Changes in Properties of Substantia Gelatinosa Neurons after Surgical Incision in the Rat

In Vivo Patch-clamp Analysis

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Background: Noxious information through Aδ and C afferent fibers is transmitted to substantia gelatinosa, a process that plays an important role in plastic changes of nociceptive processing in pathophysiological conditions. In this study, changes in properties of substantia gelatinosa neurons and their sensitivity to systemic administration of lidocaine after surgical incision were investigated using the in vivo patch-clamp technique.

Methods: Under urethane anesthesia, in the current clamp mode, spontaneous activities and responses of substantia gelatinosa neurons to nonnoxious air-puff stimuli and noxious pinch stimuli were recorded before and after 1-cm-long incisions had been made in hairy skin of the hindquarters of rats. Systemic administration of lidocaine (2 mg/kg) was applied at 30 min after the incision.

Results: Stable recordings for 30 min or more after the incision were obtained from 18 substantia gelatinosa neurons that were classified as multireceptive (n = 8), nociceptive (n = 5), and subthreshold (n = 5) neurons. Action potential firing disappeared immediately after completion of the wound closure in most multireceptive and nociceptive neurons, and sustained spontaneous action potential firing was observed in 23% of these substantia gelatinosa neurons. Responsiveness of these substantia gelatinosa neurons, but not that of subthreshold neurons, increased after the incision. Systemic administration of lidocaine reversed spontaneous firings of action potentials of the substantia gelatinosa neurons and reversed the increased responsiveness of the neurons.

Conclusions: The results suggest that (1) changes in properties of substantia gelatinosa neurons after incision vary depending on the classification of substantia gelatinosa neurons and (2) systemic administration of lidocaine can reverse increased responsiveness of substantia gelatinosa neurons after incision.

Analgesia for postoperative pain or surgical injury-induced pain not only may lead to increased patient comfort, but also may reduce morbidity after surgery. However, optimal postoperative pain therapy has still not been established, because postoperative pain management strategies are based mainly on results of studies performed using other types of persistent pain models and because it has been shown that neurochemical and electrophysiological mechanisms of different pain states, such as postoperative, inflammatory, and cancer pain, differ. An incision made in glabrous and hairy skin of rodents causes persistent, reduced withdrawal thresholds to mechanical stimuli (mechanical hyperalgesia and allodynia), and time courses of primary hyperalgesia and secondary hyperalgesia in these animal models are similar to those in several clinical studies.

Based on results of behavioral and electrophysiological studies, mechanisms of enhanced sensitivity to pain (allodynia and hyperalgesia) in incision models are thought to differ from those in other types of tissue injury-induced pain in which tissue injury is caused by application of chemical irritants such as capsaicin, mustard oil, and bradykinin. First, preemptive analgesic treatments did not prevent development of mechanical hyperalgesia after incision. Second, N-methyl-D-aspartate receptor-independent factors mainly influence the increased responsiveness of dorsal horn neurons after incision. Third, in dorsal horn neurons located in deep laminae (laminae IV–V), wide-dynamic-range neurons are responsible for the hyperexcitability in response to nonnoxious as well as noxious stimuli after incision, whereas high-threshold neurons are not involved in the hyperexcitability, especially that in response to nonnoxious stimulation, after a surgical incision has been made.

Noxious information is transmitted through fine myelinated Aδ and unmyelinated C afferents from the periphery to the superficial dorsal horn, especially to the substantia gelatinosa (SG; lamina II of Rexed). This sensory information is modified and integrated in the SG and consequently regulates the outputs of projection neurons located in lamina I and laminae IV–V. SG neurons exhibit a variety of excitatory and inhibitory synaptic responses that range in duration from milliseconds to minutes. Recent studies have indicated that the synaptic connectivity and receptor expression in the SG can be altered easily after peripheral tissue damage and nerve damage. In addition, the descending pain inhibitory influence on SG neurons also is modified under certain pathologic conditions. However, changes in properties of SG neurons in a postoperative pain state have not been elucidated.

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The aim of the present study was to determine the changes in synaptic transmission of SG neurons after incision using the recently established technique of in vivo patch-clamp recordings. To obtain pharmacological insights into the mechanisms of postoperative pain, we also examined the effects of systemic administration of lidocaine on increased excitability of SG neurons after incision.

Materials and Methods

Animal Preparation

All of the protocols of this study were approved by the Animal Care and Use Committee of Sapporo Medical University School of Medicine, Sapporo, Japan. Efforts were made to minimize the number of animals used, and the experiments followed the ethical guidelines of the International Association for the Study of Pain.22

The experimental method was described in detail previously.21,23 Briefly, male Sprague-Dawley rats (6–7 weeks of age; 200–280 g) were anesthetized with urethane (1.2–1.5 g/kg intraperitoneal), and the left carotid artery and external jugular vein were cannulated to allow for blood pressure monitoring and for drug administration, respectively. After a tracheotomy, each animal was mechanically ventilated. The lumbar spinal cord was exposed at the level from L3–L5 by a thoracolumbar laminectomy at the level from Th13 to L2, and then the rat was placed in a stereotaxic apparatus (Model ST-7; Narishige, Tokyo, Japan). After opening the dura, a dorsal root that enters the spinal cord above the level of the spinal cord was irrigated with 95% O2–5% CO2-containing saline solution (15 ml/min; NaCl, 117; KCl, 5; CaCl2, 0.5; MgCl2, 2; EGTA, 5; ATP-Mg, 5; HEPES-KOH, 5 mM. The electrode was filled with a solution having the following composition: potassium gluconate, 135; KCl, 5; CaCl2, 0.5; MgCl2, 2; EGTA, 5; ATP-Mg, 5; HEPES-KOH, 5 mM. The electrode with a resistance of 8 to 12 MΩ was advanced at an angle of 30 to 45° into the SG through the window using a micromanipulator (Model MHW-4; Narishige, Tokyo, Japan; fig. 1A). After making a gigaohm seal (resistance of at least 5 GΩ), the membrane patch was ruptured by a brief period of more negative pressure, thus resulting in whole cell configuration. Recordings were made using a patch-clamp amplifier (Axopatch 200B; Axon Instruments, Union City, CA). In the voltage-clamp mode, the holding potentials (VH) were −70 mV, at which glycine- and γ-aminobutyric acid-mediated inhibitory postsynaptic currents (IPSCs) were negligible.24 Then recordings were performed in the current clamp mode. Current and voltage data were digitized with an A/D converter (Digidata 1200; Axon Instruments) and stored on a personal computer using the pCLAMP 7 data acquisition program (Axon Instruments). Data then were analyzed using a software package (Mini Analysis, version 6.01; Synaptosoft Inc., Fort Lee, NJ).

Neurons were recorded at a depth of 30 to 150 μm measured from the dorsal surface of the spinal cord to the point of contact with the cell. This distance was identified to be within the SG using transverse slices obtained from the spinal cords of 6- to 8-week-old rats at the same lumbar level.21 The location and morphological features of the recorded cells were confirmed further in some instances by an intrasomatic injection of biocytin (0.2–0.4% in electrode solution) after obtaining synaptic responses, according to a previously described method:21 The neuron shown in figure 1B was located in the SG and possessed morphological features similar to those of cells described previously as SG neurons.25,26

Nonnoxious Stimuli and Noxious Stimuli

For cutaneous stimulation, a neuron’s receptive field (RF) was first determined by applying nonnoxious stimuli with a paintbrush across the shaved skin of the hindquarter (fig. 1C). The response to noxious stimulation was assessed by pinching the skin over the neuron’s RF with forceps. A 1-cm-long line, to be incised, was drawn in the most sensitive region of the RF, and air-puff stimuli (200 p.s.i.) delivered through a pipette (Φ 200 μm) were applied repetitively 1 to 2 mm next to the line (duration of an injection, 100 ms; frequency, 10 Hz; injection time, 10 s) by using a pico injector (PLI-100; Harvard Apparatus, Holliston, MA). The air-puff stimulation did not evoke pain or discomfort sensation in examiners in a pilot study. The noxious mechanical stimuli then were applied to the same site at which air puff was applied with toothed forceps. The toothed forceps was fixed on a rod and a weight (40 g) was placed on the forceps for a prescribed duration of 5 s, by which examiners experienced pinching pain. In a preliminary study, the frequency of excitatory postsynaptic currents (EPSCs) of SG neurons increased as the weight (5, 10, 20, 40, and 80 g) increased, and no significant accommodation was observed, thus indicating that the responses were mediated by the activation of nociceptors. The

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A series of stimuli (air-puff stimulus and pinching stimulus) were applied several times at 1-min intervals.

Both nonnoxious and noxious stimuli were applied to the RF of each neuron on the hindquarter. It has been reported that SG neurons can be classified as several types of neurons according to their response properties of EPSPs and action potentials (APs) to mechanical stimuli on the RF. Neurons are classified as multireceptive if they exhibit APs in response to nonnoxious stimuli and responded maximally to noxious stimuli (fig. 2A), and this type of neurons has been described previously in the superficial dorsal horn by others.25–28 Neurons are classified as nociceptive if they respond only to noxious pinch stimuli (fig. 2B). Neurons are classified as subthreshold neurons if they respond to air-puff stimuli and pinch stimuli with small depolarizations that fail to reach AP threshold (fig. 2C). The amplitudes of EPSPs evoked by pinch stimuli were higher than those evoked by air-puff stimuli in these neurons examined in the present study. These functionally silent neurons also have been described in the SG.28 Neurons were classed as light touch if they responded maximally to nonnoxious brush stimuli.28 Light-touch neurons also fired APs in response to pinch; however, these responses were restricted mostly to the beginning and end of pinch stimuli and were qualitatively similar to the corresponding brush responses (fig. 2D). Consequently, these responses have been interpreted as responses to the initial touch contact of the forceps during pinching, consistent with previous observations.29 In the current study, nociceptive, multireceptive, and subthreshold neurons were used. However, light-touch neurons were not used in the present study because these neurons were located deeply (approximately 120 μm from the dorsal surface of the spinal cord), that is, possibly located in lamina III, and because we could not completely distinguish these neurons from lamina III neurons, which are involved in nonnoxious but not noxious sensory information, with respect to their responses to mechanical stimuli.

**Experimental Protocol**

In the current-clamp mode, after obtaining basal data of stimuli-induced changes in voltages of SG neurons, a 1-cm-long incision was made on the marked line with a number 11 blade through the skin in the center of the RF area of the hindquarter with care taken to prevent dam-
age to superficial veins and nerves in the muscle (fig. 1C). The underlying muscle was incised longitudinally to a depth of 3 to 5 mm from the surface of the fascia of the muscle. The skin was apposed with two skin clips by a Visistat® (Teleflex Medical Research Triangle Park, NC).

Spontaneous activity was recorded in the current clamp mode before and until 30 min after the incision had been made, when behavioral hyperalgesia and increased responsiveness of deep dorsal horn neurons were maximally developed. Nonnoxious and noxious stimuli then were applied to the same sites as those stimulated before the incision. Some animals were given an intravenous injection of 2 mg/kg lidocaine (Astra Japan, Tokyo, Japan). Spontaneous activity and responses to nonnoxious and noxious stimuli then were recorded 5 min after the administration of lidocaine. Lidocaine was dissolved in 0.9% saline and adjusted to a concentration of 3 μg/μl.

Data Analysis

The air puff stimuli and pinch stimuli were applied at least three times before and after the incision and after administration of lidocaine. Spontaneous firing rates were determined by averaging the activity over 5-min periods when there was no contact with the RF. To evaluate the effects of the surgical incision on evoked activities of SG neurons, rates of APs to air-puff and pinch stimuli were subtracted from spontaneous firing rates; the subtracted rates of APs before and after the incision and after systemic administration of lidocaine were compared by one-way analyses of variance with Scheffé test and paired t tests for differences from the control values (preincision values) and from the values at 30 min after the incision. Some of the variables are expressed as percentages of control values (preincision values). All numerical data are expressed as means ±
Table 1. Physiology of Neurons Tested

<table>
<thead>
<tr>
<th>Cell Type</th>
<th>No. of Cells</th>
<th>Cell Location (μm)</th>
<th>V_R (mV)</th>
<th>Input Resistance (MΩ)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Multireceptive</td>
<td>8</td>
<td>119 ± 15</td>
<td>-60.6 ± 2.6</td>
<td>380 ± 44</td>
</tr>
<tr>
<td>Nociceptive</td>
<td>5</td>
<td>110 ± 12</td>
<td>-59.6 ± 1.4</td>
<td>272 ± 26</td>
</tr>
<tr>
<td>Subthreshold</td>
<td>5</td>
<td>100 ± 7</td>
<td>-62.2 ± 2.7</td>
<td>300 ± 29</td>
</tr>
</tbody>
</table>

Cells were classified as multireceptive, nociceptive, or subthreshold neurons (see text). Cell location was determined as the distance between the electrode tip and the surface of the spinal cord.

SEM. P values of less than 0.05 were considered statistically significant.

Results

An animal preparation could be maintained in a stable condition for more than 10 h, comparable with the previous experimental state.21 Whole-cell patch-clamp recordings were made from 39 SG neurons. Although stable recording was obtained from a single neuron for up to 3 h, 11 neurons were lost during incision and wound closure, and 10 neurons were lost within 30 min after the incision had been made. As a result, stable recordings could be maintained in 18 neurons over a period of 30 min after the incision. Data obtained from these 18 neurons thus was analyzed in the current study. All neurons studied had membrane potentials more negative than −55 mV. The number of neurons, depths of cell location, membrane potentials, and input membrane resistances are shown in table 1. RFs of all neurons examined in the current study were located on the shaved skin of the hairy hindquarter (lumbar and gluteal regions of the rat).

Spontaneous Activity and Evoked Responses of SG Neurons to Nonnoxious and Noxious Stimuli before and after Incision

In the voltage clamp mode (holding voltage, −70 mV), the mean amplitude and frequency of spontaneous EPSCs were 17.1 ± 2.4 pA and 37.7 ± 4.6 Hz, respectively, and both noxious (pinch) and nonnoxious (air-puff) stimuli applied to the RF of hairy skin elicited a barrage of EPSCs in all of the neurons examined in the present study (data not shown), consistent with results of previous studies.21-23 In the current clamp mode, none of the neurons showed any spontaneous APs before the incision had been made. A barrage of APs was observed in all multireceptive neurons and nociceptive neurons during the incision and clipping of the skin (fig. 3A). Mean rates of APs during the incision and wound closure were 2.3 ± 0.3 and 1.5 ± 0.2 in multireceptive neurons (n = 8) and nociceptive neurons (n = 5), respectively.

Occurrence of APs disappeared immediately after wound closure had been completed, and spontaneous APs were not subsequently seen in most multireceptive neurons (75%; 6/8 neurons) and nociceptive neurons (80%; 4/5 neurons). In two multireceptive neurons (25%; 2/8 neurons) and one nociceptive neuron (20%; 1/5 neurons), spontaneous AP firing was observed after the incision; mean rates of spontaneous APs were 0.12 ± 0.03 and 0.10 ± 0.02 Hz at 15 and 30 min, respectively, after the incision had been made. Responses of multireceptive neurons to nonnoxious and noxious stimuli and those of nociceptive neurons to noxious stimuli greatly increased after the incision had been made (fig. 3, B and C). The mean rates of APs evoked by pinch stimuli in multireceptive neurons significantly increased (P < 0.05; fig. 3D). The mean rates of APs evoked by pinch stimuli in nociceptive neurons also significantly increased after the incision had been made (P < 0.05; fig. 3D), and most nociceptive neurons (60%; 3/5 neurons) began to respond to nonnoxious stimuli.

The incision and wound closure elicited a barrage of EPSPs in subthreshold neurons (n = 5); however, the EPSCs did not reach AP thresholds and occurrence of APs was not seen during and after the incision in any subthreshold neurons (fig. 4A). In the subthreshold neurons, nonnoxious and noxious stimuli did not evoke APs before or after the incision had been made (fig. 4, B and C).

Effects of Systemic Administration of Lidocaine on Increased Activity of SG Neurons after Incision

The effect of intravenous administration of lidocaine (2 mg/kg) was evaluated in five multireceptive neurons, including one neuron with sustained spontaneous AP firing after the incision, and in three nociceptive neurons. Administration of lidocaine abolished sustained spontaneous AP firing (fig. 5A) and suppressed the increased responses of the multireceptive neurons and nociceptive neurons to nonnoxious and noxious stimuli (P < 0.05; fig. 5, B and C).

Discussion

Changes in Spontaneous Activity and Evoked Responsiveness of SG Neurons after Incision

Spontaneous pain seems to be present in an incision model, but the magnitude of spontaneous pain is not as great as that of other types of persistent pain models.2,4 Spontaneous activities of dorsal horn neurons located in deep laminae, including lamina V, increased immediately after the incision and suturing in hairy skin of the rat and returned to the preincision levels within 2 h after the incision in the majority of neurons.6 In the present study, AP firing ceased just after completion of the incision and wound closure in most multireceptive and...
nociceptive SG neurons (77%; 10/13 neurons), and spontaneous AP firing was observed only in 23% of the neurons (3/13 neurons) 30 min after the incision had been made. The relatively low incidence of neurons with spontaneous AP firing after the incision may reflect the relatively small magnitude of spontaneous pain-related behavior in the incision model.2,4

In the present study, most nociceptive SG neurons (60%; 3/5 neurons) began to respond to nonnoxious air-puff stimuli after the incision, suggesting functional conversion of nociceptive neurons to multireceptive neurons. In contrast, high-threshold dorsal horn neurons located mainly in deep laminae (more than 400 μm from the dorsal surface of the cord) did not respond to nonnoxious stimuli after a similar incision in our previous study, whereas these neurons were capable of responding to nonnoxious stimuli by reversal of γ-aminobutyric acid–mediated inhibition.6 Low-threshold mechanoreceptive Aβ-fibers terminate mainly in laminae III–V, whereas Aδ-mechanical nociceptors terminate in laminae I and V, and C-fiber nociceptors terminate in laminae I and II.25 Thus, high-threshold neurons located in deep laminae (laminae IV–V) may receive inputs from Aβ-fibers and Aδ-fibers, these inputs being inhibited by γ-aminobutyric acid–mediated interneurons in the spinal cord in normal conditions. Incision injury may not reduce activity of the interneurons, and high-threshold neurons do not respond to nonnoxious stimuli after incision.

However, it has been reported that the threshold of sensitized Aδ- and C-fibers to stimuli by using von Frey filaments after incision injury in glabrous skin was reduced to 28 mN and that most of these small fibers responded to brush stimuli,27 although it should be pointed out that physiologic characteristics of hairy skin and glabrous skin are different, especially after tissue injury. Thus, responses of nociceptive SG neurons to air-puff stimuli used in the present study might have been elicited through sensitized Aδ- and C-fibers. The results suggest that nociceptive SG neurons, but not

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Fig. 3. (A) A typical time course of excitatory postsynaptic potentials (EPSPs) and action potentials (APs) in the most multireceptive neurons (75%; 6/8 neurons) and nociceptive neurons (80%; 4/5 neurons) before, during, and after incision and wound closure with staples (S). The incision and wound closure elicited EPSPs with a barrage of APs, but occurrence of APs disappeared immediately after the wound closure had been completed, and spontaneous APs were not seen subsequently. (B) An example of multireceptive neurons in response to air-puff stimuli and pinch stimuli before (Pre) and after the incision had been made (Incision). (C) An example of nociceptive neurons in response to air-puff stimuli and pinch stimuli before (Pre) and after the incision had been made (Incision). (D) Mean rates of APs in response to air-puff stimuli and pinch stimuli in multireceptive neurons (upper panels) and in nociceptive neurons (lower panels) before (Pre) and after the incision had been made (Incision). *P < 0.05 versus preincision value.
high-threshold neurons located in deep laminae,⁶ may be responsible for behavioral allodynia seen in the incision model.

It has been reported that mechanoinsensitive Aδ-fibers and C-fibers, but not Aβ-fibers, were sensitized after plantar incision and that approximately 40% of the Aδ-fibers and C-fibers showed spontaneous firings.³⁰ Post-traumatic injection of bupivacaine into the incised site abolished spontaneous activities of the sensitized primary afferents³⁰ and dorsal horn neurons located in deep laminae.¹¹ Taken together, the results of the present study suggest that the increased spontaneous activity of SG neurons also was dependent on excessive afferent inputs from the injured site but not on activity of SG neurons per se. However, if subthreshold SG neurons receive inputs mainly from these mechanoinsensitive Aδ-fibers and C-fibers and if this explains why subthreshold neurons are functionally silent, some subthreshold SG neurons should begin to respond to noxious stimuli after incisional injury. However, this was not the case in the present study; none of subthreshold SG neurons (n = 5) exerted any APs to mechanical stimuli after the 1-cm-long incision had been made.

All of subthreshold SG neurons exerted large EPSCs with high frequency evoked by pinch stimuli (30.2 ± 2.5 pA, 91.2 ± 3.9 Hz), most of which were suppressed by application of tetrodotoxin (0.5 M) in Krebs’s solution (data not shown), suggesting that subthreshold SG neurons receive inputs from mechanoinsensitive Aδ-fibers and C-fibers. We recently showed that spontaneous IPSCs with high frequency (77 ± 45 Hz) and large amplitude (47 ± 26 pA) were observed in approximately 40% of SG neurons and that the high-frequency and large-amplitude IPSCs were at least in part caused by tonic spontaneous excitation of descending inhibitory pathways from supraspinal sites, which synapse on SG neurons.³¹ Thus, subthreshold SG neurons, which are thought to be functionally silent, may be a result of great tonic influence through the descending inhibitory systems from supraspinal sites. If so, it is likely that these subthreshold SG neurons are functional when the descending inhibition is disrupted,³¹ and surgical incision may not affect the inhibitory influence on SG neurons.

Effects of Systemic Lidocaine on Hyperexcitability of SG Neurons after Incision Injury

Although mechanisms of enhanced sensitivity to pain (allodynia and hyperalgesia) in postoperative pain are thought to differ from those in other types of tissue injury-induced pain,²¹¹–¹³ systemic administration of lidocaine has been shown to relieve postoperative pain in a clinical setting.³²–³⁴ We also have shown that systemic anesthesia confer no apparent benefit on the outcome of pain.
administration of lidocaine suppresses primary and secondary hyperalgesia after an experimental small incision in humans. In the present study, systemic administration of 2 mg/kg of lidocaine abolished spontaneous AP firing and suppressed increased responsiveness after the incision in multireceptive and nociceptive SG neurons. It is thus likely that spontaneous AP firing in SG neurons originates from the injured site and that systemic administration of lidocaine exerts its reversing effect on increased responsiveness of SG neurons after incision.

Previous studies demonstrated little effect of systemically administered lidocaine on normal pain thresholds but demonstrated profound effects on acute painful conditions after tissue injury induced by application of chemical irritants. Furthermore, it has been reported that intraplantar injection of a quaternary derivative of lidocaine, QX-314, after the initial phase after hind-paw injection of formalin abolished persistent phase 2 pain nociceptive behaviors. The results suggest that persistent activity in peripheral afferent fibers during phase 2 is required for the persistent pain evoked by formalin, because in contrast to lidocaine, which rapidly crosses cell membranes, QX-314 does not easily penetrate the blood–brain barrier and has only peripheral sites of action. Because the number of neurons examined in the present study was relatively small, further study is required to determine the mechanisms underlying the suppressive effects of systemic administration of lidocaine on hyperexcitation of SG neurons after incision.

Only data obtained in the current clamp mode were analyzed in the present study. Neuronal excitability results from balance between excitatory synapse transmission and inhibitory synapse transmission. Using in vivo patch-clamp recording, IPSCs and EPSCs are recorded in the same neurons by altering holding potential. For example, nonnoxious mechanical stimuli elicit both IPSCs and EPSCs in SG neurons, whereas noxious stimuli evoke a persistent barrage of EPSCs, but not IPSCs. These

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**Fig. 5.** (A) An example of the effect of systemic administration of lidocaine on spontaneously occurring action potentials (APs). In two of eight multireceptive neurons and in one of five nociceptive neurons, spontaneous APs were seen after incision and wound closure with staples (S). Immediately after systemic administration of lidocaine (2 mg/kg; arrow), the spontaneous APs ceased and were not subsequently seen. (B) Typical examples of responses to nonnoxious and noxious stimuli before (Pre) and after (Incision) the incision had been made and at 5 min after systemic administration of 2 mg/kg lidocaine (Lidocaine). (C) Changes in rates of APs in response to nonnoxious air-puff stimuli and noxious pinch stimuli before (Pre) and after (Incision) the incision had been made and at 5 min after systemic administration of 2 mg/kg lidocaine (Lidocaine). *P < 0.05 versus preincision value and postincision value at 30 min after the incision had been made, respectively.
results suggest that nonnoxious mechanical stimuli applied to the skin reduce noxious mechanical transmission in the SG by eliciting a barrage of IPSCs. If the inhibitory inputs to SG neurons are lost, as was described in previous reports after nerve injury,20 SG neurons will be excited in response to nonnoxious stimuli, possibly resulting in allodynia. Thus, the in vivo patch-clamp technique is a good tool to investigate changes in balance between excitatory and inhibitory synapse transmission in SG neurons in a postoperative pain state. Further study using in vivo patch-clamp recording thus is required to obtain insights into the mechanisms of postoperative pain, focusing on analysis of changes in EPSCs and IPSCs of SG neurons after incision injury.

In conclusion, the results of the present study using in vivo patch-clamp recording suggest that SG neurons show different changes in properties after surgical incision depending on classification of SG neurons and that systemic administration of lidocaine at a relatively low dose (2 mg/kg) can abolish sustained occurrence of APs originating from the injured site and can reverse increased responsiveness of nonnoxious and noxious stimuli.

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