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Effects of Morphine on Somatosympathetic Reflex and Arterial Blood Pressure Response Evoked by Stimulation of Peripheral Nerves

Min Gang Huh, Hai Dun Yan, Wonil Lim and Jun Kim

Department of Physiology & Biophysics, Seoul National University, College of Medicine, 28 Yongon-Dong, Chongno-Gu, Seoul 110-799, Korea

=ABSTRACT=

In the present study, the relationship between the somatosympathetic reflexes and arterial blood pressure responses to electrical stimulation of the peripheral nerve was investigated in cats anesthetized with α-chloralose. Single sympathetic postganglionic fiber activities were recorded from the hindlimb muscle and skin nerves and also from the cervical and abdominal sympathetic chains. Effects of the morphine on responses of the sympathetic nerve and arterial blood pressure to activation of the peripheral Aδ- and C-afferent nerves were analyzed. The following results were obtained.

1) Arterial blood pressure was depressed by peripheral Aδ-afferent stimulation (A-response) and was elevated during C-afferent activation (C-response).

2) Intravenously administered morphine enhanced the C-response while the A-response decreased insignificantly. Only the C-response was decreased by intrathecal morphine.

3) All the ten recorded cutaneous sympathetic fibers showed periodic discharge pattern similar to respiratory rhythm and five of them also showed cardiac-related rhythm. However, most of the muscular sympathetic fibers had cardiac-related rhythm and only four fibers showed respiratory rhythm.

4) Morphine decreased the sympathetic C-reflex elicited by the peripheral C-afferent activation and the abdominal sympathetic A-reflex was also decreased by morphine.

From the above results, it was concluded that supraspinal mechanisms were involved in the enhanced arterial pressor response to peripheral C-afferent activation by intravenous morphine.

Key Words: Sympathetic fiber activity, Morphine, Somatosympathetic reflex, Arterial blood pressure

INTRODUCTION

It is well known that excitation of peripheral afferent nerves elicits changes in sympathetic nervous activity, and cardiovascular responses, which are called 'somatosympathetic reflex' (Koizumi & Brooks, 1972; Sato & Schmidt, 1973). Peripheral nerve stimulation would elicit either pressor or depressor response depending on the stimulation intensity and frequency. In general arterial blood pressure level is depressed during stimulation of a

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peripheral afferent nerve with Aδ-intensity, low frequency stimulus (A-response) and elevated by stimulation of C-afferent fibers with high frequency stimuli (C-response) (Chung & Wurster, 1976; Chung et al, 1979). The ascending spinal pathways mediating the pressor response seem to be localized in the dorsolateral sulcus area and those mediating the depressor response in the dorsolateral funiculus (Chung et al, 1979; Mitchell & Schmidt, 1983). There is now much evidence to support the view that cardiovascular neurons located close to the surface of the rostral ventrolateral medulla are the sources of somatosympathetic reflex activity (Stornetta et al, 1989; Sun & Spyer, 1991; Goo et al, 1993).

Electrical stimulation of nociceptive somatic afferent fibers would result in two peaks in sympathetic nerve activity and, determined by conduction velocity, these would be sympathetic A- and C-reflexes, respectively (Sato & Schmidt, 1973; Whitwam et al, 1979). The somatosympathetic Aδ-reflex is known to be depressed by benzodiazepine agonist (Wang et al, 1992), and the somatosympathetic C-reflex is selectively depressed by opioids administered intravenously (Niv & Whitwam, 1983; Swenzen et al, 1988; Wang et al, 1992), in a manner related to the stimulation frequency (Wang et al, 1993). The finding that morphine administered to the brainstem via the vertebral artery produced a nonselective and slight depression of the somatosympathetic C-reflex, while intrathecal application of morphine produced a selective and marked depression of the C-reflex, suggests that the spinal cord is an important target site mediating the somatosympathetic C-reflex, which is responsive to morphine (Kato et al, 1992).

There have been few studies about the effects of morphine on the somatosympathetic arterial blood pressure response. Intravenously administered morphine decreased the arterial depressor response to stimulation of the peripheral afferent nerve with Aδ -intensity, low frequency stimuli, while the pressor response to C-intensity high frequency stimuli was enhanced by intravenous morphine (Kwon, 1988; Kim et al, 1988). However, the same authors also reported that intrathecally administered morphine decreased the pressor response. Other authors reported that fentanyl administered intrathecally abolished blood pressure response to low frequency stimulation but the pressor response to high frequency stimulation was increased by fentanyl (Wang et al, 1993).

Morphine is expected to decrease the arterial blood pressure responses to peripheral noxious stimuli, so the finding that morphine increased the somatosympathetic pressor response to peripheral C-fiber stimulation (Kim et al, 1988; Kwon, 1988) was unexpected. One can think of several possibilities. The first one is the differences in experimental conditions between the peripheral sympathetic nerve recording study and the arterial blood pressure study. For example, few studies which recorded the peripheral sympathetic nerve activity used stimuli with such high intensity and frequency as in the arterial blood pressure study. Another one is that the responses of the peripheral sympathetic nerves and arterial blood pressure would be different each other. Arterial blood pressure depends on the cardiac output and the total peripheral vascular resistance. The peripheral vascular resistance is determined by peripheral sympathetic activity. The sympathetic activities recorded from various organs are not the same and there is a functional differentiation among subretrofacial neurons of the rostral ventrolateral medulla in their relative control of the sympathetic vasoconstrictor supply to the skin and skeletal muscle. Furthermore, those neurons are organized topographically (Barman et al, 1984; Dampney & McAllen, 1988; Stein et al, 1989).

In addition, there would be a difference in the mechanism of morphine action on the arterial blood pressure response and somatosympathetic reflex. The somatosympathetic C-reflex is abolished by intrathecal injection of opioids (Swenzen et al, 1988; Wang et al, 1992; 1993), but only slightly affected

by morphine administered in the brainstem via vertebral artery (Kato et al, 1992). However, arterial pressor response to C-afferent stimulation is increased by systemic morphine and decreased by intrathecally administered morphine (Kim et al, 1988; Kwon, 1988). In the present study we attempted to analyze the relationship between the somatosympathetic reflex and arterial blood pressure response during peripheral nerve stimulation and compare the effects of morphine on them. For this, 1) the effects of morphine on the arterial blood pressure response to the peripheral nerve stimulation were determined, 2) single sympathetic postganglionic fiber activities were recorded and 3) the effects of morphine on the sympathetic fiber activity were investigated.

MATERIAL AND METHODS

Animal preparations

Experiments were performed on thirty adult cats (1.8～3.3 kg) of either sex. Animals were pretreated with atropine sulfate (Kwang Myeong Pharm., 0.1 mg/kg, i.m.), sedated with ketamine (Ketalar, Yuhan Pharm., 10～20 mg/kg, i.m.) and anesthetized with α-chloralose (Sigma, St. Louis, MO, U.S.A., 60 mg/kg, i.v.). The trachea, femoral artery and vein were cannulated for artificial ventilation, blood pressure monitoring and drug injection, respectively. The animals were paralyzed with pancuronium bromide (Mioblock, Organon Teknika B.V., Boxtel, Holland, initial dose 0.4 mg, maintenance dose 0.4 mg/hr, i.v.) and ventilated with an animal respirator (Harvard Respirator 645, tidal volume 20～30 ml, rate 20～30/min.). End-tidal PCO_2 was monitored (Normocap CO_2 & O_2 Monitor, Datex Instrumentarium, Helsinki, Finland) and maintained within the range 3.5～4.5% by adjusting the respirator. Rectal temperature was monitored and maintained within the range 37～38℃ by an electric blanket (Homeothermic Blanket Control Unit, Harvard Apparatus, Edenbridge, Kent, UK). The electrocardiogram was recorded using subcutaneous pin electrodes and cardiac pulses were recorded by Ratemeter (4522, Device Ltd., Welwyn Gardn City, Hertfordshire, U.K.). Hartmann solution was infused using infusion pump (Harvard Apparatus, Southnatick, MA, U.S.A.) at the rate of 10～15 ml/hour.

Sciatic nerves and their branches were exposed after incision of skin of both hindlimbs. Sural nerve (a pure sensory nerve), nerves to gastrocnemius muscle and common peroneal nerve (a mixed nerve) were dissected under a surgical microscope. In other groups of animal the cervical and abdominal sympathetic trunks were identified and dissected. In these group the femoral or saphenous nerve was also dissected. A laminectomy was performed at the L4 to S1 vertebrae and the lumbosacral enlargement was exposed.

After the surgical process was over, the animal was mounted on a stereotaxic frame and a mineral oil pool was made using the incised skin. The preparations was then allowed to stabilize for 50 min.

Stimulation and recording

A tripolar platinum electrode was hooked around one of the isolated peripheral nerves in one hindlimb for electrical stimulation. The most proximal pole was grounded to prevent current spread, the middle pole was connected to the negative terminal, and the distal pole was connected to the positive terminal. To determine the stimulation intensity a recording electrode was placed proximal to the stimulating electrode. Aα, β, δ and C waves in a compound action potential were identified and their thresholds for activation were determined. In most cases the threshold intensities for the Aδ-fiber and C-fiber were a couple of tens of times and several hundred times, respectively. In present study we used stimuli of 1 mA, 0.1 ms square pulses for Aδ-fiber activation, and 10 mA, 0.5 ms pulses for the activation of C-fibers. Square pulses were generated by a stimulator (Pulsemaster A300, WPI, Sarasota,

Florida, U.S.A.).

To record single fiber activities the sural and nerves to gastrocnemius muscles in remaining hindlimb were cut distally and their perineurium were removed. The nerves were dissected into fine fascicles under a surgical microscope with fine scissors and tweezers. One of the fascicles was mounted on a bipolar platinum recording electrode. The signals picked up were fed into an AC amplifier (DAM 80, WPI, Sarasota, Florida, U.S.A.) and amplified 10,000 times. Amplified signals were monitored on an oscilloscope (Nicolet 4094C, Madison, Wisconsin, U.S.A.) and simultaneously processed via a window discriminator (Frederick Haer & Co, U.S.A.), laboratory interface (CED 1401, Cambridge, U.K.) and stored in IBM personal computers. Whether the recorded nerve fiber activity was a postganglionic fiber of sympathetic nerve or not was determined by the following criteria: 1) spontaneous activity which was recorded from the proximal nerve stump cut distally in case of cutaneous nerve, 2) in case of muscular nerve, a post R-wave analysis triggered by R-waves of ECG signals was performed and whether the single fiber unit showed a cardiac-related discharge pattern or not. Furthermore each unit activity was tested for its respiration-related rhythmic discharge pattern by using endtidal PCO_2 triggered unit analysis.

At the end of each experiment the animal was sacrificed with a sufficient dose of anesthetic. All data are expressed as mean $\pm$ SE. Significant differences between groups were determined with paired or non paired Student's *t*-tests.

RESULTS

Effects of morphine on the arterial blood pressure response to peripheral afferent nerve stimulation

For cutaneous afferent activation, the sural or saphenous nerve was stimulated. For muscle afferent activation, nerves to the gastrocnemius muscles were stimulated. The common peroneal nerve was stimulated for mixed nerve activation. In Fig. 1 a typical example of arterial blood pressure response to the common peroneal nerve activation is shown. The arterial blood pressure was depressed when the common peroneal nerve was stimulated with Aδ -intensity, low frequency stimuli and was elevated when stimulated with C-intensity, high frequency stimuli. After systemic injection of morphine (2 mg/kg), the pressor response was increased and the depressor response decreased. These effects of morphine were reversed by systemic injection of naloxone (0.4 mg/kg), a morphine antagonist. The resting blood pressure level was elevated after naloxone. A total of eight experiments were performed and the results are summarized in the Table 1. In the case of cutaneous nerve the arterial blood pressure was elevated by C-afferent activation from a control value of 127.8 to 152.4 mmHg, and depressed by Aδ-afferent stimulation from 128.0 to 120.4 mmHg. In the case of muscle afferent activation, blood pressure was elevated by C-afferent stimulation from 127.6 to 151.4 mmHg and depressed by Aδ-afferent from 127.6 to 117.6 mmHg. In the case of mixed nerve activation, blood pressure was elevated by C-afferent activation from 129.2 to 173.6 mmHg and depressed by Aδ-activation from 127.6 to 107.0 mmHg.

After intravenous injection of morphine, arterial blood pressure was depressed and reached to the lowest level at 5~10 min after injection. Thereafter the pressure recovered slowly over one hour or longer. Systemic morphine depressed the resting arterial blood pressure by 20~30 mmHg at 15~30 min. In the case of cutaneous nerve, morphine depressed the arterial blood pressure from 127.8 to 94.0 mmHg, and C-afferent activation elevated it to 133.0 mmHg. The arterial blood pressure was depressed by Aδ -activation from 91.8 to 86.2 mmHg after morphine. In the case of muscle afferent activation, the arterial pressor response was

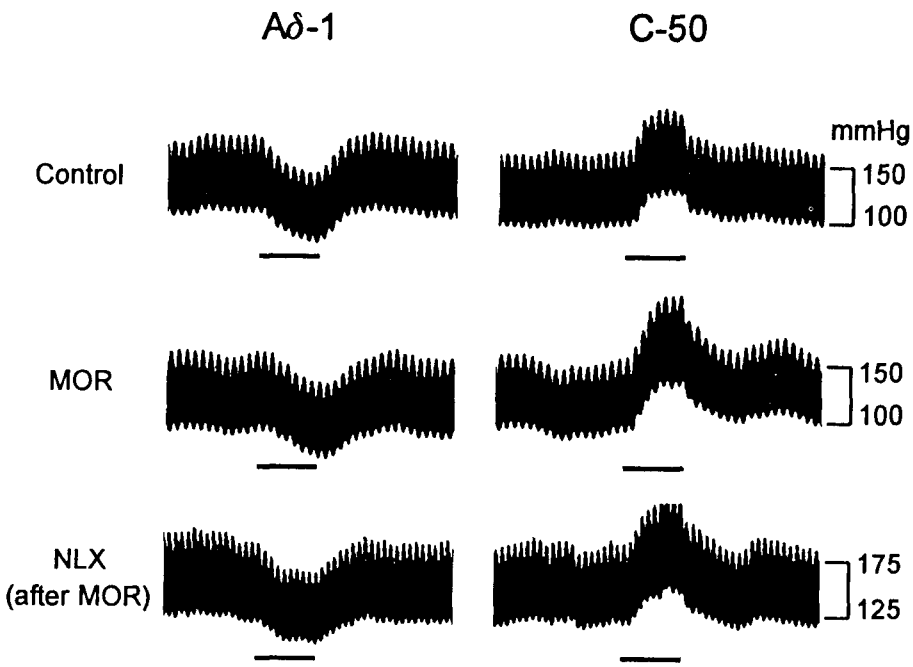

Fig. 1. An example of arterial blood pressure response to peripheral nerve stimulation in an anesthetized cat. Common peroneal nerve was isolated and stimulated with either at Aδ-intensity with low frequency (1 Hz) or at C-intensity with high frequency (50 Hz) for 20 sec. MOR, morphine; NLX, naloxone. Horizontal bars indicate the time intervals of peripheral nerve stimulation.

Table 1. Effects of morphine on the arterial blood pressure responses evoked by peripheral afferent nerve stimulation (mmHg)

	Control(n=5)		MOR(n=5)		NLX(n=4)	
	Before	After	Before	After	Before	After
Pressor response						
Common Peroneal N.	129.2±4.4	173.6±8.9	106.8±15.3	163.2± 7.6	126.8±15.5	192.3± 9.6
Gastrochemius N.	127.6±5.4	151.4±5.9	98.4± 8.6	137.6±12.0	125.5±14.8	153.5± 9.7
Sural N.	127.8±5.7	152.4±5.0	93.8± 8.7	133.0±11.0	136.5±14.5	162.5±14.3
Depressor response						
Common Peroneal N.	127.6±4.0	107.0± 8.7	97.2±13.4	82.0±11.4	134.8±16.3	106.5±12.9
Gastrocnemius N.	127.6±6.9	117.6± 4.7	93.8± 8.7	88.6± 6.7	129.0±13.5	121.3±10.3
Sural N.	128.0±7.1	120.4±10.1	91.8±11.0	86.2±11.1	138.5±15.4	125.5±17.0

MOR: morphine i.v. (2 mg/kg), NLX: naloxone i.v. (0.08 mg/kg).

before, after: before and after electrical stimulation of nerve, respectively.

Pressor responses were induced by C-intensity, high frequency stimulation and depressor responses were induced by Aδ-intensity, low frequency stimulation.

Experimental data were obtained at 30 min intervals after the administration of each drug.

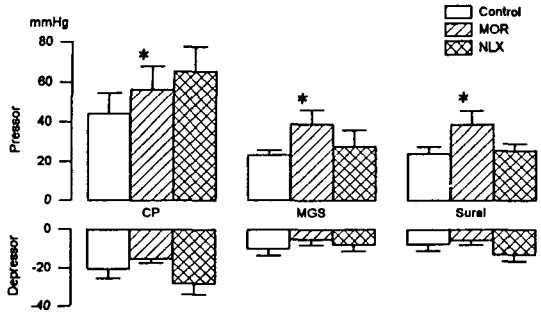

Fig. 2. Effects of morphine on the pressor and depressor response evoked by either C- or Aδ-afferent activation. CP, common peroneal nerve; MGS, nerve to medial gastrocnemius; Sural, sural nerve (, p<0.05).*

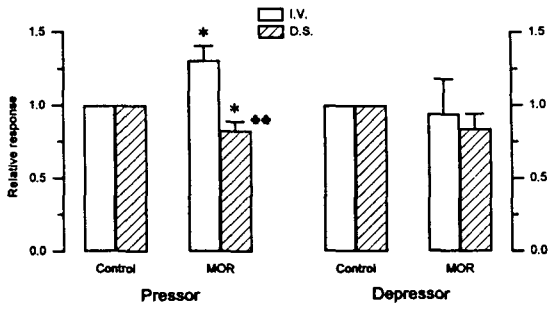

Fig. 3. Comparison of the effects of morphine via the two routes of administration. I.V., intravenous application; D.S., direct spinal application (, p<0.05; **, p<0.01).*

from 98.4 to 137.6 mmHg and the depressor response was from 93.8 to 88.6 mmHg. In the case of mixed nerve stimulation, the pressor response was from 106.8 to 163.2 mmHg and the depressor response, from 97.2 to 82.0 mmHg. In summary, during the state of arterial blood pressure depression by systemic morphine, the pressor response to peripheral C-afferent stimulation was increased significantly and the depressor response to Aδ-afferent stimulation was decreased, but was not significant statistically, as shown in Fig. 2.

To study the site of morphine action on blood pressure responses to peripheral afferent activation we compared the morphine effects between the routes of administration, i.e. intravenous or direct spinal application. By intravenous morphine administration, the amplitude of pressor response was increased from 44.4 to 56.4 mmHg and depressor response was decreased from 20.6 to 13.2 mmHg. However, direct administration of morphine to the spinal dorsal surface decreased the pressor response to C-afferent activation from 65.3 to 53.5 mmHg and decreased the depressor response, from 27.5 to 23.0 mmHg. The results suggest that a supraspinal mechanism may be involved in the enhanced arterial

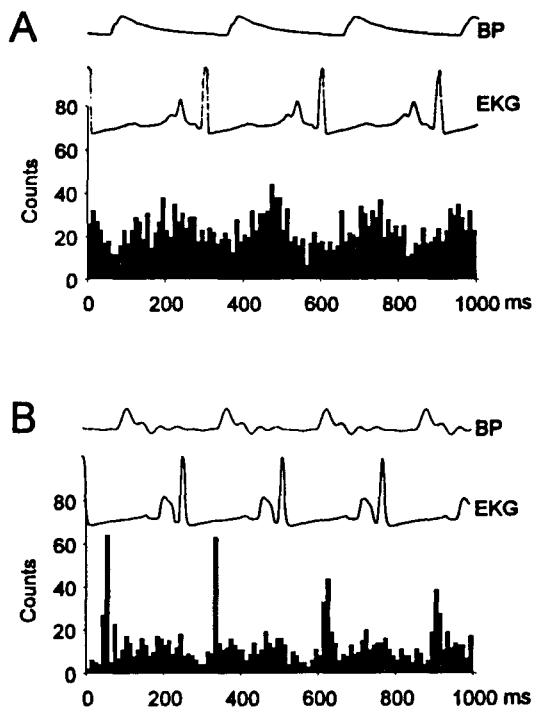

Fig. 4. Examples of cervical (A) and abdominal (B) single sympathetic nerve fiber activity. The sympathetic fibers showed cardiac-related periodic discharge patterns. The post R-wave histograms were compiled from 500 sweeps of activities (100 bin, 10 ms bin width).

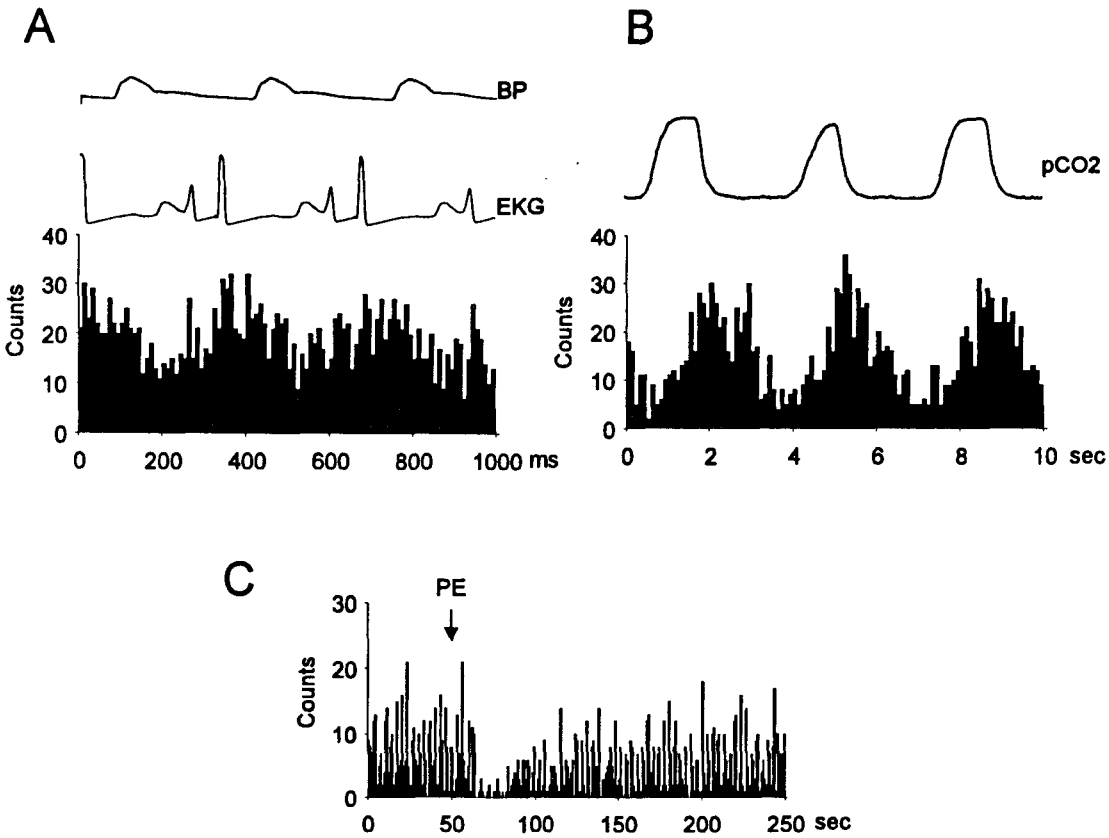

Fig. 5. An example of single cutaneous sympathetic nerve fiber activity recorded from the saphenous nerve. This unit showed both cardiac-related (A) and respiration-related (B) rhythms. In C, phenylephrine (PE, 1 mM, 0.2 ml, i.v.) was administered at 50 seconds to activate the baroreceptor activity.

pressor response during application of intravenous morphine to peripheral C-afferent activation.

Activity of peripheral sympathetic postganglionic nerve

The next step of the study was to record the single or multiunit peripheral sympathetic fiber activities. Fig. 4 shows examples of single fiber activities recorded from cervical (A) and abdominal (B) sympathetic trunks. The post R-wave histograms, compiled from 500 sweeps with 100 bins of 10 ms bin width, clearly showed the relation of their discharge pattern to cardiac rhythm. A total of six fibers from the cervical sympathetic trunk were recorded and some of them also showed the respiratory related periodic discharge pattern. Among the four abdominal sympathetic fiber activities recorded, two showed a cardiac related discharge pattern.

Cutaneous sympathetic fiber activities were determined by spontaneous activity recorded from the cut end of a nerve fiber. Rhythmic discharge patterns coincided with cardiac and/or respiratory rhythms and baroreceptor responses to arterial blood pressure elevation. Fig. 5 shows an example of single cutaneous nerve fiber activity recorded from the sural nerve. The activity showed cardiac related periodicity with a cycle length of 330 ms determined by a post R-wave histogram. Fig. 5B shows a

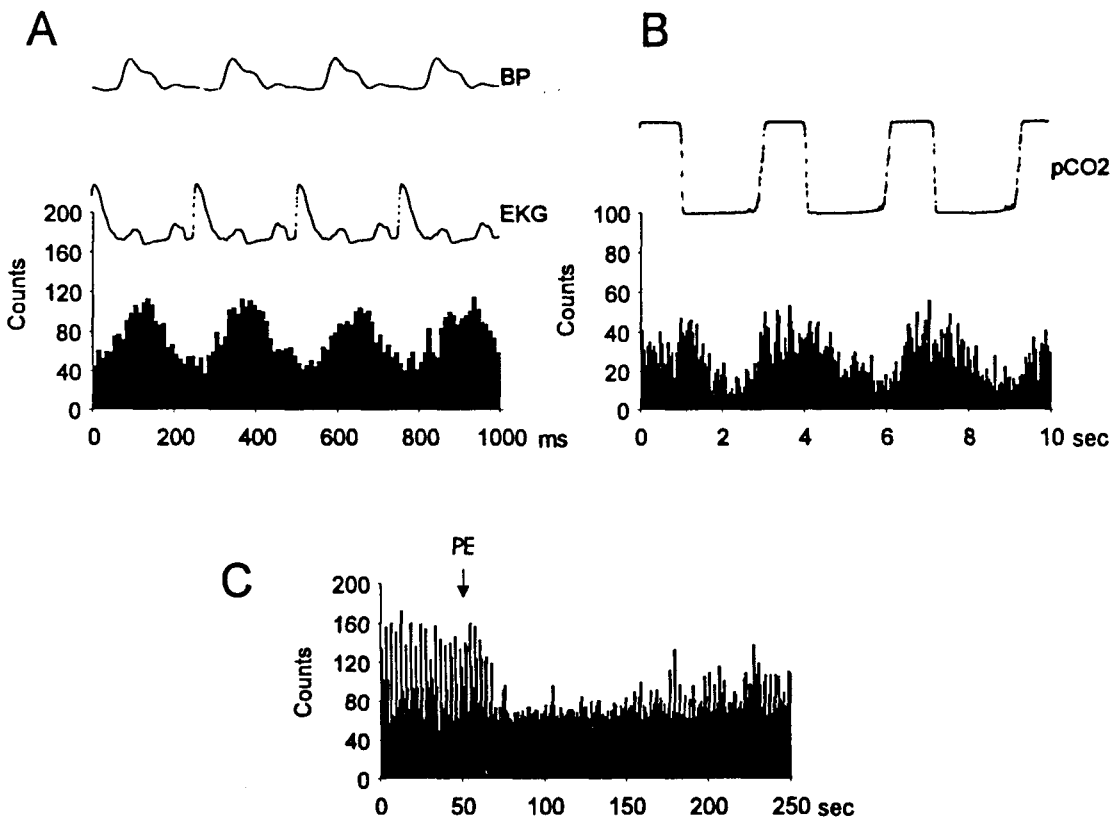

Fig. 6. An example of single muscular sympathetic nerve activity recorded from the nerve to the medial gastrocnemius muscle. This unit also showed both cardiac-related (A) and respiration-related (B) rhythms. Phenylephrine was injected at 50 s.

post-PCO_2 histogram which was compiled from 20 sweeps of activities with 200 bins of 50 ms bin width. The histogram was triggered by the signals from the PCO_2 monitor at the peak of the expiratory PCO_2 level. The recorded sympathetic fiber also showed a respiratory related rhythm of period 3.4 sec, which coincided with the respiration rate of 18 /min. As shown in Fig. 5C, the single fiber activity was reduced suddenly when phenylephrine (1 mM, 0.2 ml, i.v.) was administered to activate the baroreceptor reflex at 50 sec after the onset of a single pass time histogram (500 bins of 1 sec width) and thereafter its activity recovered slowly. A total of ten cutaneous sympathetic fiber activities were recorded from the sural or saphenous nerve. All of them showed a respiratory related discharge pattern and five of them also showed a cardiac related rhythm as summarized in Table 2.

Muscular sympathetic fiber activities were determined by the same criteria as those used in the cutaneous sympathetic fiber. Some alpha and gamma motor nerve fibers also showed spontaneous discharges but from their amplitude and shape we could easily rule out them. In Fig. 6, an example of muscle sympathetic fiber activity is shown. The unit showed both cardiac (A) and respiration related (B) rhythms, of which the cycle lengths were 250 ms and 3 seconds, respectively. Fig. 5C shows the baroreceptor response to blood pressure elevation. A total of fifteen muscular sympathetic fibers were

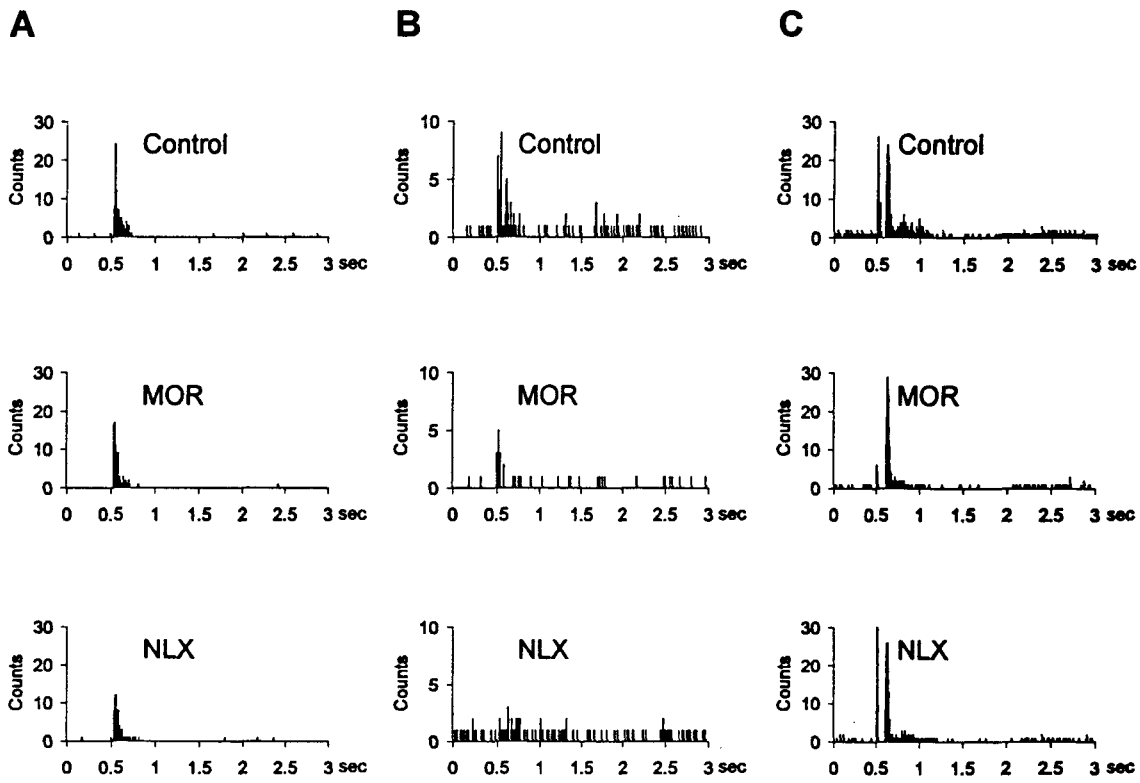

Fig. 7. Effects of morphine on the response of single fiber activities recorded from cervical (A), abdominal (B) and cutaneous (C) sympathetic nerves to three pulses of stimuli with C-intensity, at high frequency. The post-stimulus time histograms were compiled from 20 sweeps with 1500 bins (2 ms bin width).

identified and eleven of them showed cardiac-related rhythm whereas only four showed respiratory-related rhythm (Table 2).

Table 2. Rhythmic discharge patterns of the sympathetic fiber activity recorded from muscle and skin nerves

	No. of smpathetic fiber activities showing		
	Card. rhythm	Resp. rhythm	Card.+Resp. rhythm
Skin N (n=10)	5	10	5
Muscle N (n=15)	11	4	4

Card, cardiac; Resp., respiratory

Effects of morphine on the response of sympathetic fiber to peripheral nerve stimulation

Fig. 7 shows the effect of morphine on the response of single peripheral sympathetic fiber activity to the three train pulses of stimuli with C-intensity, 50Hz. The post-stimulus time histograms were compiled from twenty sweeps with 1500 bins of 2 ms width. The pulses were applied 500 ms after the onset of each sweep. The number of action potentials during the Aδ-response of the cervical sympathetic fiber (Fig. 7A) determined by the latency after stimulation before and after morphine administration was reduced to 302 and 275, respectively. The number of action potentials elicited by C-

Table 3. Effects of morphine on responses of the cervical and abdominal sympathetic nerve fiber to peripheral afferent nerve stimulation

	MOR	NLX
CSC (n=10)		
Resting	88.6±19.2	177.8±51.9
Aδ-response	113.1± 7.8	135.5±21.4
C-response	58.9±11.8	93.3±32.8
ASC (n=4)		
Resting	83.6±11.0	107.5± 5.0
Aδ-respons	48.7±27.0	60.7±15.0
C-response	71.0±21.3	126.6±16.1

Data of resting state were obtained during the first 500 ms intervals.

All the data were shown as percentile change to control responses.

CSC: cervical sympathetic chain.

ASC: abdominal sympathetic chain.

stimuli decreased from 17 before morphine injection to 9 after morphine injection. Fig. 7B shows an example of the abdominal sympathetic fiber activity. The number of action potentials during A-reflex decreased from 41 to 9 and the number during the C-reflex decreased from 11 to 4 after morphine injection. Naloxone partially reversed the morphine effect of morphine on both cervical and abdominal sympathetic fibers. The results obtained from 10 cervical sympathetic fibers and four abdominal fibers are summarized in Table 3. Morphine injection induced no significant changes in the single fiber activity during resting state (88.6+19.2%, n=10). In the case of the Aδ-reflex, the response of the abdominal sympathetic fiber was decreased to 48.7+ 27.0% by morphine. However, the Aδ-reflex of the cervical sympathetic fiber increased insignificantly. Morphine injection decreased the C-reflexes of both cervical and abdominal sympathetic fibers to 58.9+11.8% and 71.0+21.3%, respectively.

Fig. 7C shows the effects of morphine on the response of single cutaneous sympathetic fiber activity. The number of action potential during the A-reflex was reduced from the control of 582 to 427 after morphine injection. The number during the C-reflex was markedly decreased from 206 to 36 by morphine. The changes of activities recorded from muscular sympathetic nerve fibers were not influenced by morphine, but the number of nerves studied was too small to show any statistical significance.

DISCUSSION

The results of the present study can be summarized as follows: 1) arterial blood pressure was depressed by Aδ-intensity, low frequency (A-response) peripheral nerve stimulation and was elevated by high frequency C-afferent activation (C-response). 2) Intravenously administered morphine enhanced the C-response significantly but decreased the A-response insignificantly. Only the C-response was decreased by direct spinally administered morphine. 3) All the recorded cutaneous sympathetic single fiber activity showed a periodic discharge pattern related to respiration rhythm and two-thirds of the muscular sympathetic fibers showed a cardiac-related discharge pattern. 4) Morphine decreased the sympathetic C-reflex elicited by peripheral C-afferent activation but there was no significant change in the A-reflex.

The changes in arterial blood pressure caused by stimulation of the peripheral afferent nerves coincide with previous reports from other authors (Chung & Wurster, 1976; Chung et al, 1979; Mitchell & Schmidt, 1983). Here, stimulation with C-intensity can activate both C- and Aδ-afferent fibers. Thus the response to C-stimulation in the present study could be the combined result of the activation of both C- and Aδ-afferent fibers. It is more likely, however, that C-responses in present study are due to activation of the C-afferent fiber because arterial blood pressure was not significantly changed by Aδ

-intensity, high frequency stimulation (data were not shown in present study).

We do not know the physiological meaning of the A- or C-response but it would be likely that A-response and C-response are related with Aδ-pain and C-pain, respectively. Thus, one can expect that administration of morphine would depress arterial blood pressure response evoked by activation of the peripheral afferent nerve. However, intravenous morphine enhanced the pressor response to C-afferent activation. The enhanced effect was due to a true morphine action because naloxone could reverse it. Other authors have reported that morphine administered to the brainstem via the vertebral artery produced a nonselective and slight depression of the somatosympathetic C-reflex (Kato et al, 1992). The A-response is less sensitive to intravenous morphine than C-response (Sato et al, 1985), which is supported by the report that the C-reflex is more selectively and markedly depressed by intravenous opioids than the A-reflex (Niv & Whitwam, 1983). This suggests that the mechanism of morphine action would be different between nociceptive Aδ- and C-afferent processing (Kato et al, 1992).

In the present study, morphine was administered intrathecally to investigate whether the mechanism of enhancement of the C-response by morphine is spinal or supraspinal. Intrathecal morphine decreased the C-response. This means that the spinal nociceptive C-afferent process would be decreased by direct spinal morphine action, which is supported by the well known contention that most of the spinothalamic tract (STT) neurons are inhibited by morphine (Duggan et al, 1976; Wilcockson et al, 1986), although some of the STT cells can be excited by morphine (Wilcockson et al, 1986). It seems that the C-reflex is sensitive to opioids (Niv & Whitwam, 1983; Swenzen et al, 1988; Wang et al, 1992). The present study also showed that C-reflexes recorded from the abdominal & cervical sympathetic fibers were depressed by morphine. These findings suggest that the spinal dorsal horn is an important target site for the antinociceptive actions of morphine. However, the result that the arterial pressor response to stimulation of the peripheral C-afferent nerves was enhanced by intravenous morphine suggests that the enhancing mechanism of morphine on the pressor response would exist at a supraspinal level.

It is well known that spontaneous activities recorded from the single peripheral sympathetic nerve fiber are closely correlated with cardiac and respiratory rhythms (Preiss et al, 1975; Gilbey et al, 1986; Boczek-Funcke et al, 1992; Haebler et al, 1993). In general the relationship between sympathetic nerve activity and cardiac or respiratory rhythm is different according to animal species or innervating organs (Gilbey et al, 1986; Boczek-Funcke et al, 1992; Zhou & Gilbey, 1992). For example muscular sympathetic fibers are sensitive to the baroreceptor activation and have cardiac related rhythm, and can be activated by noxious stimuli, visceral stimuli and chemoreceptor activation. However, the cutaneous sympathetic fibers are less activated by baroreceptor activity and inhibited by noxious stimuli to skin or viscera (Blumberg & Jaenig, 1985; Jaenig, 1988), although some of cutaneous sympathetic fibers could be activated strongly by noxious stimuli (Gregor & Jaenig, 1977). It seems that the relationship between peripheral sympathetic nerve fiber activity and cardiac-related rhythm is more complex than has been considered and muscular sympathetic nerve has a closer relationship with respiratory rhythm than cutaneous sympathetic nerve (Jaenig & McLachlan, 1986).

In the present study, all the recorded cutaneous sympathetic fibers showed respiratory related rhythm and five of them also showed cardiac related rhythm. Most of the muscular sympathetic fibers showed cardiac related rhythm and a half of them showed respiratory related rhythm. These findings support the reports of other authors above, except in that cutaneous sympathetic fibers are strongly influenced by respiratory rhythm.

The effects of morphine on the cervical responses seems to be different to the effect on abdominal sympathetic fibers. In the case of the cervical sympathetic fiber, morphine did not change the A-reflex but decreased the C-reflex to a half the control level. On the other hand, both A- and C-reflexes in abdominal sympathetic fiber were decreased by morphine. Since the cutaneous sympathetic response to peripheral afferent activation would be different, to that of muscular sympathetic activity (Jaenig, 1988; Haebler et al, 1994), the cervical sympathetic response to peripheral afferent activation might be different, to that of abdominal sympathetic activity, but do not know of any report supporting the possibility.

In conclusion it seems that supraspinal mechanisms are involved in the enhanced arterial pressor response to peripheral C-afferent activation by intravenously administered morphine.

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