

Changes of Afferent Transmission to the SI Cortex by Transient Co-Stimulation of Receptive Field Center and Outside in Anesthetized Rats

Yu-Mi Yang, Sabina Lim¹, Chung-Kil Won², and Hyung-Cheul Shin

Department of Physiology, College of Medicine, Hallym University, Chunchon 200–702; ¹Department of Acupuncture, College of Oriental Medicine, Kyunghee University, Seoul 130–701; ²Department of Pharmacology, College of Medicine, Korea University, Seoul 136–701, Korea

We have characterized the aftereffects of impulse activities on the transmission of afferent sensory to the primary somatosensory (SI) cortex of the anesthetized rats (n=22). Following conditioning stimulation (CS, 10 sec, either 5 Hz or 200 Hz) to the receptive field (RF), quantitative determination of the changes of afferent sensory transmission was done by generating post-stimulus time histogram of unit response to the testing stimulation (TS, at 0.5 Hz) to the RF center (RFC) for 60 min. In one group of experiments, CS was delivered to the RF center (RFC). In another group of experiments, CSs were simultaneously given to both RFC and RF outside (RFO, either forepaw or hindpaw). CS of 5 Hz to RFC exerted irreversible facilitation of sensory transmissions evoked by TS. Simultaneous CSs of 5 Hz to RFC and hindpaw RFO exerted reversible suppression of afferent transmission. However, CSs of 5 Hz to RFC and forepaw RFO did not significantly altered afferent sensory transmission to SI cortex neurons. CS of 200 Hz to RFC exerted irreversible suppression of sensory transmissions up to 60 min of experimental period. Simultaneous CSs of 200 Hz to RFC and RFO did not significantly altered afferent sensory transmission to SI cortex neurons. The profiles of CS-induced modulation of afferent sensory transmission were significantly different between two CS conditions. Thus, this study suggests that activity-dependent modulation of afferent transmission from a RF center to the SI cortex may be significantly altered when remote body part was simultaneously activated.

Key Words: Cortex, Somatosensory, Transmission, Impulse, Receptal field, Plastics, Frequency, Stimulation

INTRODUCTION

Previously, we have reported that there is a significant change of the excitability of afferent peripheral nerve fibers, which is strongly dependent on the previous impulse activity (Shin et al, 1995; Won et al, 1996). The changes of activity-dependent excitability in presynaptic axonal tree have been known to act as spatiotemporal filter of impulse trains coming from axon trunk, governing subsequent activation of

postsynaptic neurons (Raymond, 1979). This suggests that activity-dependent excitability changes occurring in the primary afferent fibers may also trigger a series of modulations of afferent sensory transmission ascending to the primary somatosensory (SI) cortex.

Recently, we have shown that sensory transmission, evoked at 0.5 Hz, to SI cortex of anesthetized rats is subject to strong and long lasting modulations after transient (10 sec) stimulation of the receptive field (RF) center (Yang et al, 1998). This modulation has activity-dependent characteristics such that low frequency (5 Hz) stimulation induced facilitation but high frequency (200 Hz) exerted suppression of sensory transmissions to the SI cortex. This suggested that

Corresponding to: Hyung-Cheul Shin, Department of Physiology, College of Medicine, Hallym University, Chunchon 200-702, Korea. (Tel) 82-33-240-1645, (Fax) 82-33-255-1640, (E-mail) hcshin@sun.hallym.ac.kr

cutaneous sensory processing in touch behaviors might involve continuous changes of the excitability of SI cortex neurons, and that the sensory transmission to the SI cortex is an intrinsically active process that is dependent on short-term prior somatosensory experience.

Generally, touch behaviors can be classified into two types; touch between subject's body and external object(s) and touch between subject's body parts (Blakemore et al, 1998, 1999; Bolanowski et al, 1999). Co-activation of different body parts are predominant during normal touch behaviors. However, no study has been done to test the presence of the activity-dependent modulations of afferent sensory transmission between remote body parts. In this study, profiles of the activity-dependent modulations of afferent transmissions to the SI cortex were characterized in anesthetized rats following transient co-activation of spatially separated body parts.

METHODS

Preparation of animal

Sprague-Dawley rats (200~300 g, n=34) were anesthetized with urethane (1 g kg^{-1} body weight, i.p.). Animals were mounted in a stereotaxic frame and a relatively large (2~3 mm diameter) craniotomy was performed over the SI cortex using the bregma as the initial point of reference. Four-channel multi-array recording electrode (tungsten microwire, A-M systems, USA, $75 \mu\text{m}$ diameter, teflon coated) was driven into layer IV of the forepaw area of SI cortex (rostro-caudal, 1.5 mm rostral- 0.5 mm caudal from bregma; mediolaterally, 3.5~4.5 mm lateral from midline; 0.5~1.2 mm deep from brain surface) with a micro-drive. More detailed methods for surgery and the recording of single neurons were described elsewhere (Shin et al, 1993, 1994, 1995, 1997; Jung & Shin, 2000).

Stimulation and recording

Cutaneous receptive fields (RF, mainly from forepaw) were identified by listening to the recorded signal through an audio speaker while using a fine tipped probe to tap whiskers lightly until the zone responding was defined most intensely and reliably. A bipolar concentric stimulating electrode ($50 \mu\text{m}$ tip, $100 \mu\text{m}$ o.d., 0.5 mm tip separation, David Kopf,

Tujunga, CA) was inserted under the center of the RF and the electrode was fixed firmly to prevent any movement. Responses of individual cells to testing stimulation (TS) of indwelling electrodes (single 0.1 ms pulses, 0.5 Hz, $50\sim 500 \mu\text{A}$) were characterized by generation of post-stimulus time histograms (PSTHs). Conditioning stimulations (CS) to the RFC were delivered through the same electrode for 10 sec, but with different frequencies (low frequency: 5 Hz, high frequency: 200 Hz). Conditioning stimulations (CS, either 5 Hz or 200 Hz, 10 sec, $50\sim 500 \mu\text{A}$) were also delivered simultaneously to both RFC center (RFC) and RF outside (RFO, either forepaw or hindpaw).

Statistical analysis of data

PSTHs were constructed for quantitative measurements of magnitude of short latency evoked unit responses (EURs: 5.8 ± 0.3 to 10.4 ± 0.3 ms post-stimulus). The firing rates (spikes s⁻¹) were determined during the epochs defined as: (No. of spikes/no of sweeps) X (1000/No. of ms in epoch). CS-induced modulations of afferent sensory transmission during 60 min of post-CS period were expressed in terms of the percentage change from the averaged EUR value calculated during the pre-CS control period (15 min). The method of the analysis of histograms was the same as that reported in our previous papers (Shin et al, 1994, 1995). Statistical analysis was undertaken with the student's t-test. All results are presented as means \pm s.e.m.

RESULTS

Fig. 1 shows the aftereffects of CS (5 Hz and 200 Hz) to either RFC alone or both RFC and RFO (either forepaw or hindpaw) on the afferent somatosensory transmission in four SI cortical neurons. The stability of the afferent sensory transmission was ensured by monitoring EURs of three histograms (200 sec duration for each histogram) generated during the 10 min control period before 10 sec of CS application (Fig. 1. PSTHs A, B, C, D, CONs). CS of 5 Hz to RFC alone resulted in irreversible facilitation of TS-activated EUR of a SI cortex neuron (Fig. 1. PSTHs in A, after 20 min: +23.60%, after 60 min: +48.30%). However, simultaneous CSs of 5 Hz to RFC (forepaw digit 5) and RFO (hindpaw digit 2) exerted reversible suppression of afferent transmission to a SI neuron

(Fig. 1. PSTH B, after 20 min: -15.95% , after 60 min: -6.21%).

CS of 200 Hz to RFC alone resulted in irreversible suppression of TS-induced EUR of a SI cortex neuron (Fig. 1. PSTHs in C, after 20 min: -26.10% , after 60 min: -46.10%). However, simultaneous CSs of 200 Hz to RFC (forepaw digit 4) and RFO (hindpaw digit 3), did not exert any change on the afferent transmission to a SI neuron (Fig. 1. PSTHs in D, after 20 min: $+0.04\%$, after 60 min: -8.90%). Fig. 1E and

1F show temporal changes of afferent sensory transmissions to above four SI neurons before and after CS.

Fig. 2 and Table 1 show the overall averaged after effects of CS (5 Hz and 200 Hz) to either RFC alone or both RFC and RFO (either forepaw or hindpaw) on the afferent somatosensory transmission in SI cortex neurons ($n=164$). Control experiments ($n=9$) without any CS to the periphery did not change the afferent sensory transmission in the SI cortex. CS of 5 Hz to RFC exerted reversible facilitation of sensory

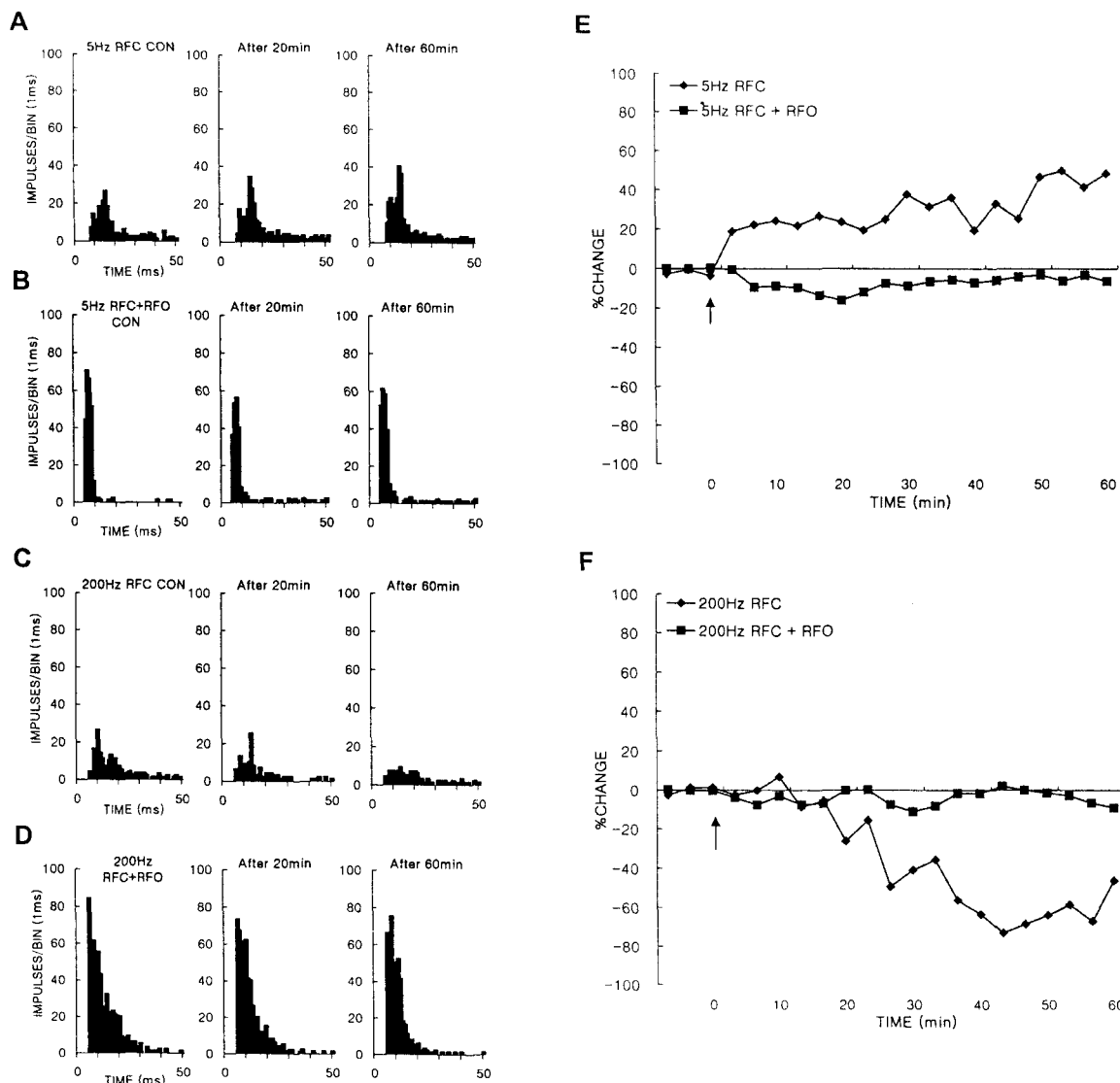


Fig. 1. CS-induced aftereffects on the SI cortical unit responses evoked by TS. PSTHs shown in A to D represent neurons' responsiveness to the TS stimulation in different conditions. In each panel, a neuron's activities were illustrated for three durations, control period (CON), 20 and 60 min after an experimental conditioning. A. with CS to RFC at 5 Hz, B. with CSs to both RFC and RFO at 5 Hz, C. with CS to RFC at 200 Hz, D. with CSs to both RFC and RFO at 200 Hz, E.&F. Percentage temporal changes of sensory response of the SI cortex neurons in A to D. Arrow: time of CS.

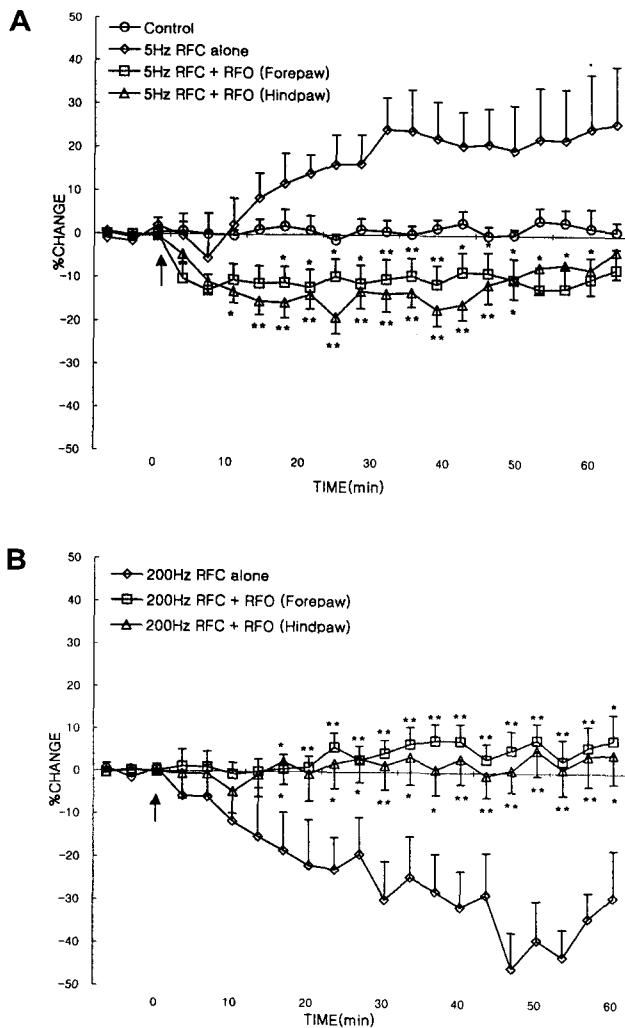


Fig. 2. Averaged temporal changes of afferent sensory transmission through SI cortex neurons following different CSs. A. Afferent transmission without any CS (Control), after RFC stimulation alone at 5 Hz (5 Hz RFC alone), after combined CSs (RFC+RFO) at 5 Hz but with different RFO site. B. after RFC stimulation alone at 200 Hz (200 Hz RFC alone), following costimulation of CSs (RFC+RFO) at 200 Hz but with different RFO site. ** $P < 0.01$, * $P < 0.05$, compared with RFC alone.

transmissions evoked by TS (Control $0.88 \pm 2.6\%$, $n=9$; 5 Hz: $+24.34 \pm 7.4\%$, $n=7$, $p < 0.01$, after 30 min of CS, 5 Hz RFC alone in Fig. 2A). Simultaneous CSs of 5 Hz to RFC and hindpaw RFO exerted reversible suppression (13~18%, 7~23 min and 33~40 min post CSs, $p < 0.05$) of afferent transmission to SI cortex neurons ($n=40$). However, simultaneous CS of 5 Hz to RFC and forepaw RFO did not significantly altered afferent sensory transmission to SI cortex neurons ($n=49$, $p < 0.05$, Fig. 2A).

Significantly different profiles of CS-induced modulation of afferent sensory transmission were obvious between RFC alone and RFC+RFO in Fig. 2A, regardless of the location of the RFOs.

CS of 200 Hz to RFC exerted irreversible suppression of sensory transmissions evoked by TS ($-29.79 \pm 9.0\%$, $n=11$, $p < 0.01$, after 30 min of CS, Fig. 2B) up to 60 min of experimental period. Simultaneous CSs of 200 Hz to RFC and RFO did not significantly altered afferent sensory transmission to SI cortex neurons (forepaw RFO: $n=26$, hindpaw RFO: $n=22$, $p < 0.05$, Fig. 2B). CS-induced modulation of afferent sensory transmission were also significantly different between two CS conditions, RFC alone and RFC+RFO in Fig. 2B, regardless of the location of the RFOs.

DISCUSSION

In this study, afferent modulation following transient co-activation of two separated body parts was significantly suppressed, compared to the control value obtained in the absence of any CS, only when RFC and RFO were activated at low frequency, especially if the RFO was located at hindpaw. This activity-dependent modulation of afferent transmission following simultaneous CSs to both RFC and RFO may be related to the somatosensory evoked potential (Kakigi et al, 1985) and magnetic field studies (Kakigi et al, 1996; Naka et al, 1998) reporting the presence of interference effects between remote body parts. In fact, sensory modulations between remote body parts have been routinely used in acupuncture and the changes of SEP following electro-acupuncture have also been reported (Kawashima, 1991; Kumar et al, 1995).

The delayed appearance of the changes of afferent transmission following simultaneous stimulation to both RFC and RFO also suggests a possibility of multisynaptic convergence of inputs ascending from separate afferent pathways. It is well known that a SI cortex neuron has a discrete RF on the periphery. But, this does not mean that the neuron has no direct input from remote body parts. In fact, several studies have demonstrated extensive convergence of dual afferents to a neuron from both forelimb and hindlimb (Kang et al, 1985; Roberts & Wells, 1990). Thus, the delayed appearance of the afferent modulation following simultaneous activation of the RFC and RFO (hindpaw) could be mediated by unmasking of pre-existing

Table 1. Mean % change of afferent transmission after different CSs

Group	Stimulation site	<i>n</i>	Time	% Change	<i>p</i> value
Control	RFC	9	30 min	0.88 ± 1.14	
			60 min	1.04 ± 0.81	
	RFC	7	30 min	24.34 ± 7.36	*
			60 min	25.97 ± 13.32	†
Low frequency (5 Hz)	RFC + RFO (Forepaw)	49	30 min	-10.15 ± 4.55	‡
			60 min	-7.59 ± 4.77	
	RFC + RFO (Hindpaw)	40	30 min	-13.56 ± 4.05	‡
			60 min	-3.50 ± 6.15	
	RFC	11	30 min	-29.79 ± 9.00	*
			60 min	-28.97 ± 11.00	*
High frequency (200 Hz)	RFC + RFO (Forepaw)	26	30 min	4.50 ± 3.13	§
			60 min	7.86 ± 6.22	
	RFC + RFO (Hindpaw)	22	30 min	1.58 ± 5.68	§
			60 min	4.49 ± 6.89	

* $P < 0.01$, † $P < 0.05$ compared with control, ‡ $P < 0.01$ compared with 5 Hz RFC alone, § $P < 0.01$, || $P < 0.05$ compared with 200 Hz RFC alone.

afferent inputs from RFO (Nicoletis et al, 1993).

It has been reported that a self-produced tactile stimulus is perceived as less ticklish than the same stimulus generated externally. fMRI study also indicated that more activity was found in somatosensory cortex when the stimulus was externally produced (Blackmore et al, 1998). Although this fMRI study did not examine the activity-dependent modulation of afferent sensory modulation, it is similar to the current study in terms of the classification of the peripheral RF stimulations, if we disregard the state difference of the animal. A self-produced low frequency tactile behaviour involves simultaneous activation of both RFC and RFO as in this study, while passive touch behaviour is possible by RFC stimulation alone. The weaker perception of the self-produced tactile stimulus may be related to the movement-induced general suppression (Shin & Chapin, 1990) of afferent sensory transmission and the biasing source from the descending motor command (Shin & Chapin, 1989). But that may also be partly produced by the co-activation of the RFC and RFO as observed in the current study.

The results of this study demonstrated that activity-dependent modulation of afferent sensory transmission arising from the forepaw RFC to the SI cortex was substantially altered when the RFC and the RFO were simultaneously stimulated for very short period of time. Simultaneous CS stimulation of the RFO with

the RFC generally acted to abolish the afferent sensory transmission induced following RFC stimulation alone. This suggests that the magnitude of the activity-dependent afferent sensory modulation could be small in normal touch behaviour where several parts of the body are simultaneously stimulated and that processing of sensory input ascending from a discretely localized peripheral RF, without simultaneous activation of other body parts, may be subject to greater modulatory influences.

In this study, afferent modulations following co-stimulation of the different body parts were also significantly different between low and high frequency stimulations, regardless of RFO location. This and our previous (Yang et al, 1998) studies strongly suggest that the informations about previous impulse history in the SI cortex may have been memorized and they exert significant modulations on the subsequent sensory processing in the SI cortex of rats. This may be termed either as the impulse history (activity)-dependent sensory processing or as the short-term memory trace of the afferent somatosensory processing in the SI cortex. The observed activity-dependence may be responsible for the generation of the previously reported use-dependent or experience-dependent synaptic changes of the SI cortex neurons (Li et al, 1996; Coq & Xerri C, 1998). The results of this study also suggest that cutaneous sensory processing in normal touch behaviors may involve continuous changes

of the excitability of SI cortical neurons and the sensory transmission to the SI cortex is intrinsically active processes that is dependent on short or long-time prior somatosensory experiences.

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