

Persistent Neuronal Firing in Primary Somatosensory Cortex in the Absence of Working Memory of Trial-specific Features of the Sample Stimuli in a Haptic Working Memory Task

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Abstract

■ Previous studies suggested that primary somatosensory (SI) neurons in well-trained monkeys participated in the haptic–haptic unimodal delayed matching-to-sample (DMS) task. In this study, 585 SI neurons were recorded in monkeys performing a task that was identical to that in the previous studies but without requiring discrimination and active memorization of specific features of a tactile or visual memorandum. A substantial number of those cells significantly changed their firing rate in the delay compared with the baseline, and some of them showed differential delay activity. These firing changes are similar to those recorded from monkeys engaged in active (working) memory. We conclude that the delay activity is not necessarily only observed as was generally thought in the situation of active memorization of different features between memoranda after those features have been actively discrim-

inated. The delay activity observed in this study appears to be an intrinsic property of SI neurons and suggests that there exists a neural network in SI (the primary sensory cortex) for haptic working memory no matter whether the difference in features of memoranda needs to be memorized in the task or not. Over 400 SI neurons were also recorded in monkeys well-trained to discriminate two memoranda in the haptic–haptic DMS task for comparison of delay firing of SI neurons between the two different working memory tasks used in this study. The similarity observed in those two situations suggests that working memory uses already-existing memory apparatus by activating it temporarily. Our data also suggest that, through training (repetitive exposure to the stimulus), SI neurons may increase their involvement in the working memory of the memorandum. ■

INTRODUCTION

Working memory refers to an active STM system that is capable of temporarily maintaining and manipulating sensory information and then executing the sensory information-related behavioral action (Fuster, 1997; Baddeley, 1992). Studies over the past three decades have demonstrated that, in certain areas of the primate cerebral cortex, some cells undergo sustained activation of discharge when the animal needs to retain information about a sensory stimulus for a subsequent action (Fuster, 1997). Such “memory cells” are thought to be the neural substrate of working memory.

Memory cells have been found in various areas of the association cortex of monkeys depending on the nature of information provided by the cue in delay tasks, such as in pFC (Romo, Brody, Hernandez, & Lemus, 1999; Rao, Rainer, & Miller, 1997; Miller, Erickson, & Desimone,

1996; Funahashi, Bruce, & Goldman-Rakic, 1989; Niki, 1974; Fuster & Alexander, 1971), inferotemporal cortex (Chelazzi, Duncan, Miller, & Desimone, 1998; Gibson & Maunsell, 1997; Colombo & Gross, 1994; Miller, Li, & Desimone, 1993; Fuster, 1990; Miyashita & Chang, 1988; Fuster & Jervey, 1982), and posterior parietal cortex (Chafee & Goldman-Rakic, 1998; Bracewell, Mazzoni, Barash, & Andersen, 1996; Colby, Duhamel, & Goldberg, 1996; Constantinidis & Steinmetz, 1996; Barash, Bracewell, Fogassi, Gnadt, & Andersen, 1991; Andersen, Bracewell, Barash, Gnadt, & Fogassi, 1990; Koch & Fuster, 1989; Gnadt & Andersen, 1988).

Our previous studies demonstrated that neurons in the primary somatosensory (SI) area were activated during the delay period when the monkey performed a haptic–haptic (HH) DMS task (Bodner, Zhou, & Fuster, 1997; Zhou & Fuster, 1996). Some of those cells showed differential delay activity depending on the features of the memorandum actively touched by the animal during the sample period. These findings indicate that SI cortex participates in active retention of haptic information in addition to being important

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for haptic perception. Furthermore, in monkeys well-trained to perform a visuo-haptic (VH) cross-modal DMS task, some SI cells were activated by a visual icon that was associated with the haptic choice and displayed delay activity (Zhou & Fuster, 1997, 2000). Chapman and her colleagues investigated the neural activity in the SI cortex of monkeys with an instructed delay tactile discrimination task (Meftah el, Bourgeon, & Chapman, 2009), in which a visual stimulus was used as an instruction cue. They found that the visual cue could induce a sustained increase or decrease in discharge in SI during the 2-sec delay period, when the monkey was required by the task to discriminate the tactile stimuli after the delay. Those data indicate that SI cortex may also play an important role in retention of nontactile information when it is associated through learning with the tactile stimulus.

Results of a recent study showed that neurons in secondary somatosensory (SII) cortex of monkeys were also involved in working memory of information of a vibration frequency (base stimulus) for a later comparison with another vibration frequency (comparison stimulus; Salinas, Hernandez, Zainos, & Romo, 2000). Many SII neurons in this study showed stimulus frequency-specific firing modulation during the memorization period, and when the animal did not need to remember the stimulus, the frequency-specific modulation was diminished significantly. Existence of memory cells in both sensory and association cortices demonstrates that neural networks for working memory are globally distributed in different cortical areas.

In a recent study (Constantinidis & Steinmetz, 2005), some neurons in the posterior parietal cortex were shown to be able to represent the location of a salient visual stimulus, although the monkey was only trained to perform a fixation task and not a task in which the animal had to actively detect the location of the stimulus. These results are similar to the previous results in monkeys trained to actively locate a salient stimulus (Constantinidis & Steinmetz, 2001). The researchers proposed that posterior parietal cortex neurons could automatically detect and encode the location of the salient stimulus in those animals that were trained only for fixation task, although compared with the results in monkeys that were trained to perform an active-detection task, a significantly lower percentage of neurons with selectivity for the salient stimulus was observed (Constantinidis & Steinmetz, 2005). More recently, some prefrontal neurons of monkeys untrained to a working memory task were found to show selective persistent activity in the delay period of the task related to the location and feature of the salient stimulus (Meyer, Qi, & Constantinidis, 2007). This indicates that some neurons in the pFC of untrained monkeys represent the location and identity of visual stimuli that have no behavioral significance.

In this study, two groups of monkeys were used. In one group, monkeys (named as “untrained” here) were not required to actively discriminate and memorize specific features of a tactile or visual memorandum for sub-

sequent haptic choices in performance of haptic delay tasks. In the other, monkeys (used as controls, named as “well-trained” here) were required to actively discriminate and memorize those specific features in the corresponding haptic tasks. We compared SI cells recorded from those two groups of monkeys to address the following questions: (1) Does the delay activity shown in SI cells of the “well-trained” monkeys also exist in SI cells of the “untrained” monkeys? (2) If yes, does behavioral training have any impact on the delay activity of SI cells?

METHODS

Animal

Two (one male and one female) rhesus monkeys (*Macaca mulatta*), weighing 7–10 kg, were used for this study. They had never been trained in any other cognitive tasks before. They were individually housed and fed an *ad libitum* diet. Intake of water was restricted 1 day before and during experimental sessions. Animal care and surgical procedures were approved by the animal care and use committee at the Johns Hopkins University.

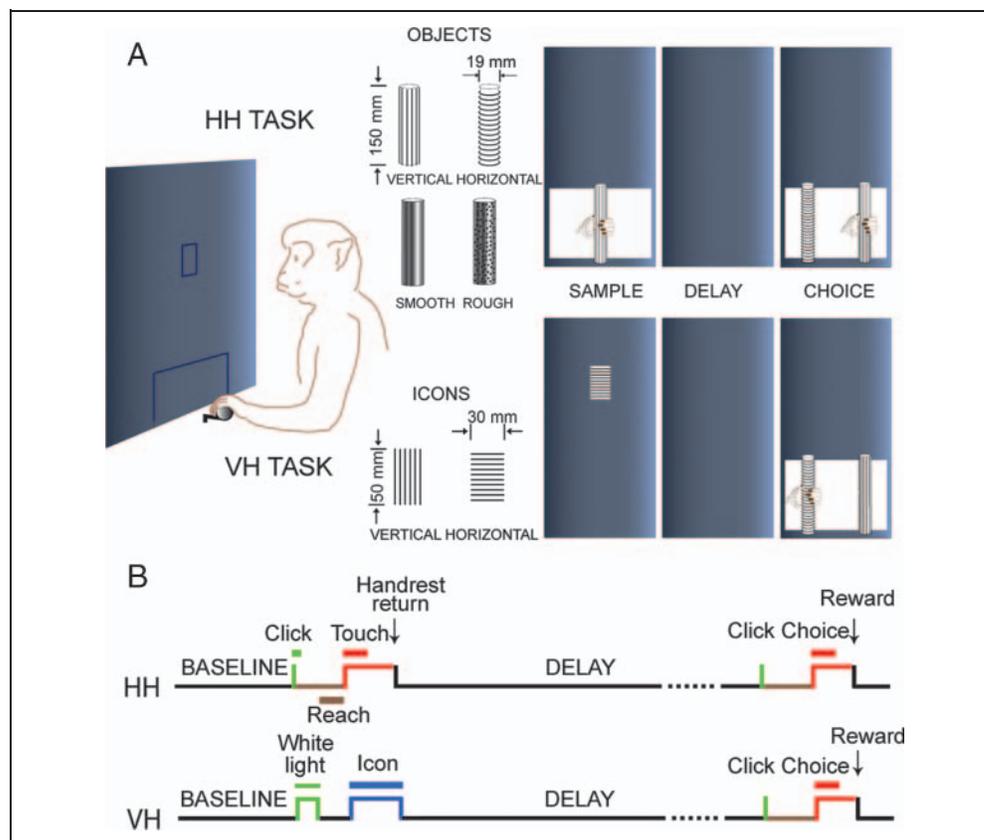
Behavioral Task

The monkey sat in a primate chair in a sound-attenuated chamber and was trained to learn the procedure of the behavioral tasks (one monkey was trained for over 1 year, and the other for 4 months).

HH Task

A trial started with a click signaling that the sample rod (either the rod with horizontal bars on its surface or the rod with vertical bars) was accessible for the monkey to touch in a fixed central position in front of the animal. About 1.5 sec later, the monkey’s operating hand reached out to touch the rod (Figure 1A, top). After the sample touch the monkey returned its hand to a handrest initiating the delay period, a random length in the range of 10.5–12 sec. The monkey had to rest its operating hand on the handrest during the whole delay period (also during the baseline period). Any break of the contact between the hand and the handrest during the period led to the trial being aborted automatically. At the end of the delay, the objects moved to proper positions to be ready for the animal’s choice. Five seconds later, a second click signaled two rods (one horizontal and one vertical) were presented side by side. The monkey reached out again to grasp and pull the objects. A pull of either rod ended the trial and led to an immediate reward with about 1.5–2 ml of water. The rod was entirely hidden from view in the task. The monkey could not see the objects either during training or during recording. The presentation of the sample object and the position of the objects in the choice period were randomized from trial to trial. To explore the impact of behavioral

Figure 1. Schematic diagram of behavioral tasks. (A) Top: Events of the HH task. Either horizontal or vertical rod is presented during the sample period. Monkey's palpation of the sample object is followed by the delay period (10.5–12 sec). In the choice period, the horizontal and vertical rods are presented side by side. The monkey pulls either one of the objects to get 1.5–2 ml of water. Bottom: Events of the VH task. The monkey watches the visual icon (horizontal or vertical) in the center of the screen while the operating hand rests on the handrest during the cue period that is followed by the delay period (10.5–12 sec). The choice period in the VH task is the same as that in the HH task. (B) The events of the HH task and the VH task.



training on the delay activity of SI neurons in the monkeys, a second pair of rods (one with a smooth surface and the other with a rough surface) were also used during the recording of single units.

In this study, the animal was not required by the task to actively discriminate between the two objects either in the period before the delay, which we called the sample period, or in the period after the delay, which we call the choice period. Monkeys were rewarded so long as they successfully progressed through sample and delay periods to the response (a pull of either rod) of the trial. We referred to the two periods as the “sample” and “choice” periods to be consistent with our previous studies (Zhou & Fuster, 1996, 2000), in which the animal had to recognize the sample object and retain information about the sample to make a correct choice.

VH Task

A trial started with the presentation of an alerting light (a white rectangular icon, dimension = 3×5 cm, duration = 0.5 sec) on a computer screen at eye level. Two seconds after the offset of the white light, a visual cue (a patterned icon with the same dimension as the white light but with duration of 2 sec) was presented at the same position as the alerting light just presented. The eye movement was monitored and recorded continuously by an eye tracking system (ISCAN ETL-200, ISCAN, Inc., Burlington, MA). A

pair of patterned icons was used. Black and white patterns of parallel stripes (3.50 mm apart) with horizontal direction were shown in one icon, and those with vertical direction were shown in the other (Figure 1A, bottom). The offset of the visual cue was the beginning of the delay. The rest of the trial was the same as the corresponding part of the trial in the HH task. The visual cue and the position of the tactile objects in choice period were arranged randomly in trials. Similar to the previous HH task, the VH task did not require the animal to either discriminate the visual cues or actively memorize them during the delay for the subsequent haptic choice.

Implantation of Recording Chamber

After the monkey was able to follow the task performance procedure in both the HH task and the VH task, surgical operations were performed. Under strictly sterile conditions and general anesthesia with isoflurane at a maintenance level of 1.5–3.0, the recording chamber (Crist Instrument Co., Inc., Hagerstown, MD) with 22-mm diameter was implanted on the parietal area. The location of the recording chamber on each animal was determined by the individual MRI atlas (3T, Johns Hopkins Hospital). The central sulcus and intraparietal sulcus were clearly visible in the opening (Figure 2), and therefore, the recording chamber covered a small part of the motor area, SI, SII, and posterior parietal cortex.

Single-unit Recordings

When the monkey performed the HH and VH tasks, two or three glass-coated tungsten electrodes (1~2 M Ω , Nano Biosensors Ltd., Nazareth, Israel) were introduced into the SI area through a multielectrode system (NAN Electrode System, Plexon, Inc., Dallas, TX). The single-unit activity was recorded extracellularly, monitored, and collected by the Plexon system (Plexon Inc.). The neuronal signals with the event markers were saved on the hard disk for further off-line spike sorting and data analysis. Before starting regular daily recording sessions in the project, we first mapped the hand area in SI by examining receptive fields of cells in the animal's hand to ensure that cells recorded would be within the hand area. In many cases during recording, the receptive field of a cell was also examined. For a given unit in the VH task, the eye movement throughout a trial was monitored and recorded for off-line analysis to exclude the effect of eye movement on the unit firing. Trials in which the animal closed its eyes were not included in analysis. The unit activity of at least 10 trials for each sample/cue (horizontal or vertical) was recorded in the task. The event-locked average spike frequency histograms of units were displayed on-line during recording. In addition to the pair of stimuli with parallel bars on their surfaces, a pair of stimuli with different texture features (one smooth and the other rough) was used in the task. SI cell recording started from the first day when the monkey performed the HH task with this pair of novel stimuli.

Data Analysis

The following events in the HH task were used for the data analysis: (1) click before the sample period, (2) hand lifted from the handrest for sample touch, (3) first touch of

the sample rod, (4) last touch of the sample rod, (5) hand back to the handrest, (6) the click at the end of the delay period, (7) hand off for choice, (8) the first touch of the object in the choice period, and (9) the pull at the choice. The first five events defined the end of baseline (unit firing during the period of 10 sec before Event 1), the sample period (between Events 3 and 4) and the beginning of the delay period (Event 5). In the VH trials, the events were (1) the alerting white light, (2) the visual icon on, (3) the visual icon off, (4) the click at the end of the delay, (5) hand off for choice, (6) the first touch of the object in the choice period, (7) the pull at the choice. The first three events defined the end of baseline (unit firing during the period of 10 sec before Event 1), the cue period (between Events 2 and 3) and the beginning of the delay period (Event 3). After off-line spike sorting by the Off-line Sorter (Plexon, Inc., Dallas, TX), the files were exported to NeuroExplorer software (Plexon, Inc., Dallas, TX). The average firing frequency locked to a certain event, such as click, first touch of the sample object, was calculated by using Matlab software (Mathworks, Natick, MA). Differences in average firing rate between each task period and the baseline were submitted to the Student's *t* test by using intertrial variance as the basis of the error term ($p < .05$). The difference of responsiveness of a unit between the group of horizontal trials and the group of vertical trials was also assessed by calculating the difference of the difference in average firing rate with respect to the baseline by the Student's *t* test ($p < .05$). The unit delay activity was defined as the averaged unit firing during the period of 10 sec (the period of 0.5–10.5 sec after the monkey returned its hand to the handrest) with respect to the baseline activity. In some cases, the unit activity during the first 5 sec or the second 5 sec of the delay period was directly tested because, in addition to the sustained delay activity throughout the whole delay period, there are two other types of delay

Figure 2. Anatomical locations of recording sites and distributions of neurons in SI cortex of two monkeys in HH (HH_Hor_Ver and HH_Rgh_Smth) and VH tasks. CS = central sulcus; IPS = intraparietal sulcus; A = anterior; P = posterior; M = medial; L = lateral. Recording grids are shown in gray color. Top: Recording sites and numbers of neurons from Monkey 2. Bottom: Recording from Monkey 1. Left: Recording sites and numbers of neurons in the HH task with horizontal and vertical objects. Middle: Sites and numbers in the HH task with smooth and rough objects. Right: Recording in the VH task.

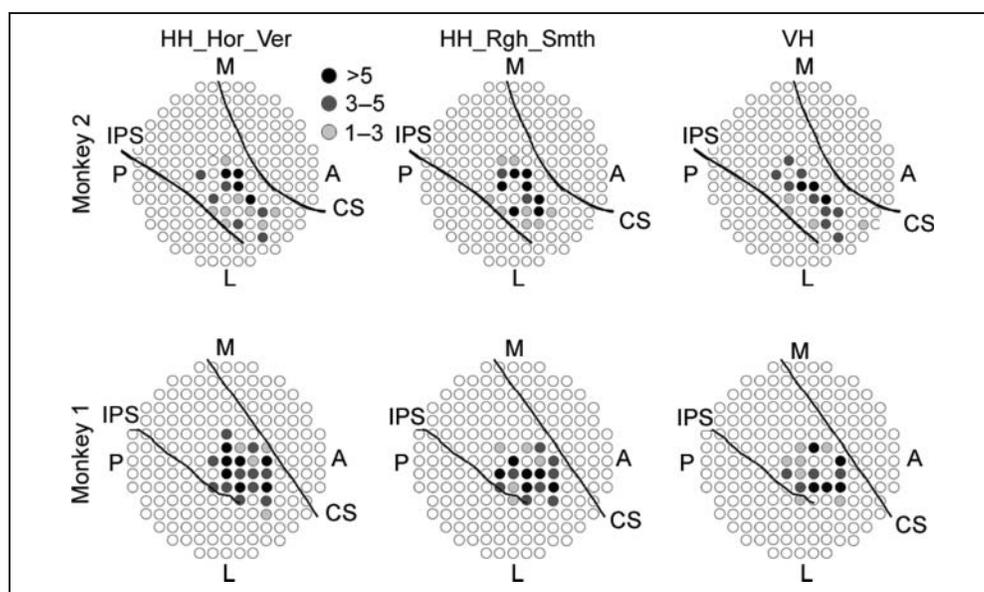


Table 1. Units in HH and VH Tasks in Untrained Monkeys and in the HH Task in Trained Monkeys

Task	Total	Click	Touch			Delay		
			E	S	Diff_touch	E	S	Diff_delay
HH_Hor_Ver (well-trained)	402	31 (7.7)	177 (44.0)	109 (27.1)	37	98 (24.3)	79 (19.6)	22
HH_Hor_Ver	232	6 (2.6)	122 (52.6)	32 (13.8)	21	44 (19.0)	82 (35.3)	15
HH_Rgh_Smth	181	5 (2.8)	97 (53.6)	33 (18.2)	16	23 (12.7)	86 (47.5)	3

Task	Total	White Light	Icon			Delay		
			E	S	Diff_icon	E	S	Diff_delay
VH	172	6 (3.5)	5 (2.9)	23 (13.4)	2	14 (8.1)	32 (18.6)	4

E = excitatory; S = suppressive; Diff_touch = differential sample activity; Diff_delay = differential delay activity; Diff_icon = differential responses to icons; HH_Hor_Ver = the HH task with horizontal and vertical rods; HH_Rgh_Smth = the HH task with smooth and rough rods. Numbers in parentheses indicate percentages of all recorded units.

activities: Cue-coupled cells whose firing rate decreases gradually from its initial high firing rate and preparatory set cells whose firing rate accelerates as a behavioral or motor response approaches (Fuster, 1997). For the response of the cell to the alerting signal (click or white light), the criteria were the same as used previously (Zhou & Fuster, 2004). Briefly, the onset of the alerting activity was defined as the time of the earliest bin among three consecutive bins (bin size = 20 msec), in all of which the unit firing was higher (or lower) than that in all but 1 of 25 bins (500 msec) before the onset of the alerting signal.

The averaged firing frequency in both baseline and delay periods of each cell (Figure 5C) was calculated by normalizing the frequency (bin size = 50 msec) of each trial to the maximal delay response (maximal deviation from zero) in each cell. The grand-averaged firing frequency was created by taking the average of all the normalized values from the cells in the corresponding bins.

RESULTS

Neuronal activities were recorded from the hand representation area of SI cortex in two monkeys performing the HH task and/or the VH task (Table 1). A total of 585 SI cells were recorded in the study. Two hundred and thirty-two cells were recorded in the HH task with horizontal and vertical objects; 181 cells were recorded in the HH task with smooth and rough objects; and 172 cells were recorded in the VH task. Among them, 61 cells were recorded in both HH (horizontal vs. vertical) and VH tasks.

Neuronal Responses in the HH Task (Horizontal vs. Vertical)

Sample Period Activity

When the monkey performed the task, 154 cells showed the touch-related activity in the sample period compared with the activity in the baseline (Table 1). Most of them

(122) showed activation (Figure 3A), and the remaining cells showed suppression (Figure 3B). Twenty-one (13.6%) of the 154 touch-related cells showed differential activities that preferred either the horizontal rod or the vertical rod (Figure 3C).

In addition, many neurons were activated or suppressed during premovement (the period from the click to the initiation of the hand movement), hand projection, and/or retraction (Figure 4A and B).

Delay Activity

During the delay period of the task, 126 cells displayed significant change in firing frequency; 44 cells (Figure 5A and C, top) showed increased delay activity, and 82 cells (Figure 5B and C, bottom) showed decreased delay activity. Fifteen (11.9%) of the 126 delay cells showed differential delay activity that depended on which sample rod the animal had touched during the sample period (Figure 6). In those 126 delay cells, 42 (33.3%) did not show premovement activity (Figure 4C); 43 (34.1%) showed premovement activity opposite to the delay activity in respect to excitation/suppression. In addition, 40 delay cells recorded in the task were also recorded in the VH task: Compared with the firing rate at baseline, 24 (60.0%) did not show any significant changes in firing rate during the delay in the VH task (Figure 7); the remaining 12 (40.0%), however, did show the delay modulation in the VH task similar to that in the HH task.

Neuronal Responses in the HH Task (Smooth vs. Rough)

One hundred eighty-one cells were recorded in the hand area of SI cortex (Table 1), 130 of which showed significant responses to the sample touch. Of these, 97 cells displayed elevated firing rates and 33 cells displayed depressed firing rates in response to the touch. Sixteen

(12.3%) of the 130 touch-related cells showed differential responses to smooth or rough objects.

One hundred nine cells changed their firing rates during the delay period compared with the baseline activity, 23 of which showed excitation and the rest showed suppression. However, three cells displayed the differential activity between smooth trials and rough trials. In addition, 40 (36.7%) of the delay cells did not show significant premovement activity; 40 (36.7%) showed premovement activity opposite to the delay activity in respect to excitation/suppression.

Neuronal Responses in the VH Cross-modal Tasks

Cue Period Activity

When the monkey performed the VH task, 172 cells were recorded (Table 1). Most of those cells (144) did not change their firing frequency when the visual icon was presented. Only 28 cells showed significant changes in firing rate in responses to the visual icon, 5 of which in-

creased the firing rate and the other 23 decreased the firing rate.

Delay Activity

Forty-six cells displayed delay activities: 14 showed excitation and the rest showed suppression. There were four cells that showed differential delay activity.

Activity Related to the Alerting Light

Six cells showed responses to the alerting light.

Comparison between Well-trained and Untrained Monkeys in HH Tasks

In this study, data were also collected as controls from other two monkeys. SI cells were recorded when they performed the HH task (DMS), in which they had been trained to actively discriminate and memorize the sample

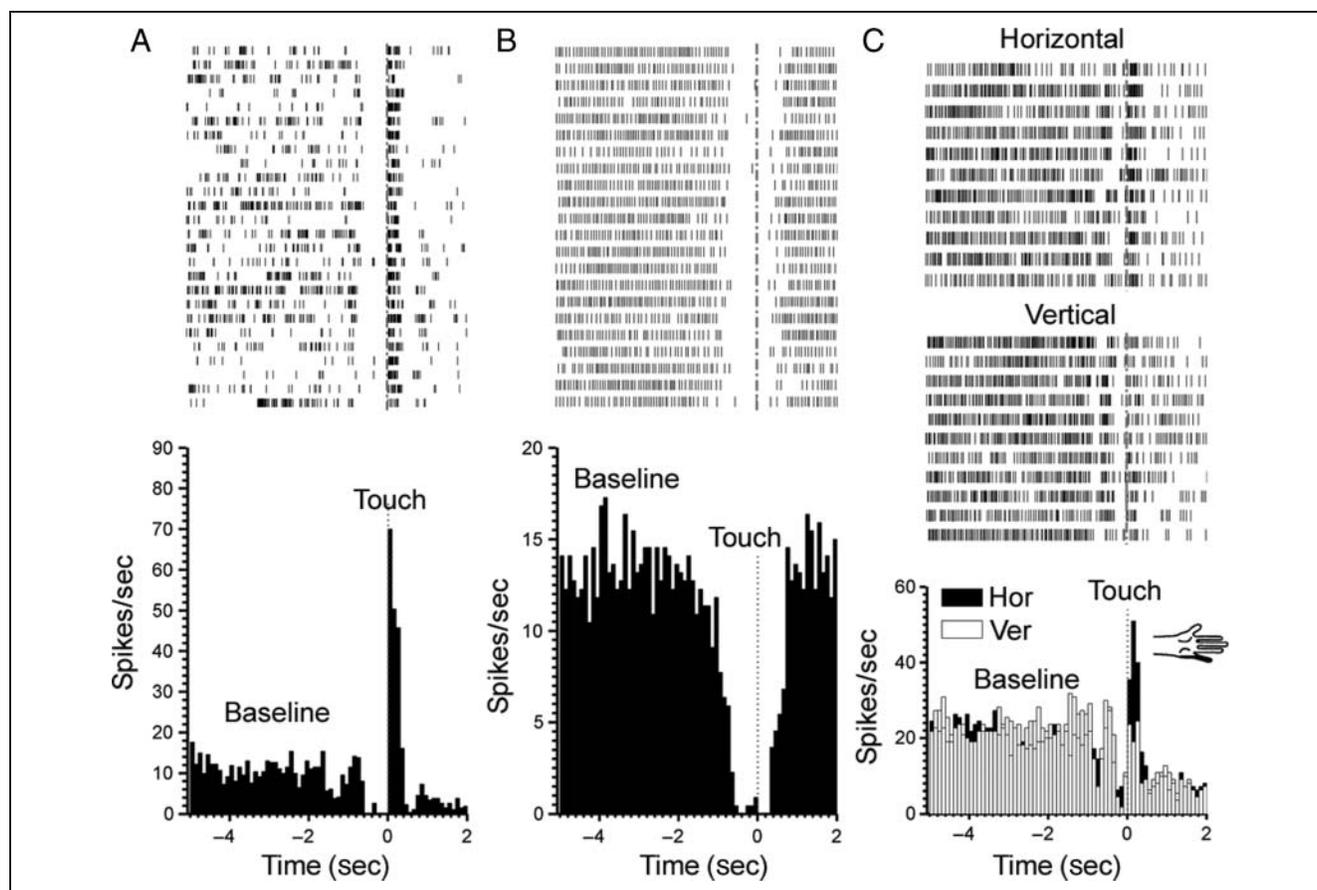


Figure 3. Rasters and perievent histograms (bin size = 0.1 sec) of touch-related neurons in the hand area of SI cortex in the HH task. The time-locking event is the first touch of the sample in A, B, and C. (A) A touch-activated neuron. The average firing rate in the sample period increases significantly from the baseline level. (B) A touch-suppressed neuron. The average firing rates in the sample period decrease significantly from the baseline level. This neuron is also suppressed during the premovement and projection period before the sample touch. (C) A differential sample touch cell. The firing rate of the cell is significantly higher in touch of the horizontal rod ($p < .01$). The receptive field of the unit is indicated in a diagram of the monkey's hand.

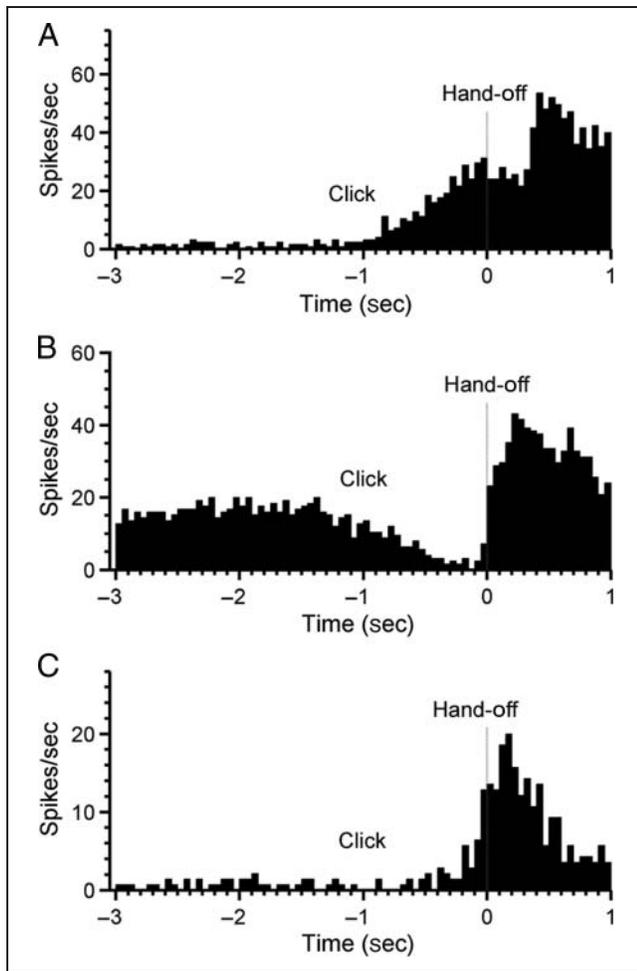


Figure 4. Average spike–frequency histograms (bin size = 50 msec) from three neurons showing activities during the time span between the click and the onset of the hand movement toward the sample object. The time-locking event is the hand-off for sample touch. (A) The neuron shows accelerating premovement activity beginning 1 sec before the hand movement (hand-off). (B) The neuron shows decreasing premovement activity. (C) The neuron does not show any significant premovement activity.

stimuli (the same rods used for the “untrained” monkeys, vertical vs. horizontal) for a choice at the end of the delay (a pull on one of the two objects). If the object the animal pulled in the choice period matched the object touched previously by the animal in the sample period, the animal was rewarded with water for this correct choice (Zhou & Fuster, 1996). The correct choice rate of those two monkeys (“well-trained”) was 75% or above. An analysis of comparison was carried out between the data from the “untrained” monkeys and the “well-trained” monkeys to investigate the impact of sample-specific working memory training on the SI unit firing. The comparison showed that there was a significant difference ($p < .05$, χ^2 test) in percentage of delay-related cells between two datum sets (Table 1; Figure 8). However, there was no such significant difference in delay differential cells between the datum sets. In addition, a significant higher percentage of click

cells were recorded in the trained animal ($p < .01$, χ^2 test). No significant difference in percentage of sample responsive cells between the datum sets was observed.

DISCUSSION

The main finding of this study is that cells in SI cortex of monkeys that have not been trained to actively memorize the specific features of haptic sample stimuli to guide subsequent haptic discrimination of the stimuli at choice in the tactile delay tasks show significant changes in single-unit firing rate in the delay compared with that at their baseline. This delay activity is of the same type observed in SI cells recorded from animals that have been trained to memorize the sample-specific features for subsequent sample-matching at choice in the tasks.

The delay activity has long been considered the cortical neural substrate of working memory, such as that recorded in pFC (Fuster, Bodner, & Kroger, 2000; Romo et al., 1999; Rainer, Asaad, & Miller, 1998; Miller et al., 1996; Funahashi, Bruce, & Goldman-Rakic, 1993; Funahashi, Chafee, & Goldman-Rakic, 1993; Fuster, 1973), posterior parietal cortex (Constantinidis & Steinmetz, 1996; Koch & Fuster, 1989), inferotemporal cortex (Fuster & Jervey, 1982), and premotor cortex (Romo, Hernandez, & Zainos, 2004). Our present results, however, indicate that this cortical delay activity is not necessarily observed, as was generally thought, only in the situation when the animal has to actively maintain stimulus-specific information in the short-term for subsequent execution of a task (making a correct choice between stimuli), which the animal has been well trained to perform. Existence of such delay cells in our “untrained” animals therefore suggests that, instead of representing active memory of specific features of a sample stimulus, the delay activity in SI observed in this study may represent some constant features of a stimulus (sensory memory of physical properties of the stimulus, such as size, shape, etc.) or the procedure of task performance.

Cells showing selective delay activity in the HH task (horizontal vs. vertical) of this study are most likely involved in retention of information about the surface features of the tactile sample stimuli. Behavioral actions may not contribute significantly to the selectivity. Our assumption is based on the following observations: (1) The “untrained” monkeys in the study showed significant behavioral bias toward one of the object positions (left or right) at choice, but this bias might not result in the delay differential activity, because the object position (left or right) was randomized. The chance for presentation of each of those two objects (horizontal or vertical) on one side is still around 50%. (2) Through our observation, the animal did not show any special postures during the delay after they touched the sample object. The selective activity of the SI cells suggest that the neural network in SI cortex may retain sensory information for at least a short term, even in the situation where this retained

information may not be used by the animal for performing the task.

The relatively low number of such selective delay cells may be because of the limited haptic sample stimuli used in the task (only one pair of rods tested in the study for each cell), and those stimuli might not be the optimal ones to most of the cells. The low number may also be because of the active touch that activates various different receptors (from joints, muscles, etc.) receiving information about common features of the sample object (such as the shape and size of the rod) besides information about orientations of parallel bars on the surface of the rod. This may therefore reduce the impact of the difference in surface features between the rods on the delay activity.

When we discuss the nondifferential delay activity shown in this study, other factors, such as arousal or preparation for motor response, cannot be simply ruled out. Nevertheless, we can assume that at least some of these nondifferential cells may participate in the retention of common features of the tactile objects (e.g., shape, size). Our assumption is based on comparisons of delay activities between the cross-modal task and the unimodal task and comparisons between the delay activity and the pre-movement activity.

In both the HH and VH tasks, requirements of attention during the delay and motor response were basically

the same. The majority of the delay cells tested in both tasks, however, showed significant delay activity in the HH task but not in the VH task. Therefore, this significant delay activity in our study was very likely associated with the tactile sample touch but not with changes in arousal level or motor preparation. Some other studies also showed that most SI neurons were biased to only one sensory modality (Liu, Denton, & Nelson, 2007).

If the delay activity of a cell was because of the preparation for movement, similar activity should also be expected during the pre-movement period before the animal's hand was lifted from the handrest for sample touch. The majority of the delay cells, however, did not show such activity during the pre-movement period.

We assume that the persistent neuronal firing changes in the delay in this study are likely to be the neural substrate of task-related events: the activation of the memory network that is built through repetitive exposure to the stimulus in performance of the task before the unit recording. This assumption was supported by the result of differential delay cells recorded in the monkeys. By comparing results of recordings in SI in use of the pair of objects with different texture (rough vs. smooth) on their surfaces, with recordings in the same area of SI using the pair of objects with horizontal or vertical ridges, we found that differential cells appeared essentially only when the

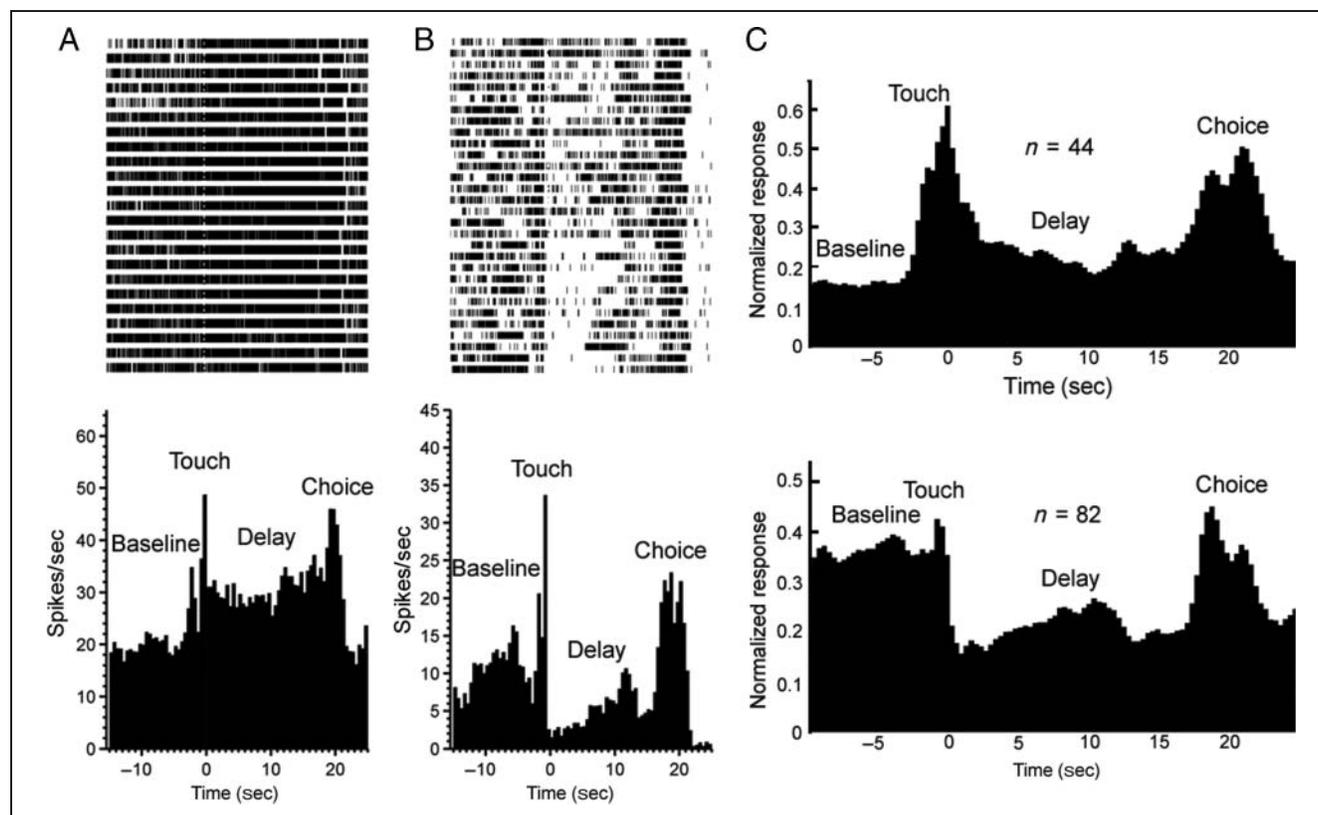
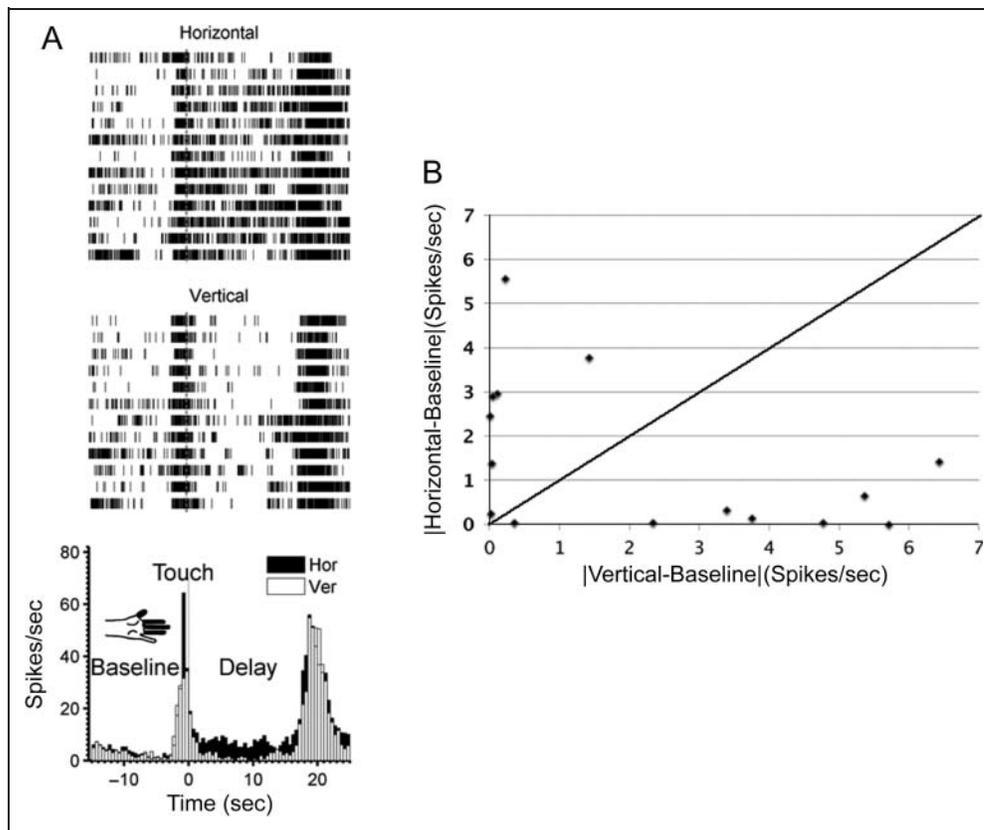


Figure 5. Rasters and peri-event histograms (bin size = 0.5 sec) of the delay neuronal activity in the HH task. The time-locking event is the onset of the delay period (hand back to the handrest after the sample touch). (A) A neuron showing significant activation during the delay ($p < .01$). (B) A neuron showing significant suppression during the delay ($p < .01$). (C) Grand-averaged firing frequency of 44 delay-activated cells (top) and 82 delay-suppressed cells (bottom).

Figure 6. Rasters and perievent histograms (bin size = 0.5 sec) of the delay-differential activity in the HH task. (A) A neuron showing differential delay activity. The firing rate of the cell is significantly higher in horizontal trials ($p < .01$). The cell also shows the significant differential activity in the sample period ($p < .01$). The receptive field of the unit is indicated. (B) Differences in firing rate of 15 differential cells between baseline and delay period. Each dot represents one neuron. x axis: Absolute difference in averaged firing rate between the delay and the baseline in vertical trials. y axis: Absolute difference in averaged firing rate between the delay and the baseline in horizontal trials. Note that there are seven cells showing horizontal selectivity, and eight cells showing vertical selectivity.



sample used in the task was from the latter pair of objects. That is, the differential delay cells appeared only after the monkey had been exposed to the objects (horizontal vs. vertical edges) repeatedly for a certain period (months). There was, however, no significant difference in sample

differential activity between trials of those two pairs of objects. Combining all the results from the HH task with two pairs of objects, it suggests that behavioral training (repetitive exposure to the stimulus) has a significant impact on the delay activity. This repetitive exposure (training)

Figure 7. Average frequency histograms (bin size = 0.5 sec) from a unit during performance of the HH task (A; trials [22] with both horizontal and vertical objects) and the VH task (B; trials [22] with both horizontal and vertical icons). The time-locking event for the histogram in A is the return of the hand to the handrest; the time-locking event for the histogram in B is the off-set of the visual stimulus (icon). In the HH task, the cell is suppressed during the projection (time from hand-leaving to the first touch of objects) and activated during the sample period. It also exhibits significant decreased firing rate during the delay. In the VH task, the cell shows no clear change in firing rate during both the visual cue and the delay periods.

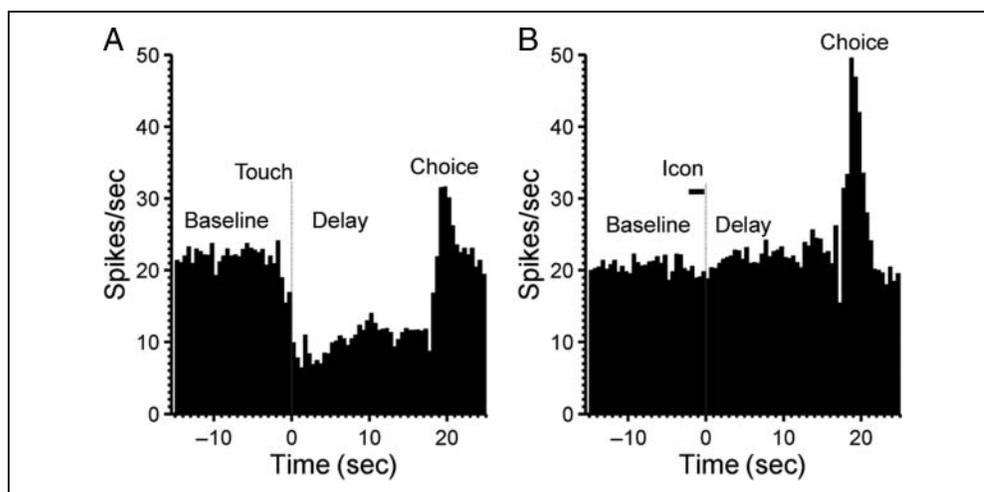
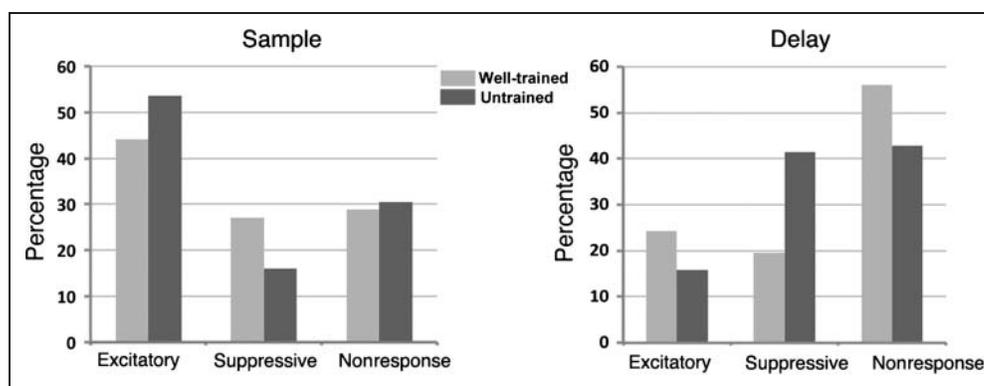


Figure 8. Percentage histograms between “well-trained” and “untrained” monkeys in sample and delay periods in the HH task. Each bar represents the percentage of units in one category (e.g., excitatory) of all recorded units in the “well-trained” or “untrained” monkeys. Note that in the delay of the suppressive cells is significantly higher ($p < .05$, χ^2 test) than that of the excitatory cells in the “untrained” monkeys, but not in the “well-trained” monkeys. This phenomenon between the “well-trained” and “untrained” monkeys, however, does not exist in the sample period.



may thus play an important role in building the long-term memory network, the neural apparatus that may be used by both long-term and working memory of the stimulus.

Researchers have proposed that working memory seems to rely largely on the temporary activation of subsets of long-term memory networks (Lewis-Peacock & Postle, 2008; Zhou, Ardestani, & Fuster, 2007; Curtis & D’Esposito, 2003; Fuster, 1995, 2003; Ruchkin, Grafman, Cameron, & Berndt, 2003; Quintana & Fuster, 1999; Ericsson & Kintsch, 1995; Crowder, 1993; Cowan, 1988). The present result shows that the activity of cortical cells during the delay period when the animal does not need to actively memorize the stimulus for a subsequent action is similar to that of cells during the delay period engaged in active (working) memory. The similarity in delay activity between the two different situations thus suggests that the delay activity in those situations may be generated from neural networks that are composed of similar components. That is, working memory may use already existing long-term memory apparatus by activating it temporarily when the same stimulus has to be actively memorized for a short-term for action.

In a recent study by Harris, Miniussi, Harris, & Diamond (2002), researchers found that performance of a tactile working memory task was significantly disrupted when a TMS pulse was delivered to SI contralateral to the stimulated hand early in the delay at 300 or 600 msec. This effect was not observed when a TMS pulse was delivered at 900 msec or later. They suggested that the neuronal activity maintained in SI constituted the neural substrate of the working memory trace itself and was essential to optimal tactile working memory performance. We therefore believe that it is a reasonable assumption that because neural processes for performance of a tactile working memory task require accurate information about the tactile stimulus, the original sensory memory trace of

the stimulus in the somatosensory cortex to be held for a certain period is essential to those processes and, consequently, to performance of the tasks. Potentially, the delay activity (assumed to be the internal representation of memory trace of the stimulus) could serve to prime or adjust the sensitivity of networks in SI cortex in response to haptic input or in relation to the timing of anticipated haptic inputs. After cortical areas at higher levels have started the process for executing the task by receiving the ascending sensory information, the original sensory information may still be maintained in parallel in SI but may not be as critical as before to the task performance. In other words, as long as it has been established through repetitive stimulation with a tactile object as suggested in this study, the memory neural network in SI will be activated by the same tactile stimulus no matter whether this sensory information will be used later or not.

In this study, we did not attempt to train the “untrained” monkeys to actively retain information of the sample stimulus in the tasks, as it would be technically difficult to record a few hundred more cells again in the same SI area for the control data after a long period of pause in recording (normally over a year for training the monkey to learn the DMS task). We therefore recorded “trained” data from another pair of monkeys. By comparison between “untrained” and “trained” data in this study, we find that the percentage of delay-activated cells from the “untrained” monkeys is significantly lower than that from the “well-trained” monkeys. This suggests that training of the animal in a working memory task may be a significant factor in building the tactile working memory network in SI cortex through cortical plasticity. That is, training in working memory may take already-existing long-term memory apparatus as a basis and modify it to build networks that operate working memory more efficiently. This is consistent with other studies (Pasupathy & Miller, 2005; Messenger, Squire, Zola, & Albright, 2001). Interestingly,

but not surprisingly, because SI cortex is the modality-specific SI area, the percentage of cells that responded to the sample touch in untrained monkeys is similar to the percentage in “well-trained” monkeys. The result showing the similarity in the percentage of cells for sample touch but a difference in the percentage of cells for delay between “trained” and “untrained” animals may also support our above assumption that the training enhances the activity of SI networks for working memory. This agrees with previous reports (Hempel et al., 2004; Desimone, 1996) suggesting that training may lead to a change in predominance of cortical mechanisms, such as enhancement mechanism and suppressive mechanism, which mediate the training effects of working memory. In our studies, the training appeared to strengthen the enhancement mechanism for active working memory (more delay activated cells but fewer delay suppressed cells found in well-trained monkeys).

Evidence has shown that attention affects the neuronal activity of somatosensory cortex including SI and SII (Nelson, Staines, Graham, & McIlroy, 2004; Meftah el, Shenasa, & Chapman, 2002; Burton & Sinclair, 2000; Johansen-Berg, Christensen, Woolrich, & Matthews, 2000; Steinmetz et al., 2000; Burton et al., 1999; Hsiao, O’Shaughnessy, & Johnson, 1993). Therefore, besides the effect of training, an alternative interpretation of a higher percentage of memory cells in well-trained monkeys is that higher attention level enhances the delay firing. Nevertheless, no difference was observed in the percentage of cells activated in the sample period between trained and untrained monkeys, suggesting that changes in attention level may not be a major factor, although its effect may still exist. In addition, more click cells and a higher percentage of visual tactile cross-modal active cells observed in well-trained monkeys (Zhou & Fuster, 1997, 2004) may also suggest an effect of training on the response of SI neurons to task-related events.

In conclusion, the results of our present study show to our knowledge for the first time the delay activity in a population of SI neurons in monkeys who are not required to discriminate and actively memorize the sample stimulus in tactile delay tasks. This suggests that there exist neural networks in SI (the primary sensory cortex) for retaining information about the tactile stimulus, even in the situation where this retained information may not be used later by the animal for certain behavioral actions. The similarity in delay firing of SI cells recorded in two different situations in this study suggests that working memory may use already-existing memory apparatus (the long-term memory networks) by activating it in the short term. Our data also suggest that, through training, neurons in SI cortex may increase their involvement in memory of a stimulus.

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