Functional Properties of Trigeminal Nociceptive Neurons in the Subnucleus Reticularis Ventralis of the Cat

Yasuo Nishikawa, Natsu Koyama, Akinori Hasegawa,
Yoshihisa Fujino and Toshikatsu Yokota

*Department of Physiology, Medical College of Shiga, Otsu and
Department of Physiology, Osaka Dental University, Osaka, Japan*

(Received 22 April 1991)

Abstract

Trigeminal nociceptive neurons within the subnucleus reticularis ventralis (SRV) of the caudal bulbar lateral reticular formation were studied in urethane-chloralose anesthetized cats. They were called SRV neurons. Most of them were excited by pressure to the ipsilateral cornea or to both corneas at a strength well above the human corneal pain threshold. Many of them were activated by noxious mechanical stimulation of the pinna, face and/or tongue. A significant fraction of SRV neurons was responsive to tapping of the ipsilateral nose dorsum and/or electrical stimulation of tooth pulp afferents. Neurons having receptive fields similar to those of SRV neurons were found in lamina VII of the first cervical cord suggesting that SRV neurons may be trigeminal lamina VII neurons. Trigeminal tractotomy just rostral to the obex did not eliminate responses of SRV neurons to trigeminal inputs. Neurons relaying trigeminal inputs to SRV neurons were electrophysiologically identified in the nucleus reticularis parvocellularis (Rpc) which is ventromedially adjacent to the subnuclei oralis and interpolaris of trigeminal spinal tract nucleus. Thalamic neurons having complex trigeminal receptive fields similar to those of SRV neurons were found in the intralaminar nuclei, i. e., nuclei centralis lateralis, centralis medialis and parafascicularis. About half of SRV neurons tested were antidromically activated by electrical stimulation of the nucleus centralis lateralis. It was also found that a significant proportion of SRV neurons was antidromically activated by electrical stimulation of the mesencephalic reticular formation (MRF). These findings suggest that SRV neurons receive trigeminal nociceptive inputs relayed through the Rpc and project directly or indirectly via the MRF to the intralaminar nuclei.

Key Words: trigeminal pain, subnucleus reticularis ventralis, trigeminal lamina VII, intralaminar nuclei, reticular formation

INTRODUCTION

The caudal bulbar lateral reticular formation (LRF) which is ventromedially contiguous with the trigeminal subnucleus caudalis, can be subdivided into subnucleus reticularis dorsalis and subnucleus reticularis ventralis²⁴⁾. Wide dynamic range (WDR) neurons receiving trigeminal inputs are located in the lateral part of the subnucleus reticularis dorsalis^{37,38)}. Another class of trigeminal nociceptive neurons is located in the dorsolateral part of the subnucleus reticularis ventralis (SRV). They are called SRV neuron. The trigeminal WDR neurons may play much the same role as WDR neurons in the dorsal horn of the spinal cord. In contrast, the role played by SRV neurons in conscious experience of pain is still unknown.

In order to gain some insight about functional significance of SRV neurons, we have studied properties of SRV neurons. In the first series of experiments, we have clarified receptive field characteristics of SRV neurons, and then explored the caudal half of the first cervical cord for neurons having receptive field characteristics similar to those of SRV neurons in an attempt to identify the spinal structure homologous with the dorsolateral part of the SRV. In the second series of experiments, we have studied afferent connections of SRV neurons. In the third series of experiments, we have studied possible projection sites within the thalamus of SRV neurons, and have examined similarity between SRV neurons and nociceptive neurons in the homologous structure of the spinal cord in relation to their efferent connections.

METHODS

Experiments were carried out on young adult cats. Each animal was initially anesthetized with ketamine hydrochloride (20 mg/kg), and anesthesia was maintained with an intravenous

dose (3.5 ml/kg) of urethane-chloralose solution (urethane 125 mg/ml and chloralose 10 mg/ml) supplemented as required.

The maxillary and mandibular canine teeth on both sides were prepared for electrical stimulation.

The dorsal surface of the caudal medulla oblongata was exposed by removing the arch of the first cervical vertebra together with an area of skull extending bilaterally from the foramen magnum to the cerebellar tentorium. After reflecting the dura, the pia and arachnoidea were dissected away at selected sites. The exposed medulla oblongata was then covered with 3.5% agar in Ringer-Locke solution. A portion of the parietal bone was removed for insertion of recording microelectrodes or stimulating electrodes into the thalamus or midbrain.

During exploration with microelectrodes, neuromuscular transmission was blocked by intravenous administration of pancuronium bromide (0.4 mg/kg). Subsequently, the animal was artificially respired through an endotracheal tube. End-tidal CO₂ % was monitored and maintained between 3.5~4.5%. The mean arterial pressure was continuously monitored by a catheter in the right femoral artery and was kept above 90 mmHg if necessary by infusion of lactate-Ringer solution. The level of anesthesia was checked intermittently by allowing the animal to recover from the relaxing drug. A thermistor probe was placed in the oesophagus and the body temperature was maintained at $37 \pm 0.5^\circ\text{C}$ by an electric heating pad under the abdomen.

The lateral half of the medulla oblongata caudal to the obex was explored with glass capillary microelectrodes which were filled with 2 % pontamine sky blue in 0.5 or 1 M Na acetate. Responses of single units were analyzed with respect to electrical stimulation of tooth pulp and mechanical stimulation of receptive fields. Single unit activities were displayed on an oscilloscope

Fig. 1 SRV Unit. **A**: receptive field of the unit. **B**: location of the unit (indicated by an arrow). **C**: responses to noxious pinch of the pinna, to repetitive tapping of the nose dorsum, to stroking a probe across the corneal receptive field and to noxious pinch of the infra-orbital skin. Upper trace shows peristimulus time histogram, whereas lower trace shows spike discharges. Periods of stimulus application are indicated by horizontal bars. Abbreviations; Cu: nucleus cuneatus. SRD: subnucleus reticularis dorsalis. SRV: subnucleus reticularis ventralis. Subnucl. Caud.: subnucleus caudalis.

Fig. 2 Locations of SRV units at different rostrocaudal levels. Locations of individual units are shown by filled squares. In each drawing of histological section, distance from the obex is shown in mm.

and led to a window discriminator. Discriminator pulses were used by a spike counter for construction of peristimulus time histograms. The firing rates and window discriminator pulses were recorded on a chart recorder.

Stereotaxic coordinates and micromanipulator micrometer readings were recorded for all recording sites. Locations of all nociceptive units were marked by depositing a small amount of dye. For this purpose, $5 \mu\text{A}$ cathodal current was passed through the microelectrode tip for 10 min.

At the termination of each experiment, the animal was perfused through the beating heart with one liter of normal saline followed by 3 liters of 10% formol-saline. Dye marks were identified in $50 \mu\text{m}$ cresyl violet-stained sections.

RESULTS

Receptive field distribution

A total of 515 units were recorded from the SRV. Of these, 510 units (99.0%) were activated by dragging a probe across the cornea ipsilateral-

ly or bilaterally at a strength above the human corneal pain threshold²⁷, 432 units (83.9%) were excited by ipsilateral or bilateral noxious mechanical stimulation of the pinna (358 units), face (198 units) and/or tongue (136 units), 208 units (40.4%) responded to tapping of the dorsum of the ipsilateral nose and 154 units (29.9%) discharged in response to electrical stimulation of the tooth pulp ipsilaterally or bilaterally. Twenty seven units (5.2%) were excited only by mechanical stimulation of the ipsilateral cornea. Of 5 units which were unresponsive to the cornea, one unit responded to inputs from the face and tooth pulp, 2 units to stimulation of the pinna, face and tooth pulp and another 2 units to stimulation of the pinna, and tooth pulp. The remaining 483 units (93.8%) were responsive to the ipsilateral cornea or both corneas together with one or more additional structures. A SRV unit is illustrated in **Figure 1**, and location of SRV units are shown in **Figure 2**.

Units in the caudal C1 segment with receptive field characteristics similar to those of SRV units

The caudal half of the first cervical segment was searched for neurons with complex receptive field, similar to those of SRV neurons in 7 cats. A total of 20 units were obtained. All of them responded to noxious pinch applied to the pinna on the same side (11 units) or both sides (9 units), and had at least two separate receptive fields in the head. Dragging a probe across the cornea activated 12 units. Nine of them were excited by this stimulation ipsilaterally and 3, bilaterally. Two of them responded with a sustained discharge to noxious pinch applied to the face. One of them had a nociceptive receptive field on the maxillary division and the other on the all 3 division of the trigeminal nerve territory. Four units responded to noxious pinch applied to the ipsilateral tongue with a sustained discharge. Three units responded to tapping of the

Fig. 3 Lamina VII unit. **A**: location of the unit. **B**: receptive field of the unit. **C**: responses to electrical stimulation of tooth pulps. Arrows indicate stimulus artefacts. IUC: ipsilateral upper canine tooth. ILC: ipsilateral lower canine tooth. CLC: contralateral lower canine tooth.

ipsilateral nose dorsum and 9 units responded to electrical stimulation of canine tooth pulps ipsilaterally (2 unit) or bilaterally (7 units). Apparently, the pinna was more frequently effective in exciting units than the rest including the cornea. Histological examination revealed that all of them were located in the lamina VII. That is, they were located not in the dorsal horn, but in the intermediate zone. A lamina VII unit is illustrated in **Figure 3**.

Responses of SRV neurons after trigeminal tractotomy

In an attempt to identify neurons relaying trigeminal inputs onto SRV units, we have examined whether SRV units receive trigeminal input relayed through neurons located in structures rostral to the trigeminal subnucleus caudalis.

For this purpose, the spinal trigeminal tract was cut at a level just rostral to the obex, and thus trigeminal primary afferent inputs to the trigeminal subnucleus caudalis and its nearby bulbar lateral reticular formation were interrupted in 4 cats. After the tractotomy, the medulla oblongata 2~5 mm caudal to the obex was searched for units responsive to mechanical or electrical stimulation of the trigeminal nerve territory. Neither low-threshold mechanoreceptive (LTM), nociceptive specific (NS) nor WDR neurons were found within the trigeminal subnucleus caudalis and ventromedially adjacent subnucleus reticularis dorsalis. Within the SRV, 10 units were found which could be excited by dragging a probe across the ipsilateral cornea. Seven of them were also responsive to noxious mechanical stimulation of the pinna on the ipsilateral or both sides. Three of them were excited by tapping of the dorsum of the ipsilateral nose. Four units responded to noxious pinch to the ipsilateral face and/or tongue, and four units were activated by electrical stimulation of the maxillary and mandibular canine tooth pulps bilaterally. Histological examination after the experiments confirmed that the tractotomy was almost complete in these 4 cats. In short, responses of SRV units to stimulation of the ipsilateral trigeminal nerve territories were not eliminated by the trigeminal tractotomy. These results suggest that trigeminal inputs onto SRV neurons are at least in part relayed via neurons located more rostrally.

Antidromic responses of more rostrally located neurons to electrical stimulation of SRV

After placing a coaxial stimulating electrode in SRV on both sides, the rostral parts of trigeminal spinal tract nucleus and adjacent reticular formation were explored for units antidromically excited by electrical stimulation of the SRV in 8 cats. The criteria used to prove the

antidromic character of evoked spikes were (a) short and invariant latency; (b) stability of the threshold; (c) faithful responses to high rates (100 or 200 Hz) of stimulation; and (d) collision of antidromic responses with orthodromic or spontaneous spikes.

Antidromic responses were observed in 15 units. Thirteen units responded to the ipsilateral SRV and two units responded to the contralateral SRV. They were located in the nucleus reticularis parvocellularis (Rpc) adjacent to the trigeminal subnuclei oralis and interpolaris. Six units responded to mechanical stimulation of the ipsilateral cornea, and one of them additionally responded to tapping of the dorsum of the ipsilateral nose. The remaining 9 units responded to electrical stimulation of the ipsilateral maxillary and/or mandibular canine tooth pulp afferents. Five of them additionally responded to noxious mechanical stimulation of the ipsilateral maxillary and/or mandibular integument. These results indicate that afferent inputs onto SRV neurons except for that from the pinna could be relayed through neurons located in the Rpc adjacent to the subnuclei oralis and interpolaris.

Distribution of thalamic neurons with receptive field characteristics similar to those of SRV neurons

In order to gain some insight about possible projection sites within the thalamus of SRV neurons, units having complex trigeminal receptive field similar to those of SRV neurons were explored in the thalamus of 25 cats.

A total of 50 units were found; 24 units in the nucleus parafascicularis, 21 units in the nucleus centralis lateralis, 2 units in the nucleus centralis medialis and 3 units in the nucleus subparafascicularis. As in the case of SRV units, they were regularly excited by mechanical stimulation of the contralateral or both corneas at a strength above the human corneal pain threshold²⁷⁾. They were frequently exhibited a

sustained discharge in response to noxious mechanical stimulation of the pinna (42 units), face (12 units) and/or tongue (11 units) contralaterally or bilaterally. Tapping of the nose dorsum contralaterally or bilaterally excited 24 of them and electrical stimulation of the canine tooth pulp afferents contralaterally or bilaterally was effective in exciting 20 of them. Although SRV units usually did not respond to noxious mechanical stimulation of the trunk or electrical stimulation of the splanchnic nerve, 40 (80.0%) of the thalamic units obtained were excited by these stimuli.

Antidromic activation of SRV neurons by electrical stimulation of the nucleus centralis lateralis

Antidromic responses of SRV neurons to electrical stimulation of the contralateral nucleus centralis lateralis (CL) were studied in 12 cats. A total of 61 units recorded from the SRV were tested. Of these, 34 units (55.7%) were antidromically activated by the stimulation. The latency of the antidromic response ranged from 1.6 to 2.8 ms. The mean was 2.23 ± 0.42 ms. Units antidromically activated were excited by mechanical stimulation of the ipsilateral cornea (32 units) or both corneas (2 units). Twenty eight units responded to noxious mechanical stimulation of the ipsilateral pinna (24 units) or both pinnae (4 units). Noxious mechanical stimulation of the ipsilateral face or tongue excited 21 or 11 units, respectively. Tapping of the ipsilateral nose dorsum excited 31 of them. Two units responded to electrical stimulation of the ipsilateral maxillary and mandibular canine tooth pulps, and 8 units responded to electrical stimulation of maxillary and mandibular canine tooth pulps bilaterally. A SRV unit which was antidromically excited by electrical stimulation of the contralateral CL is illustrated in **Figure 4**.

Fig. 4 Antidromic excitation of a SRV unit following electrical stimulation of the contralateral CL. **A**: site of stimulation (indicated by an arrow), **B**: location of the unit (indicated by an arrow). **C**: receptive field. **D**: collision test. Orthodromic stimuli were applied to the ipsilateral pinna. **E**: responses to electrical stimulation of the CL at 100 Hz. Arrows in **D** and **E** indicate stimulus artefacts. Abbreviations in **A** and **B**; CeM: nucleus centralis medialis. CL: nucleus centralis lateralis. Cu: nucleus cuneatus. GL: corpus geniculatum laterale. MD: nucleus medialis dorsalis. SRD: subnucleus reticularis dorsalis. SRV: subnucleus reticularis ventralis. Subnucl. caud.: subnucleus caudalis. VPL: nucleus ventralis posterolateralis. ZI: zona incerta.

Efferent connection of SRV neurons with the mesencephalic reticular formation

In order to find neurons sending axons to the mesencephalic reticular formation, we explored the lateral part of the caudal medulla oblongata for units antidromically activated by electrical stimulation of the mesencephalic reticular

formation, in 16 cats.

In this type of experiment, it is important to know whether our stimulating electrode is activating terminals or fibers of passage which may terminate at more rostral levels. We inserted two arrays of 3 coaxial stimulating electrodes into the mesencephalic reticular formation: one at a level AP+2.0~3.0 mm and the other at a level 1~2 mm more rostral. We searched for units responding to electrical stimulation using the caudal array. After finding a unit responsive to this stimulation, antidromic features of its responses were first confirmed, and then it was further confirmed that the unit did not respond to electrical stimulation using rostral electrodes. Using these criteria, altogether 30 units were found to be antidromically activated by the caudal, but not by the rostral array of mesencephalic stimulating electrodes. All of these units were found in the SRV. The latency of the antidromic response ranged from 1.0 to 3.0 ms. These units regularly responded to mechanical stimulation of the ipsilateral or both corneas. Twenty four of them were activated by noxious stimulation of the ipsilateral pinnae. Fourteen units responded to noxious mechanical stimulation of the ipsilateral face. Five units were excited by noxious mechanical stimulation of the ipsilateral tongue and six units were activated by tapping of the ipsilateral nose dorsum. Eleven units were responsive to electrical stimulation of the tooth pulp afferents ipsilaterally or bilaterally. These results suggest that some SRV neurons send axons to the mesencephalic reticular formation.

DISCUSSION

Nociceptive nature of SRV neurons

One of the major issues raised in the present study was whether SRV neurons recorded are nociceptive or not. Of 515 SRV units recorded in the cat, 431 units were activated by noxious

mechanical stimulation of the pinna, face and/or tongue. They were obviously nociceptive neurons. Of the remaining 83 units, 12 units were excited by electrical stimulation of tooth pulp afferents. Since sensation evoked by natural stimulation of the tooth pulp is only pain, these units may be included in the category of nociceptive neurons. Of the 83 units, 44 were activated by mechanical stimulation of the cornea and by tapping of the dorsum of the nose and 27 units were activated only by mechanical stimulation of the cornea. A question now is whether stimuli applied to the cornea and nose dorsum in the present experiments were noxious or non-noxious.

It has been demonstrated on a number of occasions that a sensation akin to touch can be aroused from the cornea by a light mechanical stimulus after the operation of trigeminal tractotomy, which has the effect, in successful cases, of abolishing all corneal pain sensibility^{32,35}. This observation can easily be explained on the basis of the presence of tactile as well as pain fibers and terminals in the cornea. Previously, we assessed the sensitivity of the cornea with a Cochet-Bonnet's esthesiometer in patients with cataract and found that mechanical threshold of corneal responses in SRV neurons was well above the pain threshold in the human cornea²⁷. Assuming that painful stimuli are noxious, these results would indicate that SRV neurons receiving corneal input are nociceptive neurons. It follows that all the SRV neurons recorded in the present experiments were nociceptive neurons.

Tapping of the dorsum of the nose was apparently not tissue damaging. However, the same stimulus can elicit a glottis-closure reflex in the cat³⁶. This reflex is a protective reflex. The receptors for the reflex are located in the nasal cavity rather than in the nose dorsum itself³⁶. The anterior ethmoidal nerve supplying branches

to the mucous membrane of the nasal cavity has mainly small diameter myelinated and unmyelinated fibers⁵⁾. The innervation of the nasal cavity is thus similar to that of the cornea and tooth pulp. The anterior ethmoidal nerve constitutes the afferent limb of several upper airway protective reflexes, such as sneezing, coughing, and apnoea^{2~4)}. Stimulation of the nasal cavity may be looked upon as a warning or alerting signal to protect the airway.

Afferent connections of SRV neurons

Almost all SRV neurons recorded in the present experiments responded to mechanical stimulation of the ipsi- or bilateral cornea and many of them responded to noxious mechanical stimulation of face and /or tongue and to tapping of the dorsum of nose, but direct projection from the trigeminal nerve territory onto the SRV has not been demonstrated^{21~23,29,30)}. Furthermore, a significant fraction of SRV neurons responded to contralateral trigeminal inputs. Previous anatomical studies^{21~23,29,30)} suggest that direct afferent connections of SRV neurons with trigeminal primary afferent fibers from the contralateral trigeminal nerve territory are unlikely. It is possible that there are neurons relaying trigeminal inputs onto this subnucleus outside this structure.

In the present experiments, trigeminal tractotomy at a level just rostral to the obex did not eliminate responses of SRV units to ipsilateral trigeminal inputs, suggesting that NS neurons in the trigeminal subnucleus caudalis is not necessarily required in relaying trigeminal nociceptive inputs onto SRV neurons. It was found that trigeminal nociceptive neurons in the nucleus reticularis parvocellularis (Rpc) adjacent to subnuclei oralis and interpolaris on both sides project to the SRV. The Rpc is known to receive trigeminal primary afferent projection^{8,20,31)}. It may be concluded that in the Rpc, there are neurons relaying trigeminal nociceptive

inputs onto SRV neurons.

Efferent connections of SRV neurons

In the present experiments, it was found that some SRV neurons have efferent connections with either the nucleus centralis lateralis or the mesencephalic reticular formation. These results are consistent with one of the conclusions of the present paper that SRV neurons are functionally homologous with nociceptive neurons in the lamina VII of the spinal cord with which the caudal end of the SRV blends^{12~14,33)}. The mesencephalic reticular formation in turn has efferent connections not only with the nucleus centralis lateralis but also with other intralaminar nuclei, such as nuclei centralis medialis, paracentralis and parafascicularis^{6,9,15,17)}. It was found in the present experiments that there are nociceptive neurons in these intralaminar nuclei which have complex trigeminal receptive fields similar to those of SRV neurons. SRV neurons may directly or indirectly via the brain stem reticular formation project to the intralaminar nuclei.

Functional significance of SRV neurons

Melzack and Casey²⁵⁾ have proposed that there is a distinct motivational-affective or aversive pain system that is activated separately and in parallel with sensory-discriminative pain systems. According to this concept discriminative information, such as stimulus location, intensity and duration, is transmitted through the spinal dorsal horn and its trigeminal homologue to the ventrobasal thalamus and finally to the somatosensory cortex. Intralaminar nuclei such as centralis lateralis and parafascicularis are assumed to be involved in affective or motivational aspects of pain because of their physiological properties, such as large receptive fields and variable responses to noxious stimuli^{1,10,11,28)}, and their efferent connections with the limbic system, in particular, with the anterior cingulate gyrus and amygdala^{16,19,26,34)}. It was reported that some neurons in the

intralaminar nuclei of alert monkeys discriminate changes in the intensity of noxious stimuli that are equal to or below the monkey's own discrimination threshold⁷⁾. However, this finding does not imply that they have no role in emotional responses to pain. The relationship of some intralaminar neurons to reward and escape behavior¹⁸⁾ is rather in favor of the concept that intralaminar nuclei are involved in the motivational-affective component of pain.

The complex trigeminal receptive fields of SRV neurons suggest that capacity of SRV neurons to signal spatial information is limited. Trigeminal nociceptive input to SRV neurons could be related to arousal, aversive or motoric functions partly through their direct and indirect connections with the intralaminar nuclei.

ACKNOWLEDGEMENTS

This work was entrusted to the Department of Physiology, Medical College of Shiga by the Science and Technology Agency, using the Special Coordination Funds for Promoting Science and Technology.

References

- 1) Albe-Fessard, D. and Kruger, L., Duality of unit discharges from cat centrum medianum in response to natural and electrical stimulation, *J. Neurophysiol.*, **25** (1962) 3-20.
- 2) Angell-James, J. E. and Daly, M., Nasal reflexes, *Proc. R. Soc. Med.*, **62** (1969) 1287-1293.
- 3) Batsel, H. L. and Lines, A. J., Neural mechanisms of sneeze, *Am. J. Physiol.*, **229** (1975) 770-776.
- 4) Batsel, H. L. and Lines, A. J., Discharge of respiratory neurons in sneezes resulting from ethmoidal nerve stimulation, *Exp. Neurol.*, **58** (1978) 410-424.
- 5) Biedebach, M. A., Beuerman, R. W. and Brown, A. C., Graphic digitizer analysis of axon spectra in ethmoidal and lingual branches of the trigeminal nerve, *Cell Tissue Res.*, **157** (1975) 341-352.
- 6) Bowsher, D., Diencephalic projections from the midbrain reticular formation, *Brain Res.*, **95** (1975) 211-220.
- 7) Bushnell, M. C. and Duncan, G. H., Sensory and affective aspects of pain perception: is medial thalamus restricted to emotional issues? *Exp. Brain Res.*, **78** (1989) 415-418.
- 8) Clarke, W. B. and Bowsher, D., Terminal distribution of primary afferent trigeminal fibers in the rat, *Exp. Neurol.*, **6** (1962) 372-383.
- 9) Camans, P. E. and Snow, P. J., Ascending projections to nucleus parafascicularis of the cat, *Brain Res.*, **230** (1981) 337-341.
- 10) Dong, W. K., Ryu, H. and Wagman, I. H., Nociceptive responses of neurons in the medial thalamus and their relationship to spinothalamic pathway, *J. Neurophysiol.*, **41** (1978) 1592-1613.
- 11) Feltz, P., Krauthamer, G. and Albe-Fessard, D., Neurons in the medial diencephalon. I. Somatosensory responses and caudate inhibition, *J. Neurophysiol.*, **30** (1967) 55-80.
- 12) Giesler, G. J. Jr., Menetrey, D. and Basbaum, A. I., Differential origins of spinothalamic tract projections to medial and lateral thalamus in the rat, *J. Comp. Neurol.*, **184** (1979) 107-125.
- 13) Giesler, G. J. Jr., Yezierski, R. P., Gerhart, K. D. and Willis, W. D., Spinothalamic tract neurons that project to medial and/or lateral thalamic nuclei: evidence for a physiologically novel population of spinal cord neurons, *J. Neurophysiol.*, **46** (1981) 1285-1308.
- 14) Haber, L. H., Moore, B. D. and Willis, W. D., Electrophysiological properties of spinoreticular neurons in the monkey, *J. Comp. Neurol.*, **207** (1982) 75-84.
- 15) Jones, B. E. and Yang, T.-Z., The efferent projections from the reticular formation and the locus coeruleus studied by anterograde and retrograde axonal transport in the rat, *J. Comp. Neurol.*, **242** (1985) 56-92.
- 16) Kaufman, E. F. S. and Rosenquist, A. C., Efferent projections of thalamic intralaminar nuclei in the cat, *J. Comp. Neurol.*, **335** (1985) 257-279.
- 17) Kaufman, E. F. S. and Rosenquist, A. C., Afferent projections of the thalamic intralaminar nuclei in the cat, *J. Comp. Neurol.*, **335** (1985) 281-296.
- 18) Keene, J. J., Reward-associated inhibition and pain-associated excitation lasting seconds in single intralaminar thalamic units, *Brain Res.*, **64** (1973) 211-224.

- 19) Krettek, J. E. and Price, J. L., The cortical projections of the mediodorsal nucleus and adjacent thalamic nuclei in the rat, *J. Comp. Neurol.*, **171** (1977) 157-192.
- 20) Kruger, L., Saporta, S. and Feldman, S. G., Axonal Transport studies of the sensory trigeminal complex. In : D. J. Anderson and B. Matthews (eds.), *Pain in the Trigeminal Region*, Elsevier, Amsterdam, 1977, pp. 243-257.
- 21) Lucier, G. E. and Egizzi, R., Central projections of ethmoidal nerve of the cat as determined by the horseradish peroxidase tracer technique, *J. Comp. Neurol.*, **247** (1986) 123-132.
- 22) Marfart, C. F., The central projections of trigeminal primary afferent neurons in the cat as determined by the transganglionic transport of horseradish peroxidase. *J. Comp. Neurol.*, **203** (1981) 785-798.
- 23) Marfart, C. F. and Echtenkamp, S. F., Central projections and trigeminal ganglion location of corneal afferent neurons in the monkey, *Macaca fascicularis*, *J. Comp. Neurol.*, **272** (1988) 370-382.
- 24) Meessen, H. and Olszewski, J., *A Cytoarchitectonic Atlas of the Rhombencephalon of the Rabbit*, Karger, Basel, 1949.
- 25) Melzack, R. and Casey, K. L., Sensory, motivational and central control determinants of pain: a new conceptual model, In : Kenshalo, D. R. (ed.), *The Skin Senses*, Thomas, Springfield, Ill, 1968, pp. 423-443.
- 26) Molinari, M., Bentivoglio, M., Minciacchi, D., Granato, A. and Macchi, G., Spinal afferents and cortical efferents of the anterior intralaminar nuclei: an anterograde-retrograde tracing study, *Neurosci. Lett.*, **72** (1986) 258-264.
- 27) Nishida, Y. and Yokota, T., Neurons in and near the trigeminal subnucleus caudalis excited by mechanical stimulation of the cornea, *Neuro-ophthalmol. Jpn.*, **3** (1986) 35-43.
- 28) Peschanski, M., Guilbaud, G. and Gautron, M., Posterior intralaminar region in rat: neuronal responses to noxious and nonnoxious cutaneous stimuli, *Exp. Neurol.*, **72** (1981) 226-238.
- 29) Panneton, W. M. and Burton, H., Corneal and periocular representation within the trigeminal sensory complex in the cat studied with transganglionic transport of horseradish peroxidase, *J. Comp. Neurol.*, **199** (1981) 327-344.
- 30) Shigenaga, Y., Chen, I. C., Suemune, S., Nishimori, T., Nasion, I. D., Yoshida, H., Sato, H., Okamoto, T., Sera, M. and Hosoi, M., Oral and facial representation within the medullary and upper cervical dorsal horns in the cat, *J. Comp. Neurol.*, **243** (1986) 388-408.
- 31) Torvik, A., Afferent connections to the sensory trigeminal nuclei, the nucleus of the solitary tract and adjacent structures, *J. Comp. Neurol.*, **106** (1956) 51-132.
- 32) Sjöqvist, O., Studies on pain conduction in the trigeminal nerve. A contribution to the surgical treatment of facial pain, *Acta Psychiat. Neurol. Scand.*, Suppl. **17** (1938) 1-139.
- 33) Trevino, D. L., Maunz, R. A., Bryan, R. N. and Willis, W. D., Location of cells of origin of the spinothalamic tract in the lumbar enlargement of cat, *Exp. Neurol.*, **34** (1972) 64-77.
- 34) Vogt, B. A., Rosene, D. L. and Pandya, D. N., Thalamic and cortical afferents differentiate anterior from posterior cingulate cortex in the monkey, *Science*, **204** (1979) 205-207.
- 35) Weinberger, L. M. and Grant, F. C., Experiences with intramedullary tractotomy. III. Studies in sensation, *Arch. Neurol. Psychiatr.* (Chicago), **48** (1942) 355-381.
- 36) Yokota, T., Trigemino-vagal reflex elicited by tactile stimulation in cats, *Jpn. J. Physiol.*, **22** (1972) 533-543.
- 37) Yokota, T., Neural mechanisms of trigeminal pain, *Adv. Pain Res. Ther.*, **9** (1985) 211-232.
- 38) Yokota, T. and Nishikawa, N., Reappraisal of somatotopic tactile representation within trigeminal subnucleus caudalis. *J. Neurophysiol.*, **43** (1980) 700-712.

Address for correspondence: Toshikatsu Yokota, M. D., Department of Physiology, Medical College of Shiga, Seta, Otsu 520-21, Japan.
Telephone: 0775-48-2146