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Mechanism of Transmission and Modulation of Renal Pain in Cats; Effects of Transcutaneous Electrical Nerve Stimulation on Renal Pain

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Transcutaneous electrical nerve stimulation (TENS) has widely been employed as a method of obtaining analgesia in medical practice. The mechanisms of pain relief by TENS are known to be associated with the spinal gate control mechanism or descending pain inhibitory system. However, most of the studies concerning the analgesic effects and their mechanisms for TENS have dealt with somatic pain. Thus, in this experiment, we investigated the analgesic effects of TENS on renal pain as a model of visceral pain, and the characteristics of the dorsal horn cells with renal inputs. The renal pain was induced by acute occlusion of the ureter or renal artery.

The main results are summarized as follows:

1) The renal nerve was composed of Aβ, Aδ and C fiber groups; the thresholds for each group were 400~800 mV, 1.1~1.5 V, and 2.1~5.8 V, respectively.

2) The dorsal horn cells tested received A and/or C afferent fibers from the kidney, and the more C inputs the dorsal horn cells had, the greater was the response to the stimuli that elicited the renal pain.

3) 94.9% of cells with renal input had the concomitant somatic receptive fields on the skin; the high threshold (HT) and wide dynamic range (WDR) cells exhibited a greater responses than low threshold (LT) cells to the renal pain-producing stimuli.

4) TENS reduced the C-responses of dorsal horn cells to 38.9±8.4% of the control value and the effect lasted for 10 min after the cessation of TENS.

5) By TENS, the responses evoked by acute occlusion of the ureter or renal artery were reduced to 37.5±9.7% and 46.3±8.9% of the control value, respectively. This analgesic effects lasted 10 min after TENS.

6) The responses elicited by squeezing the receptive fields of the skin were reduced to 40.7±7.9% of the control value and the effects lasted 15 min after TENS.

These results suggest that most of dorsal horn cells with renal inputs have the concomitant somatic inputs and TENS can alleviate the renal pain as well as somatic pain.

Key Words: Renal pain, renal nerve, visceral pain, TENS, analgesia

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Clinically severe renal colicky pain occurs during acute ureteral occlusion caused, for example, by renal stones. However, the detailed mechanisms implicated for the pain is still not clear.

Two types of sensory receptors in the kidney have been found; mechanoreceptors activated by an increase of renal venous or pelvic pressure, and chemoreceptors which respond to changes of the chemical environment in the renal pelvis (Aström and Crafford, 1968; Niijima, 1971; Uchida *et al.* 1971; Recordati *et al.* 1981). In addition, Ammons (1989b) reported that some dorsal horn cells with renal inputs were activated during acute ureteral occlusion. Thus, it is presumed that the above-mentioned mechanical, chemical receptors and the dorsal horn cells activated by the renal pain-producing stimuli are implicated in the transmission of the renal pain.

Transcutaneous electrical nerve stimulation (TENS) has been used to relieve pain in medical practice (Kane and Taub, 1975; Woolf *et al.* 1980). Many possible means of modulating nociceptive information have been proposed to explain the analgesic effect of TENS; peripheral nerve block mechanism (Campbell and Taub, 1973; Torebjörk and Harbe, 1974); gate control mechanism in which activities of the spinal neurons transmitting the nociceptive information are inhibited by activation of afferent fibers with large diameter in the spinal cord (Melzack and Wall, 1965); descending pain inhibitory systems (Kawashima and Basbaum, 1984) especially the role of endogenous opioids (Mayer and Price, 1976; Fields *et al.* 1980).

In the central nervous system, properties of the opiate receptors that bind with morphine have been studied by many investigators (Mayer and Price, 1976; Fields *et al.* 1980; Mansour *et al.* 1987). They could find the presence of considerable amount of enkephalin and endorphin in the periaqueductal gray and many other areas (Hughes, 1975; Kawashima and Basbaum, 1984). Furthermore, they demonstrated a profound analgesia by electrical stimulation of these areas. Based on these observations, it has been proposed that a descending pain inhibitory system blocking the nociceptive information at the level of the spinal cord exists (Reynolds 1969; Oliveras *et al.* 1974; Basbaum *et al.* 1976; Cannon *et al.* 1982), and the activation of this endogenous opioid system is regarded as one of the most important analgesic mechanisms for TENS.

However, most of the cited investigations concerning the analgesic effects and their mechanisms for TENS dealt with somatic pain.

Thus, the aim of this experiment is to investigate the characteristics of dorsal horn cells with renal inputs and the effect of TENS on renal pain as a model of visceral pain.

MATERIALS AND METHOD

Animal preparations

A total of 36 male and female adult cats (2.0 ~3.5 Kg) were used in this study. The animals were anesthetized initially with an intramuscular injection of ketamine hydrochloride (25 mg/kg). Under initial anesthesia, the antecubital vein was cannulated for drug injection and tracheostomy was performed to artificially ventilate the animal. Decerebration was made by ligation of the basilar artery and bilateral common carotid arteries, and further anesthesia was discontinued. During the experiment the animal was immobilized with gallamine triethiodide (Flaxedil, an injection of 20 mg i.v. followed by infusion at 4 mg/kg/h). The end-tidal CO_2 concentration was maintained at 3.5~4.5% and the rectal temperature was kept near 37℃ throughout the experiment by using a capnometer (model 2200, Traverse medical monitor Co.) and homeothermic heating blanket (Harvard Apparatus Co. Inc., Millis, Massachusetts, U.S.A.) respectively.

After exposing the left kidney along the 13th rib margin, the renal nerve was isolated from surrounding connective tissue. Laminectomies were performed at the level of T_{12}~L_2. Mineral oil was filled in the pool made around the exposed spinal cord to prevent drying, and the warm temperature of the pool

was maintained by the immersed heating coils.

Recordings of the compound action potential of the renal nerve

Impulses generated from the renal nerve are transmitted through the least splanchnic nerve and the celiac ganglia to the spinal cord. The compound action potential in the least splanchnic nerve was recorded to determine the composition of the nerve fiber populations.

Recordings were made with bipolar platinum electrodes, and the compound action potential was fed into interface (CED 1401, Cambridge Electronic Design Ltd., Cambridge, England, U.K.) and was signal averaged by the computer software. The electrical thresholds for each fiber group of renal afferents were determined.

Noxious stimulations and recordings of the responses of the dorsal horn cells with renal inputs

The activities of dorsal horn cells were recorded with a carbon filament-filled glass microelectrode.

In this experiment, two types of pain (renal and somatic) were induced. To activate C-fiber of renal nerve electrically, bipolar platinum electrodes were implanted with polyvinyl siloxone on the renal nerve then adequate electrical stimuli (25V intensity, 500 μsec duration, triple pulses of 50 Hz) were applied. To elicit the natural renal pains, a silk thread was looped around the renal artery or the ureter. The ends of the silk were then threaded through a small length of polyethylene tube. Pulling the ends of the thread in opposite directions caused the tube to slide towards and put pressure on the artery or ureter.

The receptive fields of the cells were searched and then three kinds of mechanical stimuli (brush, pressure, squeeze) were applied to the receptive fields of the skin. Based on their response patterns to mechanical stimulation, the cells were classified as low threshold (LT) cells which had greater response to brush than to pressure or squeeze, wide dynamic range (WDR) cells which had a greater response to a squeeze than to a brush or pressure, and high threshold (HT) cells which only respond to a noxious stimulation. Somatic pain was induced by squeezing the receptive field of the skin.

Transcutaneous electrical nerve stimulation

Transcutaneous nerve stimulation was applied to the somatic receptive field of the dorsal horn cells activated by renal nerve stimulation. The intensity of the TENS was 200~400 uA, the frequency 2 Hz, and the duration was 15 minutes. The responses of dorsal horn cells to several pain-producing stimuli (electrical activation of renal C-afferent fibers, ureteral or renal arterial occlusion, and a squeeze on the receptive field of the skin) were compared before and after the application of TENS.

Data analysis

The electrical activities of the dorsal horn cell tested were fed into a window discriminator (model 121, WPI, Inc., New Haven, CT, U.S.A.) via an AC amplifier, the output of which was compiled in post or peristimulus time histograms. The responses elicited by 3 consecutive electrical stimuli at 10 sec intervals were accumulated. Because of variations in the responsiveness of individual dorsal horn cells, the cell's activities were expressed as a percentage of those in the control state. Data were expressed as mean±standard error. Statistical analyses for the data obtained from the same cells or different cells were done by paired or unpaired t-test, respectively. Two-tailed p values less than 0.05 were considered to be significant.

RESULTS

According to the analysis of compound action potentials of the renal nerve, fiber population of the nerve was categorized as Aβ, A δ, and C groups. The electrical threshold was 400~800 mV for Aβ, 1.1~1.5 V for Aδ, and 2.1~5.8 V for C fibers. The durations of stimulation used were 100 μsec for A fiber groups,

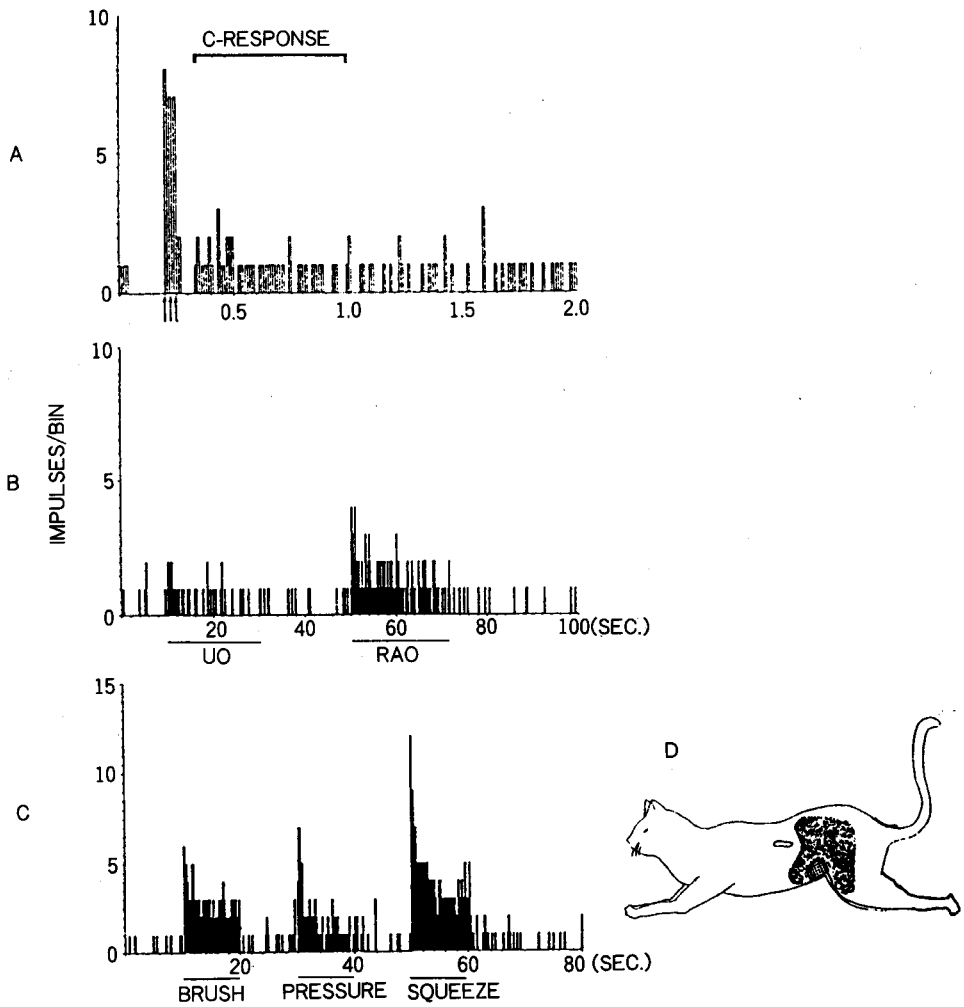

Fig. 1. *Rate histogram showing the responses of a representative neurons with renal input. A: poststimulus time histogram shows A and C-fiber responses evoked by triple electrical pulses on the renal nerve. The histogram was compiled from responses to 3 successive stimuli. Bin widths are 10 msec. B: Peristimulus time histogram from response of the cell to ureteral occlusion (UO) or renal arterial occlusion (RAO). C: Peristimulus time histogram from response of the cell to mechanical stimuli (brush, pressure, squeeze). The cell responded to both innocuous and noxious mechanical stimuli on the receptive field, representing a wide dynamic range cell. D: the receptive field of the cell is indicated by gray field, and the crossed hatched area represents the most sensitive portion of the field The time of application of electrical pulses was indicated by arrows.*

and 500 μsec for the C fiber group . Aβ fibers were fully activated at two times the threshold, and Aδ or C fibers were fully activated at five times the respective threshold intensities. The dorsal horn cells with renal input could mainly be recorded through T_{11}~L_2 of the spinal cord.

The characteristics of spinal dorsal horn cells activated by renal nerve stimulation

Characteristics of the spinal dorsal horn cells activated by renal nerve stimulation

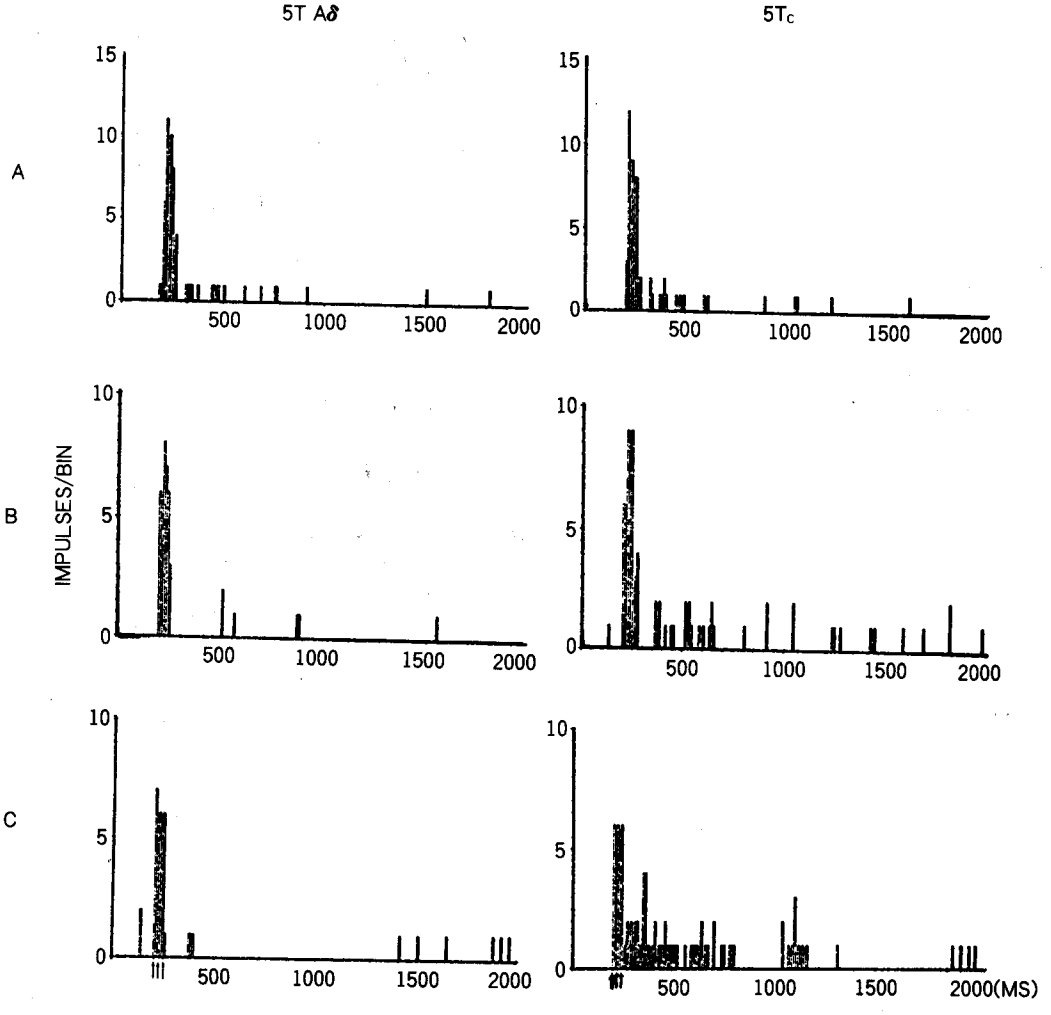

Fig. 2. *An example of analysis of the renal afferents entering the dorsal horn cells. The poststimulus time histogram was compiled from responses to 3 consecutive stimuli with 10 sec intervals. Bin widths are 10 msec. The left column shows the activities of the dorsal horn cells evoked by the strength of 5 times the threshold of Aδ fibers ($5T_{A\delta}$) to activate all A fibers The right column shows the activities of the dorsal horn cells evoked by the strength of 5 times the threshold of C fibers ($5T_C$) to activate all C afferents including A fibers. A: the cell with A fiber input, B: the cell with both A and C-fiber input, C: the cell mainly with C-fiber input.*

were analyzed. The ureter or renal artery were occluded for inducing the renal pain. Then somatic stimuli such as brush, pressure, and squeeze were applied to the receptive field of the skin to characterize the somatic responsiveness. Fig. 1 shows the responses of a representative cell responding to electrical renal nerve stimulation, renal pain-producing stimulation and the somatic mechanical stimulations applied to the receptive field of the skin.

The dorsal horn cells were classified according to the characteristics of the renal afferent fiber inputs (Fig. 2). 20 of 79 cells (25.3%) test-

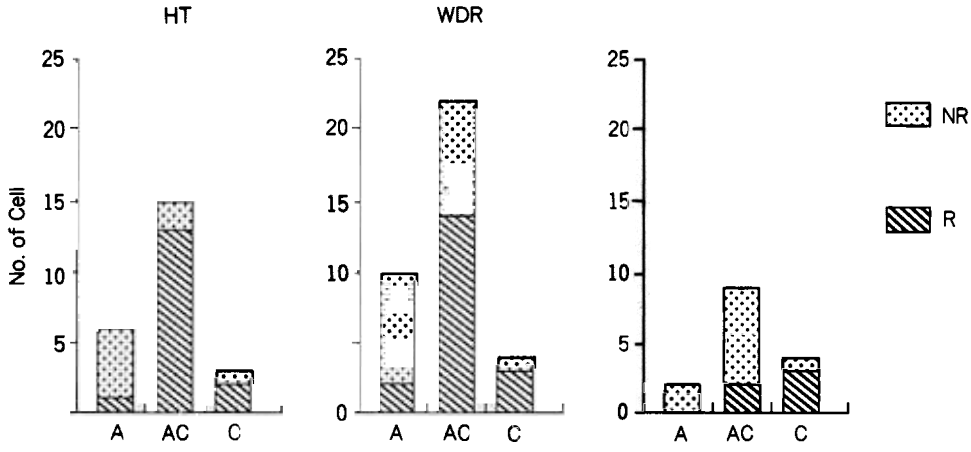

Fig. 3. *Characteristics of responses of the dorsal horn cell with renal input. Among these, the most common type is the WDR cells. The hatched portion indicates the cells responding to stimuli that elicited renal pain. The black portion indicates the cells not responding to the stimuli. The HT and WDR cells has better response to renal pain and the more C inputs the dorsal horn cells had, the greater was the response to the stimuli that elicited renal pain*
HT: high threshold cell
WDR: wide dynamic range cell
LT: low threshold cell
A: cells with A fiber inputs
AC: cells with both A and C fiber inputs
C: cells with C fiber inputs
R: response to renal stimulation
NR: no response to renal stimulation

ed were activated at the strength of 5 times the Aδ fiber threshold ($5T_{A\delta}$, duration; 100 μ sec), but not further activated at 5 times the C fiber threshold intensities ($5T_C$, duration; 500 μsec), that is, these cells responded only to A fiber inputs (Fig. 2A). 47 cells (59.5%) were activated by $5T_{A\delta}$ and exhibited further responses to $5T_C$ stimulation, which suggests that the cells had both A and C fiber inputs (Fig. 2B). The remaining 12 cells (15.2%) were little activated by $5T_{A\delta}$ but showed marked responses to $5T_C$, that is, the cells had mainly C fiber inputs (Fig. 2C).

15% of the cells with only renal A fiber inputs, 63.8% of cells with both A and C inputs, and 75.6% of the cells with only renal C fiber inputs were activated by noxious renal stimulation, indicating the tendency that the more C inputs the dorsal horn cells had, the greater the response to the stimuli that elicited renal pain (Fig. 3).

Out of the spinal dorsal horn cells activated by renal nerve stimulation, 75 cells (94.5%) had the receptive fields on the skin. According to their characteristic responses to mechanical stimuli such as brush, pressure, and squeeze, the cells could be classified into high threshold (HT) cells, wide dynamic range (WDR) cells, and low threshold (LT) cells. The proportion of the HT, WDR, LT cells in percentage was 32% (24 out of 75 cells), 48% (36 cells), and 20% (15 cells) respectively. Analyzing the responsiveness of the cells to renal stimulation, 66.7% HT cells, 52.8% WDR cells, and 33.3 % LT cells responded to renal pain-producing stimulation, suggesting that the cells associated to somatic pain responded better to renal noxious stimulation (Fig. 3).

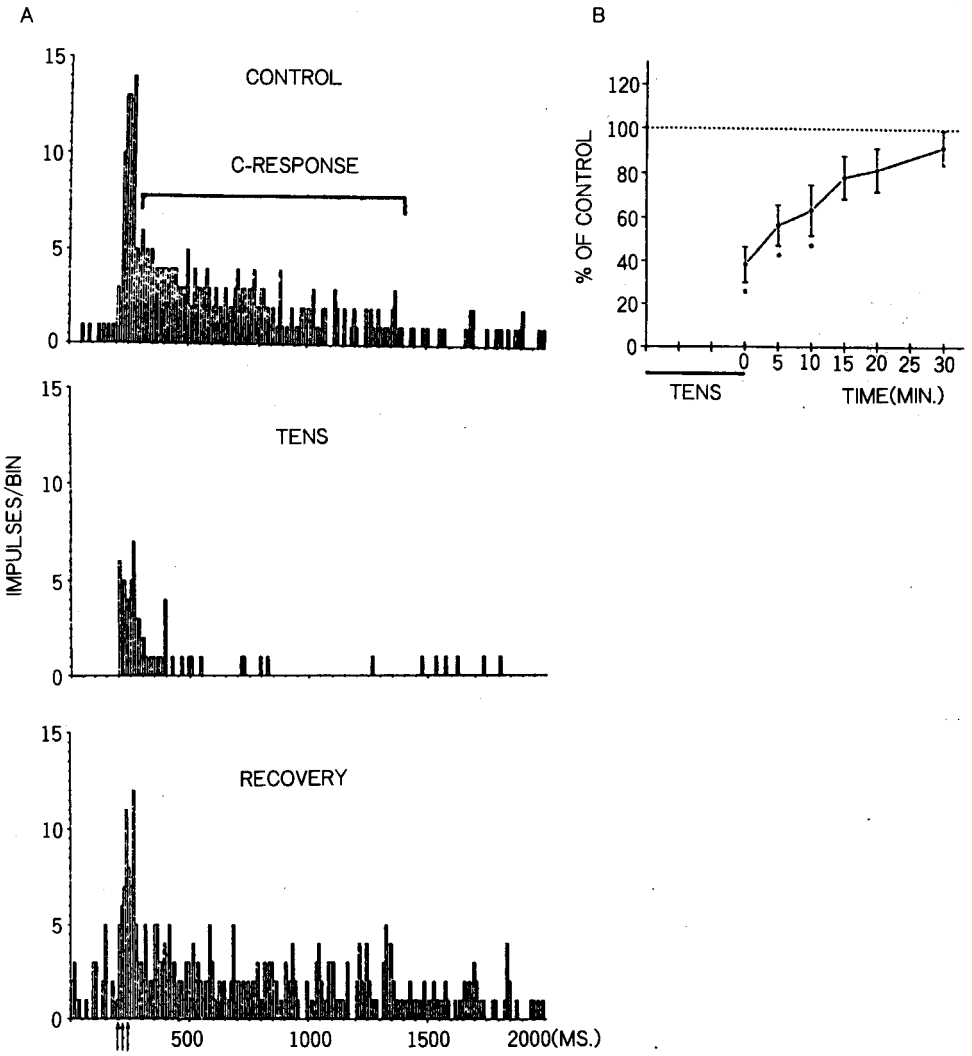

Fig. 4. *Effect of TENS on the C-response of a dorsal horn cell. A: By TENS, the C-responses are reduced initially and then gradually recovered. The histogram was compiled from responses to three consecutive stimuli with 10 sec intervals. Bin widths are 10 msec. The arrows indicate the time of application of three consecutive electrical pulses on the renal nerve. B: Activities of 19 dorsal horn cells were statistically analyzed. The C-responses are expressed as a percentage of the pre-stimulus control value. Asterisks represents statistically significant differences between control (pre-TENS) and the reduced activities by TENS.*

The analgesic effect of transcutaneous electrical nerve stimulation on renal and somatic pain

In this experiment, three types of responses, as a index of renal pain, were used; the C responses of dorsal horn cells evoked by the electrical stimuli applied to the renal nerve; the responses elicited by renal ureteral occlusion; the responses elicited by renal arterial occlusion. As for a index of somatic pain, the

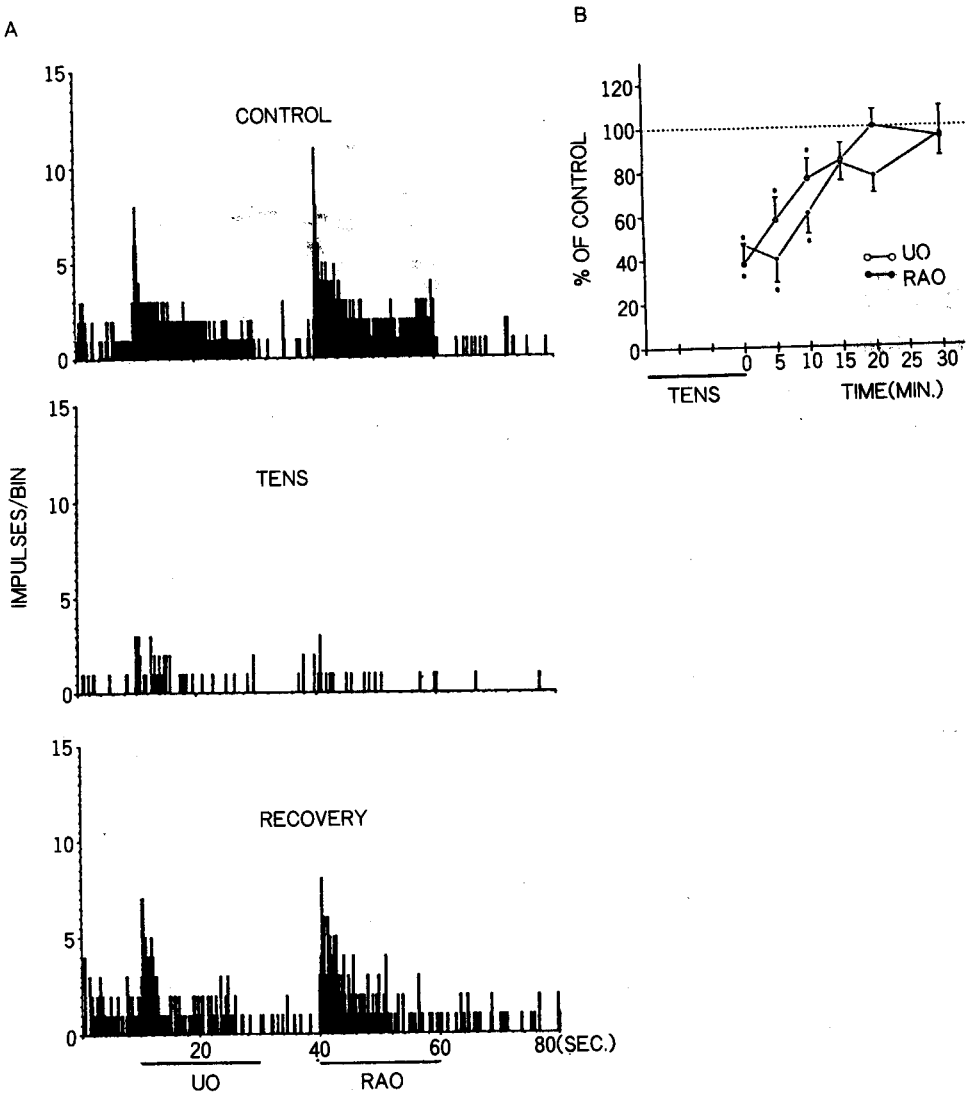

Fig. 5. *Effects of TENS on the responses of the dorsal horn cells to ureteral occlusion or renal arterial occlusion. A: By TENS, the responses of a cell to ureteral or renal arterial occlusion are reduced and then gradually recovered. Bin widths are 200 msec. B. Activities of 19 dorsal horn cells were statistically analyzed. The responses are expressed as a percentage of the pre-stimulus control value. Asterisks indicate statistically significant differences between control (pre-TENS) and the reduced activities by TENS.*
UO: ureteral occlusion
RAO: renal arterial occlusion

responses of the dorsal horn cells to noxious mechanical stimulus (a squeeze within the receptive field of the skin) were used.

The effect of TENS on C-responses of spinal dorsal horn cells

Immediately after application of TENS, C-

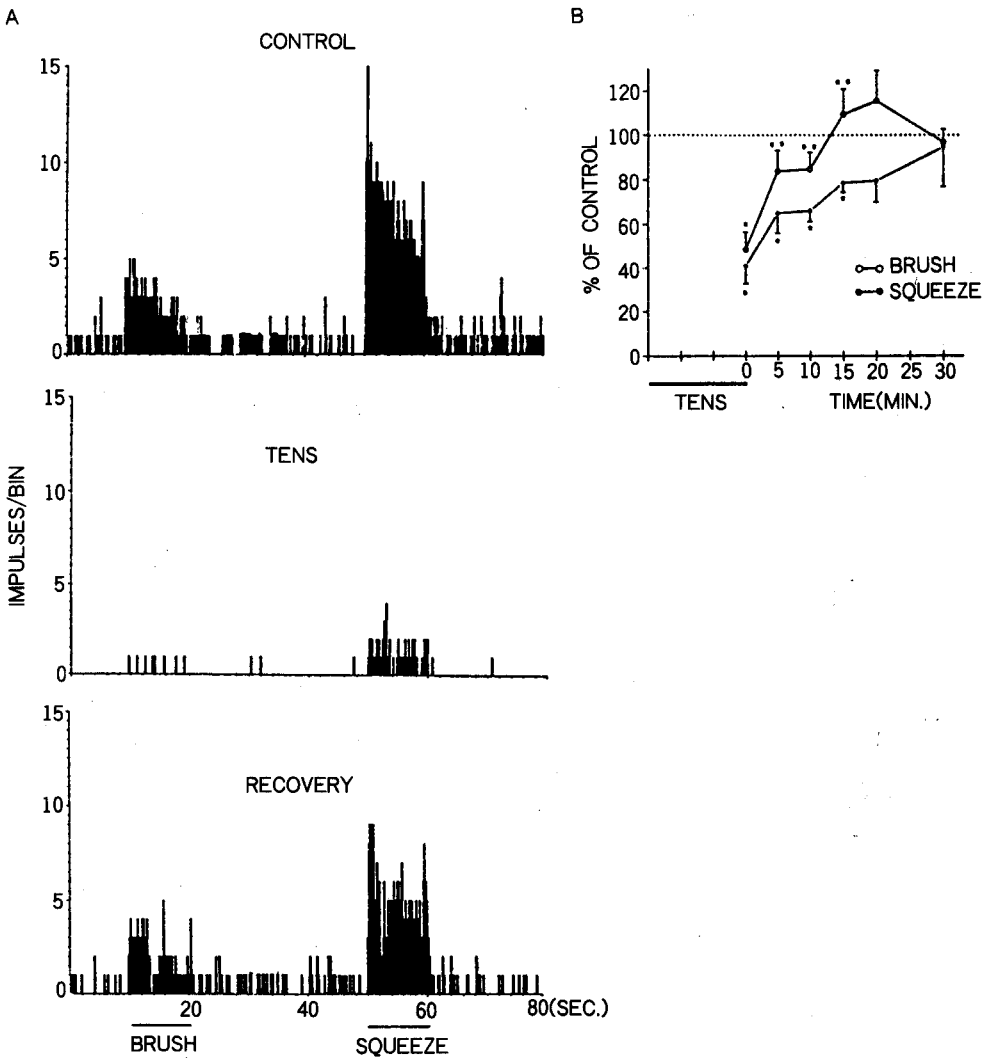

Fig. 6. *Effect of TENS on the responses of a dorsal horn cell by somatic stimulation. A: By TENS, the responses of a cell to brush or squeeze on the receptive field are reduced and then gradually recovered. Bin widths are 200 msec. B. Activities of 19 dorsal horn cells were statistically analyzed. The responses were expressed as a percentage of the pre-stimulus control value. Asterisks indicate statistically significant differences.*
**: $p< 0.05$ (compared between pre-TENS and post-TENS)*
***: $p<0.05$ (compared between brush and squeeze responses)*

response of the dorsal horn cells were reduced to 38.9±8.4 % of the control (pre-TENS) value. This reduced activities by TENS were sustained significantly ($p<0.05$) for a period of 10 min (Fig. 4), and thereafter C-responses were recovered to 78.2±9.6% of the control value at 15 min, 81.5±9.7% at 20 min, and 91.6 ±7.6% at 30 min respectively.

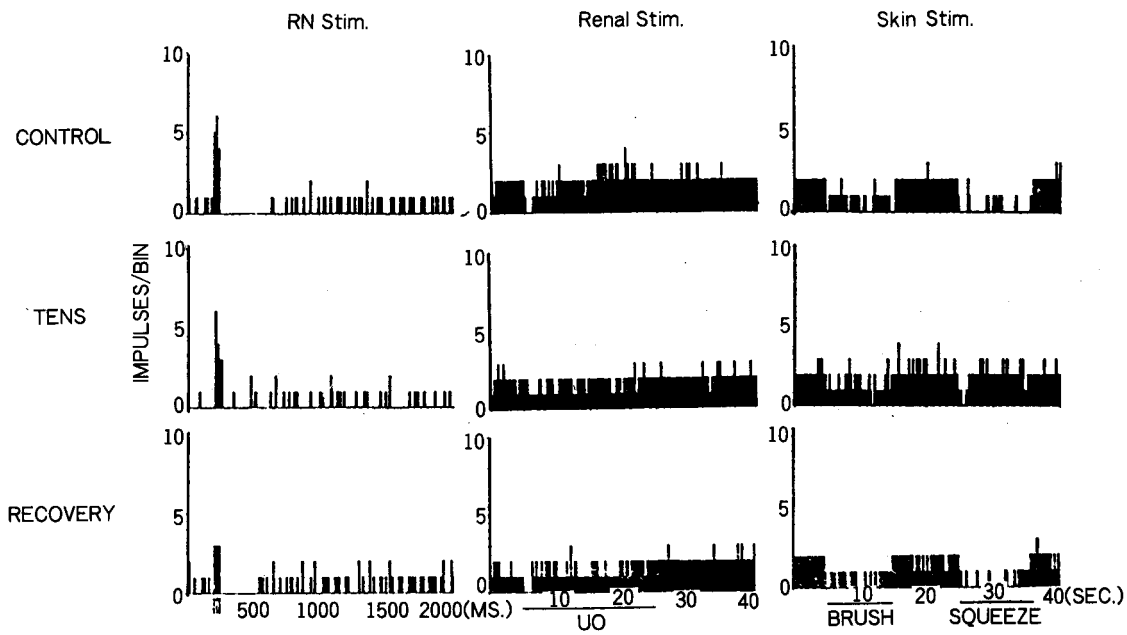

Fig. 7. *Effect of TENS on an inhibited cell by renal nerve stimulation. This cell shows inhibited response by the electrical stimulation of the renal nerve, ureteral occlusion , and somatic stimulation (upper trace). TENS reversed the inhibition of the cell (middle trace), and after TENS, the activities are recovered to pre-TENS control level (lower trace).*
RN Stim.: renal nerve stimulation
Renal Stim: renal stimulation (ureteral occlusion)
Skin Stim: skin stimulation (brush, squeeze)
UO: ureteral occlusion

The effect of TENS on the activities of the dorsal horn cells evoked by ureteral and renal arterial occlusion

The activities of dorsal horn cells evoked by ureteral occlusion were significantly ($p<0.05$) reduced to 37.5±9.7% of the control value immediately after TENS, to 57.5±14.4% at 5 min, and to 76.2±9.4% at 10 min after the cessation of TENS. The activities of spinal dorsal horn cells elicited by renal arterial occlusion were also significantly ($p<0.05$) reduced to 46.3±8.9% of the control value immediately after TENS to 39.7±10.5% at 5 min and to 60.5±9.2% at 10 min after TENS (Fig. 5).

The effect of transcutaneous electrical nerve stimulation on the activities of spinal dorsal horn cells evoked by somatic noxious stimulation

The effects of TENS on activities of dorsal horn cells evoked by somatic noxious stimulation were analyzed. The responses to noxious stimuli such as a squeeze were reduced to 40.7 ±7.9 % of the control value immediately after TENS, to 64.7±9.0% at 5 min, to 65.7±4.76% at 10 min, and to 78.4±4.2% at 15 min respectively ($P<0.05$). In contrast, response to innocuous stimuli such as a brush was not significantly reduced except immediately after TENS (48.3 ±7.9% of the control value; $p<0.05$), indicating that TENS had a more pronounced and

prolonged effect on noxious responses than innocuous ones (Fig. 6).

During the experiment, some cells inhibited by renal nerve stimulation were encountered. These cells were inhibited not only by renal pain-producing stimulation, but also by somatic stimulation. TENS reversed the inhibitions of those cells, and ultimately activated the dorsal horn cells (Fig. 7).

DISCUSSION

The kidney has rich innervation compared with its size (Mitchell, 1950; Mckenna and Angelakos, 1968) and since Bradford's report that the kidney has mainly sympathetic innervation (1889), many studies concerning the roles of the renal nerve were conducted (Dibona and Sawin, 1982; Moss, 1985; Ribstein and Humphreys, 1984; Stella and Zanchetti, 1991).

Sensory receptors of the kidney have been classified into mechanoreceptors responding to increased intrarenal pressure (Aström and Crafford, 1968; Niijima, 1971; Uchida *et al.* 1971) and chemoreceptors responding to renal ischemia or changes of the chemical environments (Recordati *et al.* 1981). The presence of specific nociceptors in the kidney has not yet been ascertained, but the above-mentioned mechanoreceptors or chemoreceptors are thought to be implicated in transmission of renal pain to the higher centers.

The information of renal pain is transmitted to the spinal cord through the renal afferent nerve fibers, and by way of ascending neural pathways of the upper spinal cord, it produces so called renorenal reflex, in which activities of the renal afferent fibers from one kidney influence those of the contralateral efferent fibers, thereby affecting the renal blood flows, blood pressure, and pulse rate (Aström and Crafford, 1968; Francisco *et al.* 1980). The higher centers associated with this visceral reflex are not specifically identified, but considering the fact that the activity of cells in the reticular formation of the brainstem (Ammons, 1987), the hypothalamus (Calaresu and Ciriello, 1981), and the solitary nucleus (Felder, 1986) are affected by stimulation of the renal afferent nerve, those areas are thought to be the locations associated with the reflex.

In this experiment, the composition of renal afferent fibers was analyzed by recording the compound action potentials. The analysis of compound action potential in the least splanchnic nerve evoked by renal nerve stimulation revealed that in addition to Aδ and C fibers, Aβ fibers that had faster conduction velocity in the range between 32.3~43.4 m/sec existed. This finding is comparable to that of Calaresu *et al.* (1978) who reported the presence of Aβ fiber group with conduction velocity of 37 m/sec. Thus it is conceivable that A responses of dorsal horn cells might be due to activation of both Aβ and Aδ afferent fibers. However, it has been reported that the activation of only Aβ fibers of the splanchnic nerve is not sufficient to activate the spinal horn cells (Hancock *et al.* 1975; Foreman *et al.* 1981; Cervero, 1983), and the Aβ fibers of the splanchnic nerve are mainly associated with the pacinian corpuscle of the mesentery outside the kidney (Sheehan, 1933) being transmitted to the gracilis nucleus through the dorsal column (Kuo and De Groat, 1985). Therefore, A-responses of dorsal horn cells observed in this experiment are likely to be the result of the activation of Aδ fibers.

In this experiment, the responses of spinal dorsal horn cells to ureteral occlusion were mainly of the slowly adapting type, that is, their activity increased sharply initially and then slowly decreased. Two other types were also observed; the rapidly adapting type whose activity increased initially and rapidly decreased, and the non-adapting type whose activity was not decreased during occlusion. Ammons (1988) also observed the similar types of dorsal horn neurons responding to ureteral occlusion.

There has been some reports that the receptors activated by renal venous occlusion were mainly of the slowly adapting (Gilmore and Tomomatsu, 1985) or rapidly adapting type (Uchida *et al.* 1971), and the mechanoreceptors of the ureter were of the non-

adapting type (Beacham and Kunze, 1969). These characteristics of receptors are different in some respects from those of the dorsal horn cell responses observed in this experiment. These discrepancies might be thought to be due to the characteristics of the adaptation of the dorsal horn cells directly receiving the renal input or to the influences of the mediation of some spinal interneurons.

During the experiment, some dorsal horn cells inhibited by renal nerve stimulation were encountered, but their functional significances in the transmission of nociceptive information is not yet clear.

We used a method of ureteral occlusion to induce the distention of the renal pelvis, but, during the procedure of the occlusion, the mechanoreceptors in the ureteral wall might also be activated by the occlusion. Therefore, it is possible that the responses of dorsal horn cells to ureteral occlusion observed were both due to direct activation of mechanoreceptors in the ureter by mechanical force applied and indirect activation of mechanoreceptors in the renal pelvis by distension of the pelvis caused by urine accumulation.

It has been known that mechanoreceptors are present in the branch of renal artery inside the kidney but absent in the renal artery outside the kidney (Niijima; 1971). Nevertheless, we could not totally exclude the possibility that a renal arterial occlusion activate mechanoreceptors in the arterial wall because the location of the occlusion was very close to the kidney. Thus, it is also possible that the responses that rapidly increased initially and then decreased to renal arterial occlusion may be the result of the deformation of the renal artery.

Some dorsal horn cells exhibited the distinctive response pattern in which the cells rapidly adapted initially, but the remaining activities of the cells were sustained or some times even increased thereafter. Ammons (1989a) also divided the dorsal horn cells into onset-response cells and onset-ischemic response cells according to the response patterns of the cells, the former being activated by mechanoreceptors in arterial wall and the latter being activated by both the mechanoreceptor and the chemoreceptors responding to renal ischemia.

Thus, it is conceivable that the initial phase of the response observed in this study was presumably due to the activation of mechanical receptors in the renal artery, and a later phase is due to the chemoreceptor activation by renal ischemia.

Of the 79 dorsal horn cells activated by renal nerve stimulation, 75 cells had a receptive field on the skin, and this finding is comparable to several reports that most dorsal horn cells with visceral input have concomitantly somatic inputs (Pomeranz *et al.* 1968; Guilbaud *et al.* 1977; Blair *et al.* 1981; Foreman *et al.* 1981).

Among dorsal horn cells having somatic receptive fields, 48%, 32%, and the remaining 20 % were WDR, HT , and LT cells respectively. 66.7% HT cells, 52.8% WDR cells, and 33.3% LT cells were activated by renal pain-producing stimulation, that is, we could find that the more closely they were associated with the nociception of the skin, the better they responded to renal pain-inducing stimulation. However, these findings differ in some respect from those of another experiment using spinothalamic tract (STT) cells in the monkey. Ammons (1989b) reported that no LT cells among STT cells with renal input were found, and WDR cells were more sensitively activated than HT cells by ureteral occlusion. These discrepancies might be due to variations among different species, or to the different types of the cells tested.

It has been known that somatic pain is inhibited by peripheral nerve stimulation (Andersson, 1979; Lee *et al.* 1985; Woolf, 1989), and TENS has widely been used as a method to excite peripheral nerve in medical practice. In this experiment, TENS reduced the activities of dorsal horn cells induced by ureteral occlusion or renal arterial occlusion for a period of 10 min. There were no statistical differences in terms of analgesic effect of TENS between on pains evoked by ureteral and renal arterial occlusion. TENS also reduced the activity of dorsal horn cells induced by somatic stimulation. The responses to innocuous stimulation such as a brush was in-

hibited only immediately after TENS while those to noxious stimulation was inhibited more pronouncedly for at least 10 min. These findings in some respects are comparable to other findings (Woolf and Wall, 1982; Chung *et al.* 1984) and suggest that the effects of TENS on noxious and on innocuous responses are different from each other.

The fact that TENS suppresses the somatic pain is well known, but analgesic characteristics and mechanisms for TENS have been interpreted diversely (Cheng and Pomeranz, 1979; Salar *et al.* 1981; Chung *et al.* 1984; Nam *et al.* 1991). For example, peripheral nerve stimulation with the low intensity and high frequency produces the analgesic effect which have rapid onset, short duration, and segmental distribution. This analgesic effect is not associated with the endogenous opioid system (Basbaum and Fields, 1984) generally being explained by the gate control mechanism in the spinal level. (Melzack and Wall, 1965; Wagman and Price, 1969; Handwerker *et al.* 1975; Woolf and Wall, 1982; Chung *et al.* 1984). In contrast, the peripheral nerve stimulation with high intensity and low frequency exhibits the analgesic effect with slow onset and long duration. This analgesic effect is thought to be associated with the endogenous opioid system (Sjö lund and Eriksson, 1979). The periaqueductal gray and the nucleus raphe magnus are known to contain endogenous opioids, and when these areas were electrically stimulated, potent analgesia is induced (Reynold, 1969; Young, 1989). If the serotonin is depleted in the raphe-spinal pathway, the analgesia does not occur, so activation of the descending pain inhibitory system is regarded as a pivotal mechanism for the analgesia. In addition to this descending inhibitory system, there are neurons containing enkephalin or dynorphin in the spinal substantia gelatinosa (Aronin *et al.* 1981) and even in spinal animals, analgesic effect of TENS associated with endogenous opioid system could be demonstrated (Woolf *et al.* 1980; Yaksh and Elde, 1981). Thus this spinal endogenous opioid system is also thought to play a role in TENS analgesia.

In recent years, a great deal of attention has been focused on the control of nociceptive transmission. But, despite of the enormous interests in the mechanism of pain control, studies for the modulation of visceral pain has largely been neglected. In this experiment, TENS was found to be effective in suppressing renal pain. However, further investigations will be needed to confirm the analgesic effect of TENS on various visceral pains and their detailed mechanisms.

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