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Excitatory and inhibitory effects of vagal afferent input on nociceptive neurons in the nucleus ventralis posterolateralis of the cat thalamus

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Abstract: Forty three nociceptive specific (NS) and 36 wide dynamic range (WDR) neurons recorded from the shell region of nucleus ventralis posterolateralis (VPL) of the thalamus were examined for responses to electrical stimulation of the cervical vagus nerve in urethane-chloralose anesthetized cats. Each neuron could be excited by manipulation of its cutaneous receptive field and by electrical stimulation of the greater splanchnic nerve (SPL). The vagus nerve stimulation excited 8 NS and 4 WDR neurons, suggesting that vagal afferents can mediate visceral pain. In the remaining 35 NS and 32 WDR units, a conditioning-test paradigm was used to examine effects of the vagus nerve stimulation on responses evoked by electrical stimulation of SPL and/or spinothalamic tract fibers in the ventrolateral funiculus (VLF). The conditioning vagus nerve stimulation inhibited responses to SPL input in 27 NS and 25 WDR units. In 18 NS and 15 WDR units effects of conditioning vagal nerve stimulation on responses to SPL and VLF stimulation were examined. Inhibition of both responses was observed in 12 NS and 11 WDR units. Following local anesthetic blockade of the midbrain periaqueductal gray (PAG) and/or nucleus raphe dorsalis (NRD), the inhibitory effect of the vagus nerve stimulation on responses of NS and WDR units to VLF stimulation was eliminated, whereas the inhibitory effect on responses to SPL stimulation was unaffected. The data suggest that vagal afferents can activate ascending antinociceptive pathway from the PAG/NRD onto the VPL, in addition to descending antinociceptive system acting upon the spinal cord.

Key words: vagus nerve, thalamus, nucleus ventralis posterolateralis, antinociception, pain, cat

INTRODUCTION

The transmission of nociceptive information is subject to regulation by endogenous pain control systems (Basbaum and Fields, 1984; Besson and Chaouch, 1987). It has been proposed that activation of vagal afferents is one way to trigger endogenous pain control systems (Randich and Gebhart, 1992; Ren et al., 1989). Foreman and his colleagues (Thies and Foreman, 1981, 1983; Ammons et al., 1983a, 1983b) showed that activation of either cervical or thoracic vagal afferents generally inhibited resting, somatic-

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evoked or bradykinin-evoked activity of thoracic spinothalamic tract neurons believed to be important in the perception of cardiac pain. Subsequently, it became evident that electrical stimulation of vagal afferents not only inhibits, but also facilitates, nociception as assessed by either nocic eptive reflexes (Ren et al., 1988) or background activity and responses of spinal dorsal horn neurons to noxious heating of the skin (Ren et al., 1989). Recently, an ascending antinociceptive system arising from nucleus raphe dorsalis (NRD) and periaqueductal gray (PAG) has been found to modulate transmission of visceral input to nociceptive neurons in the intralaminar nuclei (Anderson, 1983; Qiao and Dafny, 1988; Koyama et al., 1995) and nucleus ventralis posterolateralis (VPL) of the thalamus (Horie et al., 1991, Koyama et al., 1995). It has also been found that electrical stimulation of the nucleus raphe magnus (NRM) exerts an ascending inhibitory action on transmission of nociceptive impulses onto neurons in the shell region of the VPL of the cat thalamus (Koyama and Yokota, 1993). It is known that lesions or anesthetic blockade of the NRM attenuates antinociception produced by vagal afferent stimulation (Randich et al. 1990; Ren et al., 1990b). However, inhibitory/excitatory effects of vagal afferent stimulation on activities of thalamic nociceptive neurons have not yet been studied. The present study was undertaken to assess inhibitory/excitatory effects of vagal afferent stimulation on nociceptive neurons in the shell region of VPL.

METHODS AND MATERIALS

Experiments were performed on adult cats weighing between 2.5 and 4.0kg. Anesthesia was induced with ketamine hydrochloride (20mg/kg, i.m.), and maintained with a solution of urethane and chloralose (urethane 125mg/mℓ, chloralose 10mg/mℓ) in normal saline (dose: 3.5mℓ/kg). This was supplemented as required. Blood pressure was monitored continuously via a catheter implanted into the right femoral artery.

The left greater splanchnic nerve (SPL) was exposed retroperitoneally through an incision in the lumbosacral fascia at the lateral edge of the erector spinae muscle mass. The exposed SPL was dissected free from surrounding tissues at the level just proximal to the coeliac ganglion. A bipolar platinum hook stimulating electrode was placed on the SPL. Additional bipolar stimulating electrodes were placed on the right and left cervical vagus nerves. The stimulating electrodes were held in place with low melting point (39℃) wax to prevent the nerves from drying out.

Craniotomies were performed over VPL (to allow access for microelectrode exploration), somatosensory cortex (to allow access for antidromic stimulation), and midbrain (to allow placement of an injection cannula). In addition, a laminectomy was performed exposing the dorsum of the spinal cord at the level of C_3 and C_4 for insertion of a bipolar stimulating electrode into the right ventrolateral funiculus (VLF).

Recordings were made from single units in the VPL using glass capillary microelectrodes filled with a 2% solution of pontamine sky blue in 1 M sodium acetate. During recordings the animals were paralyzed with pancuronium bromide (0.4mg/kg; i.v.), and artificially ventilated. Tidal volume and respiratory rate were adjusted to maintain end-tidal CO_2 between 3.5 and 4.5%. Body temperature was monitored with an esophageal probe and maintained at 37.0±1℃ with an electric heating pad under the abdomen and an infrared lamp.

The peripheral receptive field characteristics of neurons in VPL were assessed using a variety of mechanical stimuli: gentle brushing of the skin with a soft brush, pressure applied to a

fold of skin using a pair of broad-tipped forceps, and pinching with a pair of fine rat-toothed forceps. The output of the oscilloscope on which the responses of single thalamic units were displayed was connected to a window discriminator that was connected to a spike counter. The output from the spike counter consisted of a count of the number of spikes in each sequential 1-s bin during a period of background, and both during and after mechanical stimulation of the cutaneous receptive field.

All units were tested for SPL input, and nociceptive units with SPL input were subjected to the study of effects of vagus nerve stimulation. Inhibitory effects were evaluated in a conditioning-test paradigm assessing the time course of vagal influences during electrical stimulation of either the SPL or the VLF at 1Hz. Conditioning stimulation applied to the cervical vagus nerve consisted of a train of 5 pulses at 400Hz. The duration of each pulse was 0.2ms. The intensity was variable. Stimulus artifacts and unit responses to stimuli were displayed on a personal computer using a dot raster processing program QP-130J (Nihon kohden Co.), and printed out after the experiment. Locations of units studied were marked by extruding a small amount of pontamine sky blue from the microelectrode tip electrophoretically (5μA DC current passed 10min).

After the experiment, the VLF stimulation site was lesioned electrolytically, with a current of 1 mA for 1 min. Animals were then deeply anesthetized, and perfused with a 1 L solution of 0.5% potassium ferrocyanide in normal saline, followed by 2 L of 10% formalin. Serial sections (50-μm thick) were cut, stained with Cresyl violet, and the locations of both the stimulation and recording sites were checked.

Data are expressed as means±S.E.M. Statistics were performed for time-course data. Analysis of mean effects were done with one-way analysis of variance. Statistical comparisons were made using Student's t-test for grouped or paired data. Data were considered significant, if $P<0.05$.

RESULTS

A total of 79 cutaneous nociceptive VPL units receiving SPL afferent input were recorded from the dorsal and ventral shell regions of the VPL (Yokota et al., 1988; Yokota, 1989). Of these, 43 units were nociceptive specific (NS) units. The remaining 36 units were wide dynamic range (WDR) units. Locations of both NS and WDR units with SPL input in the shell region of VPL are summarized in Fig. 1, and locations of their receptive fields are summarized in Figs. 2 and 3. NS units were located in the middle half of the dorsal and ventral shell regions of the caudal VPL. WDR units were located in the middle half of the dorsal and ventral shell regions of a narrow zone just rostral to the NS zone where NS units were located. NS units had a circumscribed receptive field on the contralateral integument. They did not respond to brushing and innocuous pressure but showed a sustained discharge when a noxious pinch was applied to the cutaneous receptive field (Fig. 4B). WDR units had a graded response to brushing, pressure and noxious pinch applied to the center of the receptive field (black area in Fig. 5A), responding best to noxious pinch. Outside this zone (cross-hatched area in Fig. 5A), units were unresponsive to low intensity mechanical stimuli, but responded differentially to pressure and noxious pinch. Finally, the latter area was surrounded by an area in which only noxious pinch resulted in neuronal discharges (shaded area in Fig. 5A). Cutaneous receptive fields of NS units were distributed in the posterior forearm, posterior arm, area of scapula, chest, abdomen and anterior thigh. These areas

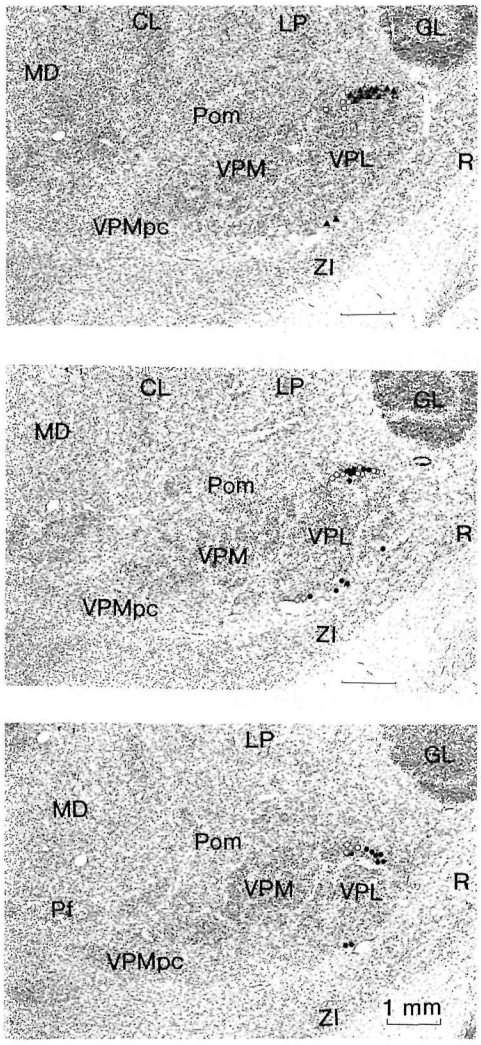

Fig. 1 Locations of nociceptive units receiving greater splanchnic nerve input. Nociceptive specific (NS) units were located in the dorsal and ventral shell regions of caudal nucleus ventralis postrolateralis (VPL). Wide dynamic range (WDR) units were located just rostral to the NS zone.

◇: NS unit excited by vagus nerve stimulation (VNS).
●: NS unit inhibited by VNS.
○: NS unit unaffected by VNS.
□: WDR unit excited by VNS.
▲: WDR unit inhibited by VNS.
△: WDR unit unaffected by VNS.
CL=nucleus centralis lateralis;
GL=corpus geniculatum laterale;
LP=nucleus lateralis posterior;
MD=nucleus medialis dorsalis;
Pom=medial region of posterior thalamic nuclear group;
R=nucleus reticularis thalami;
VPL=nucleus ventralis posterolateralis;
VPM=nucleus ventralis posteromedialis proprius;
VPMpc=nucleus ventralis posteromedialis parvocelluralis;
ZI=zona incerta.

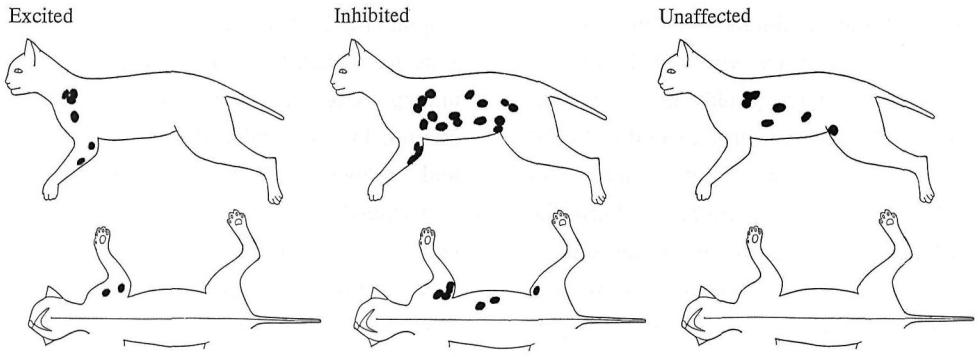

Fig. 2. Distribution of cutaneous receptive fields of NS units.

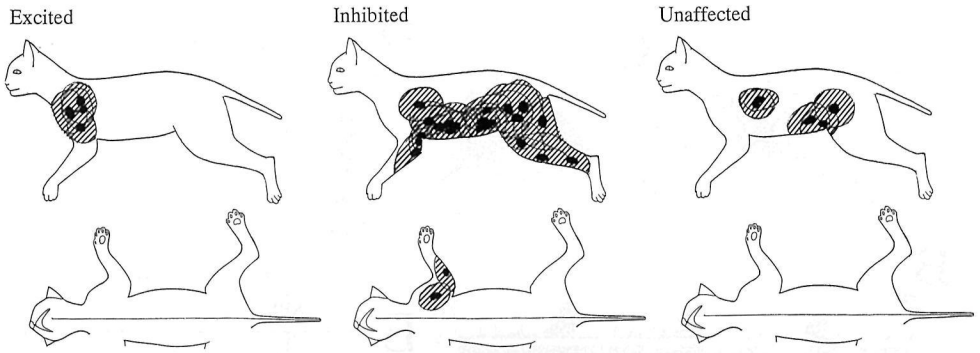

Fig. 3. Distribution of receptive fields of WDR units. Black area indicates low threshold center and shaded area indicates high threshold surround.

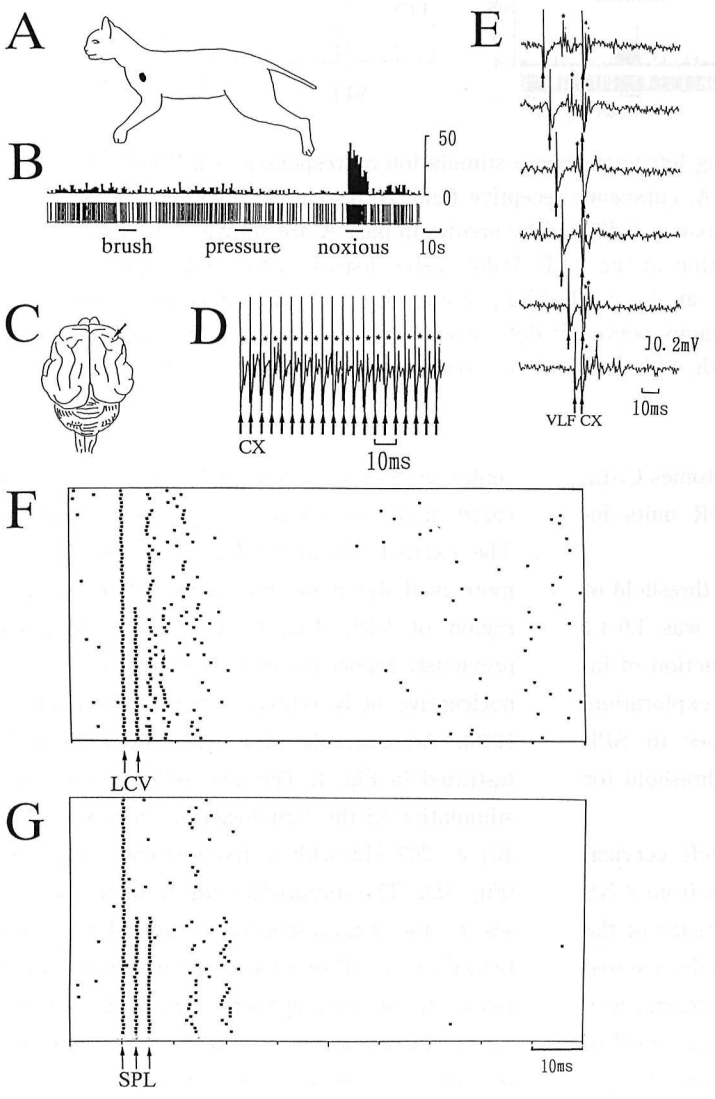

Fig. 4. Effects of vagus nerve stimulation on a VPL NS unit.
A: cutaneous receptive field.
B: responses to mechanical stimulation of the skin within the center of the cutaneous receptive field.
C: stimulation site in the SI somatosensory cortex (indicated by an arrow)
D: responses of the unit to 200 Hz stimulation of the SI somatosensory cortex (CX) shown in C.
E: collision test using the ipsilateral ventrolateral funiculus (VLF) and CX as orthodromic and antidromic stimulation, respectively.
F: responses of the unit to left cervical vagus nerve (LCV) stimulation.
G: responses of the unit to greater splanchnic nerve (SPL) stimulation.

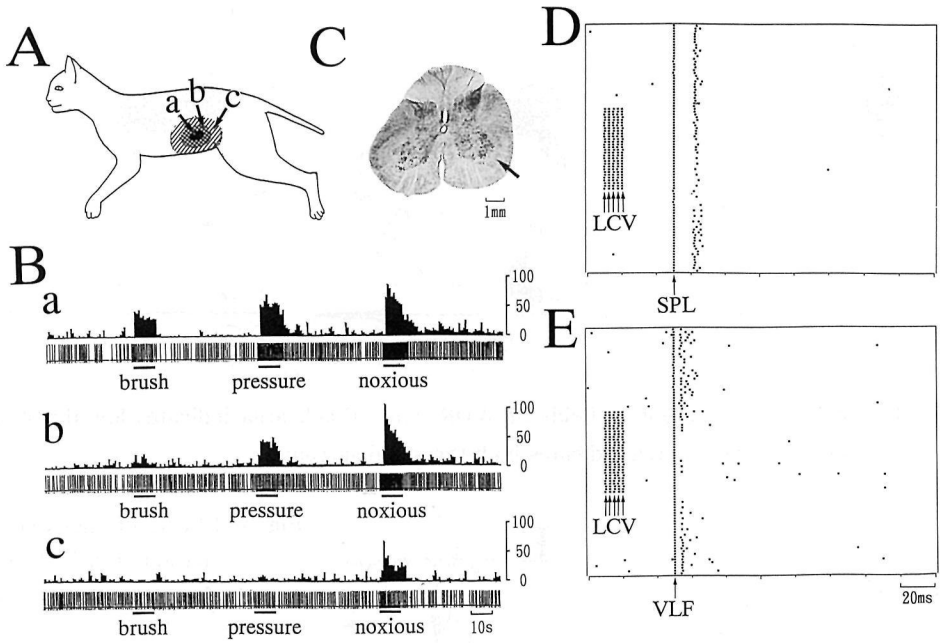

Fig. 5. Effects of conditioning left vagus nerve stimulation on responses of a WDR unit to SPL stimulation. A: cutaneous receptive field. B: responses to stimulation of corresponding three points indicated by arrows in part A are shown as a, b and c. C: site of stimulation in the VLF. D:dot raster display of the unit responses to SPL stimulation at 1.5 x threshold both with and without conditioning stimulation of the vagus nerve. E: dot raster display of the unit responses to VLF stimulation both with and without conditioning stimulation of the vagus nerve.

correspond to the dorsal root dermatomes C_8-L_3. Cutaneous receptive fields of WDR units included these areas.

In both NS and WDR units, the threshold of responses to the SPL stimulation was 1.0-4.4 times threshold for the reflex contraction of intercostal muscles measured prior to exploration. The minimum latency of responses to SPL stimulation measured at 1.5 times threshold for spike discharges was 10.5-14.6 ms.

Electrical stimulation of the left cervical vagus nerve evoked spike discharges from 8 NS and 4 WDR units. The minimum latency of the excitation was 17.2±2.8 ms. NS units excited had their receptive fields in the forearm, arm and area of scapula. These areas correspond to the dorsal root dermatomes C_8-T_1 (Fig. 2). The center of receptive field of WDR units were located in the arm and area of scapula (Fig. 3). The excited NS and WDR units were located more medially than other units within the shell region of VPL (Fig. 1), as expected from the previously reported somatotopic organization of nociceptive body representation (Yokota et al., 1988). An example of excited NS units is illustrated in Fig. 4. This unit followed electrical stimulation of the somatosensory cortex SI (Fig. 4C) at 200 Hz with a fixed latency at 1.2 ms (Fig. 4D). The antidromic nature of the responses to the somatosensory cortex SI was confirmed by a collision technique in which orthodromic stimuli were applied to the VLF (Fig. 4E). Thus this unit was a thalamocortical NS neuron receiving convergent SPL and vagal afferent

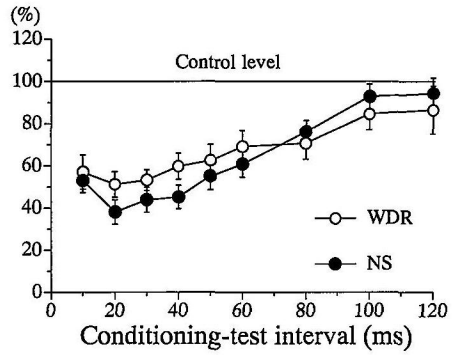

Fig. 6. Mean time courses of conditioning vagus nerve stimulation-produced inhibition of responses to SPL stimulation in NS and WDR units. Mean±S.E.M. is plotted.

inputs.

In the remaining 35 NS and 32 WDR units, effects of conditioning stimulation applied to the left cervical vagus nerve on responses evoked by test stimuli to the SPL were examined. Change in responses to test stimuli was defined as inhibition if decreased by >20% of the control value. Inhibition was observed in 27 NS and 25 WDR units. An example of WDR units inhibited is illustrated in Fig. 5, and the mean time courses of inhibition in NS and WDR units are shown in Fig. 6. The maximum inhibition was obtained when test stimuli to the SPL were applied 20 ms after the beginning of the conditioning stimuli. The maximum inhibition was 61.9±5.8% and 48.8±6.0%, in NS and WDR units respectively.

In 3 NS and 5 WDR units, effects of conditioning stimulation of the right cervical vagus nerve were also studied. Inhibition at 20-40 ms conditioning test interval was 47.3±2.7% for left vagus nerve conditioning stimulation, whereas it was 44.8±2.7% for right vagus nerve conditioning stimulation. There was no significant difference between them.

In 18 NS and 15 WDR units, effects of conditioning stimulation of the left cervical vagus nerve stimulation on responses to SPL

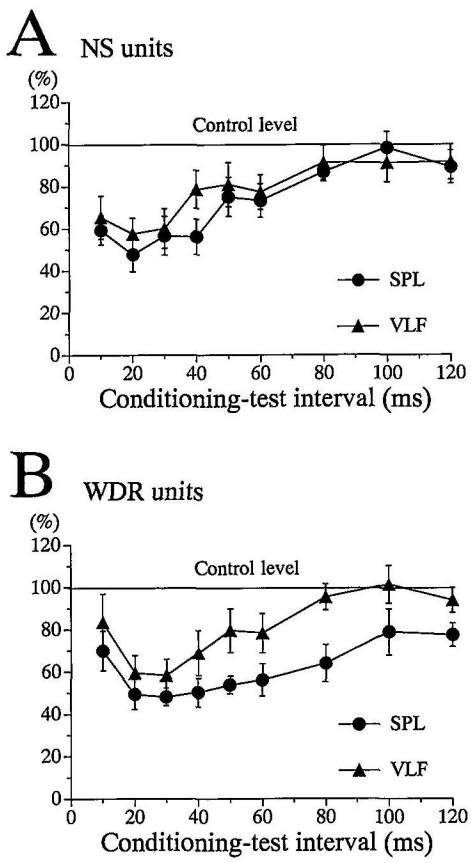

Fig. 7. Mean time courses of conditioning vagus nerve stimulation-produced inhibition of responses to SPL stimulation and to VLF stimulation. A: NS units. B: WDR units.

and VLF stimulations were examined. Inhibition of responses to SPL stimulation was observed in 16 NS and 13 WDR units, whereas inhibition of responses to VLF stimulation in 12 NS and 11 WDR units. In all the units whose responses to VLF stimulation were inhibited, responses to SPL stimulation were also inhibited. Time courses of inhibition in these 12 NS and 11 WDR units are plotted in Fig. 7. The maximum inhibition of responses to SPL stimulation was 52.4±8.1% and 51.8±4.2% in the NS and WDR units, respectively. The maximum inhibition of responses to VLF stimulation was 42.5±7.7% and 41.5±7.5% in the NS and WDR units,

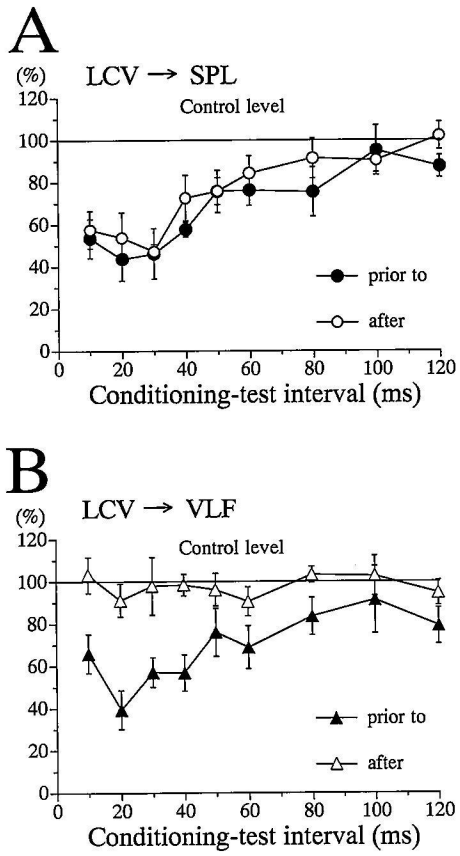

Fig. 8. Effects of lidocaine microinjection into the PAG/NRD on vagus nerve stimulation-produced inhibition.
A: effects on vagus nerve stimulation-produced inhibition of responses to SPL stimulation.
B: effects on vagus nerve stimulation-produced inhibition of responses to VLF stimulation.

respectively. In both the NS and WDR units, responses to SPL stimulation were more markedly inhibited than those to VLF stimulation.

In 4 NS and 3 WDR units, effects of microinjection (10μl) of 2% lidocaine into the midbrain just ventral to the aqueductus cerebri were studied. Results are summarized in Fig. 8. Following the lidocaine microinjection, inhibition of responses to VLF stimulation was eliminated, and inhibition of responses to SPL stimulation was unaffected. The injection sites were in the ventral part of periaqueducatal gray (PAG) and/or in the nucleus raphe dorsalis (NRD). Injection of the same amount of saline into the same midbrain sites (control injection) had no effects on inhibition produced by cervical vagus nerve conditioning stimulation.

DISCUSSION

It is well recognized that the vagus nerves are largely composed of afferent fibers (Agostini et al., 1957). The present study was the first to examine the effects of cervical vagal afferent stimulation on activities of nociceptive neurons in the shell region of VPL. The results indicate that electrical stimulation of vagal afferents either excites or inhibits some nociceptive neurons in the shell region of VPL, and that the inhibition includes an ascending antinociceptive mechanism.

1. Excitatory effect of vagal afferent stimulation

Previously it was reported that ipsilateral cervical vagus stimulation (ICVS) excited nociceptive neurons in the cervical cord of the rat (Fu et al., 1992). At the same stimulation parameters, contralateral cervical vagus stimulation (CCVS) either increased, inhibited or did not affect background activity of C_1 neurons. In the C_2-C_6 dorsal horn, ICVS either excited (16 units) or inhibited (2 units) CCVS did not increase but either decreased or did not affect background activity. In this study, projection sites of neurons excited by ICVS was not identified. It appeared possible that cervical neurons excited by ICVS might be involved in mediating descending inhibition of spinal nociceptive transmission. Conversely, if upper cervical neurons projected to brain areas processing pain sensation, then vagal afferent fibers might be involved in the sensation of pain.

In the present study, we studied effects of cervical vagus nerve stimulation on responses of nociceptive VPL neurons receiving SPL input, and found that nociceptive neurons having their receptive field in the C_8-T_1 dermatomes receive convergent inputs from both vagal and splanchnic afferents. We confirmed that some of these neurons project to the somatosensory cortex SI. These present data support the idea that vagal afferent can mediate visceral pain.

Clinically it is known that pain arising in the upper thoracic and cervical esophagus, trachea and bronchi is transmitted by sensory fibers in the vagi (White and Sweet, 1969). Jones and Chapman (1942) have shown that after most extensive thoracic sympathectomies experimental distension begins to cause distress when the balloon is drawn above the sternoclavicular joint. Distension above this level causes pain even in the presence of spinal anesthesia carried above the first thoracic segment and after transection injuries of the spinal cord as high as the fifth cervical vertebra. Grimson et al., (1947) have observed that stimulation of the cervical vagi in patients under spinal anesthesia causes a sensation of heartburn as well as pain referred to the neck. It is therefore probable that pain arising in the upper thoracic and cervical esophagus is subserved by vagal afferent fibers. This has been shown to be the case with the trachea and bronchi in bronchogenic cancer where disabling symptoms of pain and cough have been palliated by section of the homolateral vagus nerve below the origin of its recurrent laryngeal branch (Morton et al., 1951). The present data are in agreement with these clinical observations.

2. Inhibitory effect of vagal afferent stimulation

It has already been reported that electrical stimulation of the cervical vagus inhibits the tail flick elicited by noxious heat applied to the tail of conscious rats (Randich and Maixner, 1984). Electrical stimulation of afferents arising from the cardiac branch of the vagus also inhibits spontaneous activity of nociceptive spinothalamic neurons in the thoracic spinal cord of the cat and monkey (Ammons et al., 1983a; Thies and Foreman, 1981). Furthermore, responses of spinothalamic projection neurons in the thoracic spinal cord of the monkey to either electrical or bradykinin-induced activation of cardiac sympathetic afferents were inhibited by conditioning stimuli applied to the thoracic vagus nerve (Ammons et al., 1983b). Hence the inhibition of responses of nociceptive VPL neurons to SPL input as found in the present experiments, was expected. In addition, we found that conditioning vagus nerve stimulation inhibited responses of NS and WDR neurons in the VPL to VLF stimulation. The responses to the VLF stimulation do not involve any spinal mechanism. Thus the present data indicate that vagal afferents can also exert inhibitory action on synaptic transmission of nociceptive information at the level of the VPL.

3. Anatomical substrates of inhibitory effect

It has been recognized for many years that the nucleus of the solitary tract (NTS) is the principal recipient of first order visceral and gustatory afferent information conveyed by the vagus, as well as by glossopharyngeal, facial and trigeminal nerves. It has been established that terminals of vagal origin are represented primarily in the medial part of NTS throughout the caudal two thirds of the NTS in the rat, cat and monkey (Beckstead and Norgren, 1979; Kalia and Mesulam, 1980; Kalia and Sullivan, 1982). It has also been shown that the NTS is an important relay for the modulation of nociception produced by vagal afferent stimulation (Randich and Aicher, 1988; Ren et al., 1990a). Microinjection of glutamate or electrical stimulation in the NTS inhibits spinal dorsal

horn neurons and nociceptive reflexes (Du and Zhou, 1990; Lewis et al., 1987; Morgan et al., 1989; Randich and Aicher, 1988; Ren et al., 1990a), and local anesthetic blockade of the NTS abolishes or significantly attenuates these vagal inhibitory effects (Randich and Aicher, 1988; Ren et al., 1990a).

In addition to projection to the dorsal motor nucleus of the vagus, nucleus ambigus, and other visceromotor nuclei (Ross et al., 1985; Loewy and Burton, 1978; Morest, 1967; Norgren, 1978), the NTS has efferent connections with structures related to the centrifugal modulation of nociception. Beitz (1982) reported that the nucleus raphe magnus (NRM), a key station of the descending antinociceptive system, receives enkephalin and substance P input from the NTS. A direct projection from the NTS to the locus coeruleus has also been demonstrated in the cat, rat and pigeon (Arends, et al., 1988; Clavier, 1978; Sabai et al., 1977; Ward et al., 1977). Although efferent projections from the NTS to the spinal cord have been identified in the monkey (Kneisley et al., 1978), cat (Basbaum and Fields, 1979; Kuypers and Maisky, 1975; Loewy and Burton, 1978; Torvik, 1957), rabbit (Blessing et al., 1981) and rat (Basbaum and Fields, 1979; Satoh et al., 1977), other neuroanatomic studies have suggested that the NTS is unlikely to modulate spinal nociceptive transmission via a direct solitariospinal pathway (Torvik, 1957; Norgren 1978; Loewy and Burton, 1978). Hence Gebhart and his associates (Ren et al., 1990a; Randich et al., 1990) proposed as follow; Vagal afferents terminate bilaterally in the NTS. Secondary projection cells located in the NTS and cell bodies located in the locus coeruleus (LC)/locus subcoeruleus (SC) and nucleus raphe magnus (NRM) regions are important for vagal afferent stimulation-produced descending inhibitory modulation. It is well known that from both LC/SC and NRM originates noradrenergic and serotonergic descending antinociceptive system, respectively. Thus there are many brain stem sites that could be activated by electrical stimulation of vagal afferents, which, in turn, may activate descending inhibitory pathways.

In an autoradiographic study (Norgren, 1978), the rostral projection from the NTS was found to extend no further than the pons, where it terminated in the caudal parabrachial nucleus. Although anatomical data from different laboratories consistently confirmed the projection from the NTS to the parabrachial nucleus (Arends et al., 1988; Loewy and Burton, 1978; Travers, 1988), electrophysiological and neuroanatomic studies also indicated that axons ascending from the NTS innervate the PAG (Bandler and Tork, 1987; Loewy and Burton, 1978), hypothalamic paraventricular nucleus and other regions of the hypothalamus (Criello and Calaresu, 1980; Day and Sibbald, 1988; Kobashi and Adachi, 1988; Ricardo and Koh, 1978; Sawchenko and Swanson, 1981), central nucleus of the amygdala (Rogers and Fryman,1988), and other forebrain structures (Arends et al., 1988; Nosaka, 1984; Ricardo and Koh, 1978; Tanaka and Seta, 1988). Furthermore, Bandler and Tork (1987) demonstrated a reciprocal connection between the PAG and the NTS. Aghajanian and Wang (1977) found that fibers from the NTS end in the NRD but not in the median raphe nucleus. Chu and Bloom (1974) traced adrenergic fibers from the LC which receives afferent input from the NTS, to the NRD. However, there is no evidence of direct solitariothalamic projection.

It has been reported from our laboratory that electrical stimulation of the PAG/NRD inhibits synaptic transmission of nociceptive information to NS and WDR neurons in the VPL (Horie et al, 1991; Koyama et al., 1995). As mentioned above, projection from the NTS to the PAG and NRD is known to exist. In addition, local anesthetic blockade of PAG/NRD reversed

inhibitory effects of vagal afferent stimulation on responses of NS and WDR units to VLF input, in the present experiments. It is very likely that vagal afferents modulate thalamic nociception via the ascending antinociceptive system as reported previously.

4. Functional significance of inhibition mediated by vagal afferents

An important branch of the vagus which exerts inhibitory action on central nervous system neurons is the aortic nerve. Afferent fibers in this nerve respond to increased blood pressure (Stoica et al., 1965). During stressful situations such as the defense reaction, blood pressure, heart rate, cardiac output, and respiration are increased. Presumably this should lead to reduced responsiveness of nociceptive neurons in the central nervous system via the action of baroreceptors. Thus attention would be directed away from painful stimuli which would reduce organism's ability to perform the appropriate behavior. In support of the concept of an interaction between blood pressure and responsiveness to environmental stimuli is the finding that rats with chronic hypertension are less responsive to painful stimuli compared to normotensive rats (Zamir and Segal, 1979).

In conclusion, the vagus nerve is an afferent-efferent cable. Its afferent fibers connect with a great diversity of sensors and carry signals to a large number of interconnected centers in the brain. Vagal afferents can mediate some visceral pain. We have also demonstrated a potentially important effect of vagal afferent fibers on nociceptive neurons in the VPL of the cat thalamus. Vagal afferents appear to activate not only a general descending antinociceptive system but also an ascending antinociceptive system that inhibits nociceptive neurons in the VPL. This effect may have important implications for processing of information about visceral pain and somatosensory information.

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