performed trials, animals were required to hold their hands at the center position throughout the IDPs and RTPs (Fig. 1). Trial-by-trial plots of wrist position profiles showed that wrist position traces were centered within a range of $\pm 0.5^\circ$ during the period from the onset of holding at the center to the onset of wrist movements. On average, 35.0 ± 4.4 (mean $\pm$ SD) trials were analyzed for each movement direction for each neuron. Cytoarchitectonic features of monkey SI have been characterized by several investigators (Jones and Wise 1977; Jones et al. 1978; Nelson et al. 1980). Reconstruction of electrode penetration tracks demonstrated that all neurons examined

in the present study, i.e., neurons with vibration-entrained activity during the early RTPs, were recorded from SI (data not shown).

Neuronal selection and classification

During each recording session, task-related neurons were sought initially by examining each isolated neuron's activity during trials using the COM paradigm. Recordings using vibratory or visual cues alone were conducted if the neuron's activity in on-line displays appeared well modulated with movements in at least one direction. This, then, gave us recordings during three paradigms by using one of two go-cues or the two in combination. Of 406 SI neurons recorded during all three paradigms, 48 (11.8%) had significant vibration-entrained activities during the early RTPs for the VIB and/or COM trials as determined by circular statistics and were selected for further analyses. Each neuron contributed 2 cases, extension and flexion, resulting in 96 cases. Of these, 50 cases showed cutaneous and 46 showed deep receptive fields and were classified as CUTA and DEEP neurons, respectively.

Fig. 2 shows an example of the activity of a neuron in the CUTA class. This neuron had very low activity during the IDPs for both VIB and COM trials. Abrupt increases in FRs started about 20 ms after go-cue onset and continued throughout the RTPs. The activity during the first 10 vibration cycles of the RTP was entrained by vibratory stimuli. Better entrainment was observed during the COM ($r = 0.69$) than during VIB ($r = 0.42$) trials (Fig. 2a, a'; insets). This also can be seen in the corresponding raster plots (Fig. 2b, b'). During VIS trials, the change in FRs between the IDP and the early RTP was not statistically significant and, as expected, no rhythmic activity was observed (data not shown). Reconstruction of the corresponding electrode penetration indicated that this neuron was recorded from area 1 (Fig. 2c; open circle). This neuron could be activated by gentle touch at the tip of the index finger outside the task.

Fig. 3 shows an example of the activity of a neuron classified as a DEEP neuron. Vibration-entrained rhythmic activity was observed during the early RTP. In contrast to the CUTA neuron in Fig. 2, this DEEP neuron showed better activity entrainments during the VIB trials ($r = 0.56$) when compared with the COM trials ($r = 0.32$). Compared to CUTA neurons, this DEEP neuron demonstrated smaller FR increases and less entrained activity in the early RTP for both VIB and COM trials. The discharge of the neuron increased during passive extension of the metacarpo-phalangeal joint of the index finger. Reconstruction of the electrode track confirmed that it was recorded from area 3a (Fig. 2c; open triangle).

Table 1 summarizes the receptive fields of these vibration-entrained SI neurons. Most neurons showed either cutaneous or deep receptive fields associated with the stimulated hand. Some neurons had receptive fields in the wrist. A few neurons responded to deep stimulation of the forearm. None of these SI neurons responded to simple visual stimuli delivered using a flashlight. Further analyses were based on the classification determined by the type of receptive fields.

Neuronal firing rates and vibration entrainment

We analyzed the mean FRs during the late IDPs and the early RTPs in the three paradigms. During the late IDPs, the activity of the CUTA neurons was lower than for the DEEP neurons. As shown in Fig. 4a, the FRs of the CUTA neurons were 22.1 ± 1.2 and 23.0 ± 1.2 spikes/s during the VIB and COM trials, respectively. The FRs of the DEEP neurons during the VIB trials (37.2 ± 1.9 spikes/s) were significantly higher than during the COM trials (34.2 ± 1.6 spikes/s; paired t -test: $p < 0.01$). For both CUTA and DEEP classes, neuronal activities significantly increased during the early RTPs (Fig. 4b). The FR changes (Fig. 4c) were significantly greater for the CUTA (VIB vs. COM: 68.8 ± 4.9 vs. 65.0 ± 5.4 spikes/s) than for

the DEEP (VIB vs. COM: 8.5 ± 1.6 vs. 8.7 ± 1.8 spikes/s) neurons (unpaired *t*-tests between the two classes during same paradigms; $p < 0.01$).

The mean FRs per vibration cycle were slightly higher during VIB trials than during COM trials for both CUTA (VIB vs. COM: 87.7 ± 4.8 vs. 84.6 ± 5.4 spikes/s) and DEEP (VIB vs. COM: 46.6 ± 2.3 vs. 44.5 ± 2.2 spikes/s) classes. Normalized FRs plotted against time showed that, for the CUTA neurons, the peak FRs during individual vibration cycles were higher for COM trials (Fig. 5a; thinner line) when compared with VIB trials (Fig. 5a; thicker line). For the DEEP neurons, the differences in peak FRs between the VIB and COM trials were smaller (Fig. 5b) when compared with the CUTA neurons. Comparisons of FRs were then performed between cycle phases as defined in Figure 5c. During VIB trials, when compared with COM trials, the CUTA neurons showed lower FRs during a 20° phase that was centered on mean vector (PMV), but the FRs were significantly greater outside the PMVs (Fig. 5d). The DEEP neurons demonstrated greater FRs during the PMVs for VIB trials, whereas outside the PMVs, the FRs were similar between VIB and COM trials (Fig. 5e). For both CUTA and DEEP classes, the differences in FRs between extension and flexion movements were not statistically significant.

Neuronal activity during the early RTP was further analyzed for vibration entrainment, as measured by mean vector length (see Nelson et al. 2002). Fig. 6 compares the vibration entrainment between the VIB and COM trials. For CUTA neurons, significantly better entrainment was observed during COM trials than during VIB trials (paired *t*-test: $p < 0.01$; Fig. 6a). For DEEP neurons, better entrainment was observed during the VIB trials when compared with COM trials. These differences, however, did not reach statistically significant levels (paired *t*-test: $p > 0.05$; Fig. 6b). No significant difference in vibration entrainment was observed between extension and flexion movements.

During VIS trials, the FR of CUTA neurons during the late IPDs was lower than for the DEEP neurons, which was consistent with what was observed during the VIB and COM trials (Fig. 7). This difference in FRs between the two groups remained until the onset of movements (Fig. 7; arrow). As might be expected, no rhythmic activity was observed for either CUTA or DEEP neurons during the VIS trials. For both CUTA and DEEP neurons, changes in FRs between the late IPDs and the early RTPs were not significant.

Discussion

In the present study using behaving monkeys, vibration-entrained SI neurons were recorded during wrist movements and analyzed for two conditions: when the task was guided by vibratory cues only or when both vibratory and visual cues were simultaneously available. Entrained SI neurons were classified as CUTA and DEEP, according to their receptive fields. During the early RTPs, both CUTA and DEEP neurons showed increases in FRs. Moreover, the activity of CUTA neurons was significantly less entrained during VIB trials when compared with COM trials. During the same task periods, the activity entrainment of DEEP neurons was similar. These data suggest to us that the modulation of some SI responses to vibratory stimuli varies depending on the functional significance of sensory information. Suggestions of this sort would certainly be in keeping with a recent report that showed that active whisking induces touch-dependent facilitation and depression in rat SI (Derdikman et al. 2006).

Moreover, we observed that the activity of some SI neurons changed during the IDP when monkeys awaited vibratory or visual stimuli that guided wrist movements (Liu et al. 2007). These observations strongly suggested to us that central inputs from other cortical areas may modulate neuronal activity in SI. What remains unclear is the extent of the epochs during which this modulation takes place and the conditions under which it can be seen.

Early RTPs of the paradigms

During the RTP, from go-cue onset to movement onset, monkeys held their hands at the center position. Records of wrist position showed that no wrist movements were detected throughout the IDPs and RTPs for correctly performed trials (Liu et al. 2007). In the present study, neuronal activity during the early RTPs was examined. The early RTP was defined as the 175.4 ms immediately after go-cue onset (Fig. 1). We defined RTP this way because (1) it includes 10 cycles of vibration (57 Hz), providing a reasonable time period for analyzing vibration entrainment; (2) it ends about 100 ms before movement onset. We and others have previously shown that neuronal activity clearly associated with upcoming movements often begins as early as this (Glickstein 1972; Hepp-Reymond et al. 1989; Wannier et al. 1991; Lebedev and Nelson 1995). The involvement of SI in active arm reaching movements is well documented (see, e.g., Prud'homme and Kalaska 1994). Neuronal activity during the early RTPs, however, may reflect the processing of go-cue related signals or the movement planning-related information (Paz et al. 2003; Liu et al. 2005).

In the present study, vibration entrainment during the early RTPs was compared between the VIB and COM trials. The fundamental difference of the two paradigms is that, during VIB trials, the vibratory input is the only information that triggers movements and specifies targets. During the COM trials, although the same vibratory input is also present, the visual signals are available simultaneously. Thus, either vibratory or visual cues may trigger and guide wrist movements. Because they have an alternative information source that can lead to successful task completion, monkeys may pay less attention to vibratory input during the COM trials when compared with the VIB trials.

Vibration-entrained SI neurons and receptive fields

The characteristics of vibration-entrained neurons in SI have been studied under a number of conditions (Mountcastle et al. 1969; Nelson et al. 1991, 2002; Lebedev et al. 1994; Lebedev and Nelson 1995; Salinas et al. 2000; Romo and Salinas 2003). Two classes of SI neurons are thought to play essential roles in the sense of flutter-vibration: the glabrous quickly adapting (QA) neurons and the Pacinian (PC) neurons (Mountcastle et al. 1969). The QA neurons are best activated by sinusoidal mechanical stimuli in the frequency range 5–80 Hz. Discharges of these neurons occur consistently and in a relatively restricted part of the cycle of the sine wave. It is reasonable to suggest that the consistency is due to relative sensitivity to vibratory stimuli and the timing is influenced by the conduction velocity of the signal from periphery to cortex. These SI neurons have been viewed as playing an important role in frequency discrimination. The PC neurons are preferentially activated by higher frequency vibratory stimuli (80–400 Hz) delivered to peripheral tissues.

In this study, vibration-entrained neurons are classified based on receptive fields, i.e., cutaneous vs. deep, to address the functional significance of these two classes of neurons in the processing of somatosensory information. We speculate that the CUTA neurons in SI may be more involved in the discrimination of vibration frequency and the coding of its functional significance. The DEEP neurons, however, may play an important role in movement control because some of them probably receive inputs from muscles or joints. Reports show that vibrotactile adaptation enhances spatial location (Tannan et al. 2006). Our experimental design did not allow us to investigate specifically the types of fibers that carry the sensory signals from cutaneous or deep tissues. However, the source of vibratory input during the early RTPs might not involve the results of tendon-stretch because recorded profiles showed no changes in hand position (Liu et al. 2005, 2007). The angular deflection of the plate that resulted during the vibration was less than 0.06° , which would be too small to cause significant joint movements.

Processing vibratory input with or without functional significance in SI

In SI, rhythmic activity was evoked by peripheral vibratory stimuli in unanesthetized monkeys (Mountcastle et al. 1969). These authors observed well-entrained activity when suprathreshold vibratory stimuli were given. In these experiments, however, the activity recorded in SI reflected only the responsiveness of neurons to the peripheral vibratory stimulation because the animals were immobilized by neuromuscular blocking agents. No functional implication of the vibratory input was examined.

Vibratory stimuli can be used to guide motor tasks in behaviorally trained monkeys (Nelson et al. 1991, 2002; Lebedev et al. 1994; Lebedev and Nelson 1995; Salinas et al. 2000; Romo and Salinas 2003). Extracellular recordings in task-performing monkeys reveal some task-related activity that is vibration-entrained, suggesting that the entrained activity may code functionally significant information conveyed by vibratory inputs. Studies have also demonstrated that direct microstimulation in some cortical subregions where vibration-sensitive neurons are found can be used to mimic peripheral vibratory stimulation in sensory-guided tasks (Romo et al. 1998). The results from each of the studies listed above further imply that SI may be involved in processing the functional significance of the vibratory inputs. It has been suggested that periodicity and firing rate may be candidate neural codes for the frequency of vibrotactile stimuli (Hernández et al. 2000; Salinas et al. 2000; Luna et al. 2005). When judging vibration frequency, humans utilize information about stimulus velocity as coded by neurons in SI (Harris 2006). However, it remains unclear how the functional significance may be coded in the rhythmic activity of responsive neurons.

We directly compared the activity of entrained SI neurons in conditions during which vibratory input is or is not the only source of cueing signals to guide a task. The results show that when the vibratory stimuli are the only cueing signals, i.e., functionally required, the FRs of the CUTA neurons increase to some extent but are significantly less entrained (Fig. 4–Fig 6), implying that both FRs and the degree of entrainment are involved in coding of the functional significance of vibratory stimuli. Slightly decreased FRs and better-entrained activities occur when vibratory input is not a functional necessity. During VIS trials, no significant FR changes were found during the early RTPs (Fig. 7) which is consistent with observations by other authors (Hepp-Reymond et al. 1989; Wannier et al. 1991).

For those CUTA neurons, when compared with the COM trials, the smaller vector lengths during VIB trials (Fig. 2 and Fig 6a) can be explained by a decrease in activity in PMVs and an increase in activity outside PMVs (Fig. 5; see also figure 10.8 in Nelson et al. 2002). Earlier studies suggest that when vibratory stimulus amplitude increases past the range where neurons fire one spike per stimulus cycle, neurons begin to fire more than one spike per stimulus cycle. Additional spikes are commonly in anti-phase with the initial entrained activity (Mountcastle et al. 1969; see, e.g., Fig. 18). Recent studies suggest that higher-order cortical areas may influence sensory processing in SI (see, e.g., Nelson 1996; Haggard et al. 2007; Gilbert and Sigman 2007). In the present study, during VIB trials, increases in anti-phase activity were seen in the absence of visual cues, when vibratory inputs from the periphery were essential for task performance. These observations are consistent with the following hypothesis. We suggest that in COM trials, when visual cues can guide movements, vibratory responses in SI are partially suppressed by higher-order cortical areas. In VIB trials, that suppression is released, and responsive cortical neurons respond to vibratory inputs as if the amplitude of those inputs is increased. The increase in “sensitivity,” however, may saturate the activity and the anti-phase activity increases as it does when stimulus amplitude increases (Mountcastle et al. 1969). The result of the increase in anti-phase activity is that the mean vector length decreases.

It has been proposed that periodicity is less important for frequency discrimination than mean FRs (Salinas et al. 2000; Luna et al. 2005). In those experiments, the vibratory frequency of

peripheral stimuli is different. It remains unclear, however, how SI neurons may respond to the vibratory signals that are just to be detected rather than those that must be discriminated. In the present study, vibratory frequencies during early RTPs were the same for VIB and COM trials. Therefore, no frequency discrimination was required. In this situation, in addition to increases in firing rates, the degree of activity entrainment may also play a role in coding functional significance of vibratory inputs.

Studies have suggested that SI is involved not only in sensory processing but also in high-level cognitive functions (Nelson 1988, 1996; Hsiao et al. 1993; Zhou and Fuster 1996, 1997, 2000, 2004; Mima et al. 1998; Romo and Salinas 2001; Taylor-Clarke et al. 2002, 2004; de la Fuente and Romo 2006). Perhaps the subtle but statistically significant changes in FRs and entrainment that are associated with movements made in response to different types of go-cues indicate the effect of higher-level cognitive functions on the very neurons that faithfully represent externally applied vibratory stimuli in the cortex.

Acknowledgements

We thank Dr. D. L. Armbruster for detailed comments on this manuscript. This work was supported by NIH Grant NS36860 to R.J. Nelson.

References

- Batschelet, E. New York: Academic Press; 1981. Circular statistics in biology.
- de la Fuente V, Romo R. Neuronal correlate of subjective sensory experience gradually builds up across cortical areas. *Proc Natl Acad Sci USA* 2006;103:14266–14271. [PubMed: 16924098]
- Derdikman D, Yu C, Haidarliu S, Bagdasarian K, Arieli A, Ahissar E. Layer-specific touch-dependent facilitation and depression in the somatosensory cortex during active whisking. *J Neurosci* 2006;26:9538–9547. [PubMed: 16971538]
- Gilbert CD, Sigman M. Brain states: top-down influences in sensory processing. *Neuron* 2007;54:677–696. [PubMed: 17553419]
- Glickstein M. Brain mechanisms in reaction time. *Brain Res* 1972;40:33–37. [PubMed: 4338261]
- Haggard P, Christakou A, Serino A. Viewing the body modulates tactile receptive fields. *Exp Brain Res* 2007;180:187–193. [PubMed: 17508208]
- Harris JA. Psychophysical investigations into cortical encoding of vibrotactile stimuli. *Novartis Found Symp* 2006;270:238–245. [PubMed: 16649718]
- Hernández A, Zainos A, Romo R. Neuronal correlates of sensory discrimination in the somatosensory cortex. *Proc Natl Acad Sci USA* 2000;97:6191–6196. [PubMed: 10811922]
- Hepp-Reymond MC, Wannier TM, Maier MA, Rufenner EA. Sensorimotor cortical control of isometric force in the monkey. *Prog Brain Res* 1989;80:451–463. [PubMed: 2634281]
- Hsiao SS, O'Shaughnessy DM, Johnson KO. Effects of selective attention on spatial form processing in monkey primary and secondary somatosensory cortex. *J Neurophysiol* 1993;70:444–447. [PubMed: 8360721]
- Jones EG, Wise SP. Size, laminar and columnar distribution of efferent cells in the sensory-motor cortex of monkeys. *J Comp Neurol* 1977;175:391–437. [PubMed: 410849]
- Jones EG, Coulter JD, Hendry SHC. Intracortical connectivity of architectonic fields in the somatic sensory, motor and parietal cortex of monkeys. *J Comp Neurol* 1978;181:291–347. [PubMed: 99458]
- Lebedev MA, Nelson RJ. Rhythmically firing (20–50Hz) neurons in monkey primary somatosensory cortex: activity patterns during initiation of vibratory-cued hand movements. *J Comp Neurosci* 1995;2:313–334.
- Lebedev MA, Denton JM, Nelson RJ. Vibration-entrained and premovement activity in monkey primary somatosensory cortex. *J Neurophysiol* 1994;72:1654–1673. [PubMed: 7823093]
- Liu Y, Denton JM, Nelson RJ. Neuronal activity in primary motor cortex differs when monkeys perform somatosensory and visually guided wrist movements. *Exp Brain Res* 2005;167:571–586. [PubMed: 16078029]

- Liu Y, Denton JM, Nelson RJ. Neuronal activity in monkey primary somatosensory cortex is related to expectation of somatosensory and visual go-cues. *Exp Brain Res* 2007;177:540–550. [PubMed: 17006686]
- Luna R, Hernandez A, Brody CD, Romo R. Neural codes for perceptual discrimination in primary somatosensory cortex. *Nat Neurosci* 2005;8:1210–1219. [PubMed: 16056223]
- Mima T, Nagamine T, Nakamura K, Shibasaki H. Attention modulates both primary and second somatosensory cortical activities in humans: a magnetoencephalographic study. *J Neurophysiol* 1998;80:2215–2221. [PubMed: 9772274]
- Mountcastle VB, Talbot WH, Sakata H, Hyvarinen J. Cortical neuronal mechanisms in flutter-vibration studied in unanesthetized monkeys. Neuronal periodicity and frequency discrimination. *J Neurophysiol* 1969;32:452–484. [PubMed: 4977839]
- Nelson RJ. Set related and premovement related activity of primate primary somatosensory cortical neurons depends upon stimulus modality and subsequent movement. *Brain Res Bull* 1988;21:411–424. [PubMed: 3214747]
- Nelson RJ. Interactions between motor commands and somatic perception in sensorimotor cortex. *Curr Opin Neurobiol* 1996;6:801–810. [PubMed: 9000020]
- Nelson, RJ.; Lebedev, MA.; Liu, Y. Deciphering the code-dynamic modulation of neural activity during tactile behavior. In: Nelson, RJ., editor. *The somatosensory system--deciphering the brain's own body image*. Boca Raton: CRC Press; 2002. p. 243-273.
- Nelson RJ, Sur M, Felleman DJ, Kaas JH. Representations of the body surface in postcentral parietal cortex of *Macaca fascicularis*. *J Comp Neurol* 1980;192:611–643. [PubMed: 7419747]
- Nelson RJ, McCandlish CA, Douglas VD. Reaction times for hand movements made in response to visual versus vibratory cues. *Somatosens Mot Res* 1990;7:337–352. [PubMed: 2248005]
- Nelson RJ, Smith BN, Douglas VD. Relationships between sensory responsiveness and premovement activity of quickly adapting neurons in areas 3b and 1 of monkey primary somatosensory cortex. *Exp Brain Res* 1991;84:75–90. [PubMed: 1855565]
- Paz R, Boraud T, Natan C, Bergman H, Vaadia E. Preparatory activity in motor cortex reflects learning of local visuomotor skills. *Nature Neurosci* 2003;6:882–890. [PubMed: 12872127]
- Prud'homme MJ, Kalaska JF. Proprioceptive activity in primate primary somatosensory cortex during active arm reaching movements. *J Neurophysiol* 1994;72:2280–2301. [PubMed: 7884459]
- Romo R, Salinas E. Touch and go: decision-making mechanisms in somatosensation. *Annu Rev Neurosci* 2001;24:107–137. [PubMed: 11283307]
- Romo R, Salinas E. Flutter discrimination: neural codes, perception, memory and decision making. *Nat Rev Neurosci* 2003;4:203–218. [PubMed: 12612633]
- Romo R, Hernández A, Zainos A, Salinas E. Somatosensory discrimination based on cortical microstimulation. *Nature* 1998;392:387–390. [PubMed: 9537321]
- Salinas E, Hernández A, Zainos A, Romo R. Periodicity and firing rate as candidate neural codes for the frequency of vibrotactile stimuli. *J Neurosci* 2000;20:5503–5515. [PubMed: 10884334]
- Tannan V, Whitsel BL, Tommerdahl MA. Vibrotactile adaptation enhances spatial localization. *Brain Res* 2006;1102:109–116. [PubMed: 16806126]
- Taylor-Clarke M, Kennett S, Haggard P. Vision modulates somatosensory cortical processing. *Curr Biol* 2002;12:233–236. [PubMed: 11839277]
- Taylor-Clarke M, Jacobsen P, Haggard P. Keeping the world a constant size: object constancy in human touch. *Nat Neurosci* 2004;7:219–220. [PubMed: 14966526]
- Wannier TM, Maier MA, Hepp-Reymond MC. Contrasting properties of monkey somatosensory and motor cortex neurons activated during the control of force in precision grip. *J Neurophysiol* 1991;65:572–589. [PubMed: 2051196]
- Zhou YD, Fuster JM. Mnemonic neuronal activity in somatosensory cortex. *Proc Natl Acad Sci USA* 1996;93:10533–10537. [PubMed: 8927629]
- Zhou YD, Fuster JM. Neuronal activity of somatosensory cortex in a cross-modal (visuo-haptic) memory task. *Exp Brain Res* 1997;116:551–555. [PubMed: 9372304]
- Zhou YD, Fuster JM. Visuo-tactile cross-modal associations in cortical somatosensory cells. *Proc Natl Acad Sci USA* 2000;97:9777–9782. [PubMed: 10944237]

Zhou YD, Fuster JM. Somatosensory cell response to an auditory cue in a haptic memory task. *Behav Brain Res* 2004;153:573–578. [PubMed: 15265656]

Fig. 1.

The tasks. See Methods for details. Neuronal activity during the last 300 ms of the instructed delay period (*late IDP*) and the first 175.4 ms (10 vibration cycles; 57 Hz) of the reaction time period (*early RTP*) were examined.

Fig. 2.

An example of a vibration-entrained SI neuron with cutaneous receptive field during wrist extension movements for VIB (left column) and COM (right column) trials. Data are from the task period of 150 ms before and 350 ms after go-cue onset (0 ms). **a** Histogram showing mean firing rate (FR). Bin width = 2 ms. The inset is a polar coordinate ($^{\circ}$) for neuronal activities during the first 10 vibration cycles after go-cue onset, showing normalized vectors (shaded area) and mean vector length (arrow; r) determined by circular statistics (Rayleigh test). The largest circle represents the maximum r (1.0). **b** Raster plots. Same time scales as in **a**. Each dot represents a neuronal spike on a trial. Trials are aligned on go-cue onset (triangle) and ordered by reaction times (open circles). **c** Reconstruction of the location of this neuron (open circle) shown by cortical surface view (left) and histological section (right). The open triangles indicate the location of the neuron shown in Fig. 3. CS central sulcus; IPS intraparietal sulcus; SAR superior arcuate sulcus; SPCD superior precentral dimple. **a'**, **b'** COM trials, same conventions as in **a** and **b**, respectively. This neuron had a cutaneous receptive field at the tip of the index finger.

Fig. 3.

An example of a vibration-entrained SI neuron with deep receptive field during wrist flexion movements for VIB (left column) and COM (right column) trials. **a, a'** Histograms. **b, b'** Raster plots. Same conventions as in Fig. 2. The recording location was shown in Fig. 2c (triangles). The discharge of this neuron increased during passive extension of the index finger.

Fig. 4.

Scattergrams showing firing rates (*FR*) of SI neurons during VIB and COM trials. **a** *FR* during instructed delay period (*IDP*, the last 300 ms). **b** *FR* during early reaction time period (*RTP*). **c** Changes in *FR*s during the early *RTP* as compared with *IDPs*. Neurons were grouped as cutaneous (*CUTA*) or deep (*DEEP*) based on receptive fields. Solid lines represent mean *FR*s (**a**, **b**) or mean *FR* changes (**c**) of corresponding groups indicated by symbols next to each axis.

Fig. 5. Firing rates (FR) of vibration-entrained SI neurons during VIB and COM trials. **a, b** Normalized FRs for neurons with cutaneous (CUTA) and deep (DEEP) receptive fields, respectively. Markers above the abscissas indicate the beginning of each vibration cycle (57 Hz). Data represent smoothed histograms (bin width = 2 ms), which are normalized to the maximum FR during VIB (thicker line) and COM (thinner line) trials and are aligned on go-cue onset (0 ms). **c** A schematic polar coordinate for defining vibratory cycle phases that are used for analyzing neuronal activities during early reaction time periods. Arrow represents the location of a mean vector. Activities during the phase (20°) centered on mean vector (PMV),

the remaining half cycle (*RHC*), and the anti-phase half cycle (*AHC*) were compared. **d, e** Mean FRs during PMV, RHC, and AHC for CUTA (in **a**) and DEEP (in **b**) neurons, respectively.

Fig. 6.

Vibration-entrainment of SI neuronal activity during the early reaction time period as a function of changes in firing rates (FR) after go-cue onset. **a** Neurons with cutaneous (CUTA) receptive fields. The activity entrainments are determined by circular statistics (*Rayleigh test*) and measured by mean vector length. Data were normalized to the maximum vector length during VIB and COM trials. Solid lines represent the mean values of normalized vector length and are compared between the VIB and COM trials (paired *t*-test). **b** Neurons with deep (DEEP) receptive fields. Same conventions as in **a**.

Fig. 7.

Histogram showing firing rates of vibration-entrained SI neurons during the VIS trials.

Duration between the two vertical lines represents the early reaction time period during which increased firing rates and entrained activities were observed for the VIB and COM trials (see Fig. 5). Bin width = 20 ms. *CUTA* cutaneous receptive field; *DEEP* deep receptive field.

Table 1
Types and locations of receptive fields (RF) for vibration-entrained neurons in SI. Numbers represent cases.

RF type	RF location				Total
	Arm	Forearm	Wrist	Hand	
Cutaneous	0	0	4	46	50
Deep	4	4	2	36	46