Discharge Patterns of Bulbar Respiratory Neurons during Retching and Vomiting in Decerebrate Dogs

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Abstract To determine whether bulbar respiratory neurons are active in a manner similar to respiratory motor nerves, in which diverse activity patterns have been observed in dogs, the discharge of 112 bulbospinal and 155 propriobulbar respiratory neurons was observed during retching and vomiting evoked by stimulation of the vagal nerve in decerebrate, paralyzed dogs. During retching, the respiratory activities of all respiratory neurons changed. The discharge patterns during retching were classified into seven types in accordance with the discharge phase in the retching cycle and the discharge frequency. Inspiratory bulbospinal neurons (39) in the ventral respiratory group (VRG) exhibited discharge synchronous with retches at higher (14/39) or lower (4/39) frequencies than those of their respiratory discharge, discharge between retches at higher (3/39) or lower (14/39) frequencies and discharge depressed throughout the retching period (4/39). Inspiratory bulbospinal neurons (30) in the dorsal respiratory group (DRG) and expiratory bulbospinal neurons (23) in the VRG also fired with some of the seven types of discharge. No significant difference was recognized between the ratio of the numbers of inspiratory bulbospinal neurons firing with the seven types of discharge and that of expiratory bulbospinal neurons. On the other hand, the respiratory propriobulbar neurons (73) in the VRG and those (45) in the DRG seemed to be differently activated; that is, 44% of the propriobulbar neurons in the VRG fired synchronously with retches at a higher frequency than their frequency during breathing, while only 22% of those in the DRG fired at such a high frequency with retches. However, the ratio of whole inspiratory neurons (174) exhibiting the seven types of discharge was almost the same as that of whole expiratory neurons (93). During vomiting (fictive expulsion), three of five expiratory neurons fired, but most (14/16) of inspiratory neurons did not. In conclusion, all of the activity patterns which have been observed during retching in motor fibers

innervating respiratory muscles are found in both bulbospinal and propriobulbar respiratory neurons in dogs. Furthermore, since the firing patterns of inspiratory bulbospinal neurons during retching in the dogs in this study are apparently different from those in cats (MILLER *et al.*, 1990), inspiratory neurons and muscles seem to be differently organized during retching in cats and dogs.

Key words: retching, vomiting, bulbar respiratory neurons.

In decerebrate, paralyzed cats, MILLER *et al.* (1987, 1990) demonstrated that one-third of the bulbospinal expiratory neurons of the ventral respiratory group (VRG) fire synchronously with retches, whereas the remaining two-thirds are active between retches. In addition, they noted that only 10% of inspiratory bulbospinal neurons of both the dorsal and ventral respiratory groups in the caudal bulb fire concomitantly with retches, while most of the remainder are suppressed during retching. KOGA and FUKUDA (1990) recently clarified the discharge patterns of inspiratory and expiratory motor fibers to the thoracic muscles during retching in dogs. However, the following three incidents in Koga and Fukuda's study (KOGA and FUKUDA, 1990) could not be explained by the results of MILLER *et al.* (1987, 1990): 1) many inspiratory motor fibers concomitantly discharged with retches at a higher frequency than their frequency during breathing; 2) some inspiratory motor fibers strongly discharged between retches; and 3) some expiratory motor fibers were depressed throughout the retching period. The present study, therefore, was performed first to determine whether or not these discharge patterns in the respiratory motor fibers are formed in the bulb in dogs.

The second aim of this work was to study and describe the retching activities of respiratory propriobulbar neurons, since the behavior of propriobulbar neurons during retching has not been clarified, and knowledge of their behavior seems important to an understanding of the patterning of retching.

METHODS

Twelve dogs, each weighing 6–12 kg, were used in this study. Precollicular decerebration was carried out under anesthesia induced with an intramuscular injection of ketamine hydrochloride (10 mg/kg). The dogs were paralyzed with intravenous gallamine triethiodide (2 mg/kg) and artificially ventilated with a respirator (Aika, R-60) through a tracheal cannula at a rate of 10–20 strokes/min. Over the entire series of experiments, end-tidal CO₂ was maintained within a range of from 2.0 to 3.5%. Pneumothorax was induced on the left side to improve the recording stability from bulbar neurons. Arterial blood pressure was monitored through a cannula connected to the right femoral artery. Body temperature was kept near 37°C by using a heat plate under the animal and two heating lamps.

The branch of the C5 spinal nerve forming the left phrenic nerve and the branch of the L1 spinal nerve innervating the left rectus abdominis were isolated through incisions along the cervical midline and the dorsal edge of the obliquus externus abdominis, respectively. Centrifugal discharge from these nerves was led out with bipolar platinum wire electrodes. Neural discharge was converted into frequency histograms of 100 ms bins using spike counters (Dia Medical, DSE-325 A), and the histograms were recorded with a pen recorder. Animals were supported in a prone position by a stereotaxic head holder and a clamp fixed to the third thoracic vertebra. A single unitary discharge from a bulbar respiratory neuron was recorded extracellularly with micropipettes (3–5 μ m in tip diameter) filled with a water solution saturated with sodium citrate. The electrode was inserted dorsoventrally from the exposed dorsal surface of the caudal medulla oblongata. The locations of the recorded units were determined by measuring stereotaxic coordinates relative to the obex. A single-cell discharge was converted into rectangular pulses of 3 ms duration using a stimulator and was simultaneously changed into frequency histograms of 100 ms bins. Both the pulses and histograms were recorded with the pen recorder. In some experiments, activities of the phrenic nerve, the nerve to the rectus abdominis and a bulbar respiratory unit were simultaneously recorded with an oscilloscope and a long recording camera.

The supra-diaphragmatic ventral vagal trunk was isolated through an incision along the eighth rib. A retching response was produced by electrical stimulation (10 V, 0.5 ms, 10–20 Hz) of the central cut end of the ventral vagal trunk with a bipolar platinum wire electrode. Vagal stimulation was turned off when 4–5 retches were elicited. Retching could be usually elicited within 1 min of latency. However, the latency for the onset retching became longer as time elapsed after the beginning of some experiments, since retching responses were elicited about 25 times on the average per a dog. Thus, when retching could not be elicited by stimulation of the vagal nerve for over 1 min, apomorphine (0.1–0.3 mg/kg) was administered intramuscularly. At the end of retching, when the rate and period of discharge in the phrenic nerve decreased and the period of discharge in the nerve to the rectus abdominis became more prolonged, we recognized the episode as vomiting (fictive expulsion) (MILLER *et al.*, 1987; KOGA and FUKUDA, 1990). There were no significant differences in the activities of the phrenic and abdominal muscle nerves during retching and vomiting induced by vagal stimulation alone or apomorphine alone, or by vagal stimulation after apomorphine administration. Therefore, all results from retching and vomiting caused by the three kinds of stimulation were treated together in this study. Possible differences between data samples were assessed by the Wilcoxon test.

Laminectomies were performed at the C2 and Th2 vertebrae, and bipolar platinum wire electrodes were placed close to both sides of the cord to permit antidromic activation of descending axons of the bulbar respiratory neurons. A projection to the spinal cord was confirmed by collisions between spontaneously occurring and antidromically evoked spikes (LIPSKI, 1981; MILLER *et al.*, 1987;

FUKUDA and FUKAI, 1988).

RESULTS

Classification of respiratory units

Patterns of respiratory discharge. We recorded 174 inspiratory units which fired almost exclusively during phrenic discharge and 93 expiratory units which fired during the periods between phrenic discharge.

On the basis of the temporal firing patterns of the respiratory units, both inspiratory and expiratory units were further classified into six subclasses as follows (Table 1). 1) Augmenting units, which fired within the inspiratory phase and reached peak frequency at the end of the inspiration, or fired within the expiratory phase and reached peak frequency at the end of expiration, after which the discharge terminated abruptly (Figs. 2A, C, E, G, I; 3G, I). 2) Decrementing units, which began to fire at the start of inspiration or expiration, quickly reached peak frequency, and then declined slowly and stopped (Figs. 3E, 4E). 3) Constant units, which began to fire abruptly at the start of inspiration or expiration, and then continued at an approximately constant frequency for most of the inspiratory or expiratory phase (Figs. 3A, 4C). 4) Tonic units, which fired throughout the respiratory cycle with a period of increased frequency during the inspiratory or expiratory phase (Fig. 4A). These four subclasses (1)–(4)) have been previously

Table 1. Correlation between subclasses of respiratory neurons and their types of retching discharge.

	Types of retching discharge							Total
	SH	BH	TH	SL	BL	DT	AV	
A. Inspiratory units								
Augmenting	29	14	3	11	45	13	1	116
Decrementing	5	5	0	0	3	4	4	21
Tonic	6	1	0	2	2	4	0	15*
Constant	9	1	0	0	1	0	2	13
Low frequency	3	1	0	0	0	3	0	7
Late	2	0	0	0	0	0	0	2
B. Expiratory units								
Decrementing	6	0	1	10	2	3	2	24
Early and late	10	4	1	0	5	0	3	23
Constant	11	0	1	2	3	3	2	22
Augmenting	6	0	0	0	4	3	2	15
Tonic	2	0	0	0	1	4	1	8
Low frequency	2	0	0	0	0	0	0	2

Numbers of units are shown. The subclasses of respiratory neurons and the types of retching discharge are explained in the text. *Significant difference (Wilcoxon test, $p < 0.05$).

described in cats by COHEN (1979). 5) Low-frequency units, which fired at so low a frequency (12.0 ± 2.4 Hz (mean $\pm$ S.D.); 2–17 spikes per a respiratory cycle) during inspiration or expiration that they could not be classified into the categories described above. The following subclasses were exclusively observed in either inspiratory or expiratory units. 6-I) Late units, which fired during a restricted period of the late inspiratory phase and may correspond to the late inspiratory unit described in cats by RICHTER (1982). 6-E) Early and late units, which predominantly fired at the beginning and end of the expiratory phase, and decreased in firing frequency during the mid-expiratory phase (Fig. 3C). This firing pattern was observed in single active fibers from the internal intercostal nerve in dogs (KOGA and FUKUDA, 1990).

Location of units. As shown in Fig. 1, respiratory units were explored from the dorsal surface of the bulb to a depth of 7 mm in the area from 5 mm caudal to 3 mm rostral to the obex. Areas where respiratory units were densely recorded are enclosed by broken-line rectangles in Fig. 1. The two areas seem to correspond to the dorsal and ventral respiratory areas (COHEN, 1979). Therefore, in this work, the respiratory units situated in the medial rectangles to a depth of 3.5 mm from the dorsal surface of the bulb were classified as belonging to the dorsal respiratory

Fig. 1. Positions of respiratory units whose discharge was observed during retching. Each dot represents an inspiratory unit (left side) or an expiratory unit (right side). The units in the small medial rectangles, to a depth of 3.5 mm, were classified as the dorsal respiratory group. The units in the lateral rectangles, which were deeper than 3.5 mm, were classified as the ventral respiratory group. The units found outside both these rectangles were classified as "others."

group (DRG), and those in the other rectangles, which were deeper than 3.5 mm, were considered to be in the ventral respiratory group (VRG) (FUKUDA and FUKAI, 1988). Units found outside of these areas were classified as "others."

Forty-seven percent of the inspiratory units and 32% of the expiratory units projected to the spinal cord. Thirty out of the 82 inspiratory bulbospinal units and 8 out of the 30 expiratory bulbospinal units projected to C2 but not to Th2.

Discharge of respiratory units during retching (retching discharge)

Retching was defined as a series of bursts of coactivation of the phrenic nerve and the nerve to the rectus abdominis in response to vagal stimulation and/or apomorphine injection.

Classification of retching discharge of respiratory units. Recently MILLER *et al.* (1987, 1990) observed discharge of bulbar respiratory neurons during retching and vomiting in cats, and classified the discharge in accordance with its temporal patterns. In this study, retching discharge was divided into the following seven types on the ground of the criteria not only of the temporal patterns but also of the discharge frequency which was compared with the frequency of the respiratory discharge. 1) Discharge synchronous with retches at a higher frequency than the respiratory firings during quite breathing (SH-type) (Figs. 2B, 3B). 2) Discharge synchronous with retches at a lower frequency than the respiratory firings (SL-type) (Figs. 2F, 3F). Many units of the SH-type (77/90) and SL-type (21/25) also fired during periods between retches, but the frequency was lower than that during periods of retches. The retching discharge from expiratory neurons classified as the ABD type by MILLER *et al.* (1987) and that from inspiratory neurons categorized as "Active" by MILLER *et al.* (1990) seem to be included in the SH- and SL-types. 3) Discharge between retches at a higher frequency than the respiratory firings (BH-type) (Figs. 2D, 3D). 4) Discharge between retches at a lower frequency than the respiratory firings (BL-type) (Figs. 2H, 3H). Many units of the BH-type (20/27) and BL-type (37/66) also fired with retches, but the frequency was lower than that between retches. The retching discharge from expiratory neurons classified as the INT type by MILLER *et al.* (1987) seems to be included in the BL-type. 5) Tonic discharge throughout the retching period at a higher frequency than the respiratory firings (TH-type). 6) Depressed discharge throughout the retching period (DT-type) (Figs. 2J, 3J). Neurons of this type may correspond to inspiratory neurons categorized as "Silent" by MILLER *et al.* (1990). 7) Discharge mainly modified by artificial ventilation rather than by retching (AV-type) (Fig. 4). Inspiratory units which discharged only during restricted periods of the late phase of coactivations and which were categorized as "End" by MILLER *et al.* (1990), could not be found in this study. However, as shown in Fig. 2F, there were some inspiratory units (5/174) which sometimes fired in a manner similar to the units categorized as "End."

Vomiting (fictive expulsion) could only be elicited on rare occasions at the end of the retching chain. Thus, the behavior of only 21 respiratory units during

Fig. 2. Firing patterns of inspiratory units during breathing and retching. From top to bottom, the traces in A and B show the action potentials of the phrenic nerve, those of the nerve to the rectus abdominis and discharge of an inspiratory unit. These activities were recorded simultaneously with a long recording camera. Similarly, the traces in C-J show the frequency histograms of centrifugal discharge of the phrenic nerve, those of the nerve innervating the rectus abdominis, rectangular pulses representing discharge of an inspiratory unit and frequency histograms of the discharge. Each trace in A-B, C-D, E-F, G-H, and I-J was recorded from the same nerves and unit. The traces in A, C, E, G, and I were recorded during quiet breathing, and the traces in B, D, F, H, and J were recorded during retching. Vertical broken lines have been added to provide a visual reference. DRG, dorsal respiratory group; VRG, ventral respiratory group. These explanations also apply to Figs. 3 and 4. Examples of retching discharge are shown: B (SH-type), D (BH-type), F (SL-type), H (BL-type), and J (DT-type). Refer to the text for types of retching discharge.

vomiting could be clarified.

Correlations between the types of retching discharge and classes of respiratory units

Inspiratory units. All seven types of retching discharge were found in inspiratory bulbospinal units, and all except the TH-type were found in inspiratory propriobulbar units (Fig. 5A). No significant difference, however, was found between the ratio of the numbers of bulbospinal units exhibiting the seven types of retching discharge and that of the propriobulbar units ($p < 0.05$, Wilcoxon test).

Fig. 3. Firing patterns of expiratory units during breathing and retching. Examples of retching discharge are shown: B (SH-type), D (BH-type), F (SL-type), H (BL-type), and J (DT-type).

Fig. 4. Examples of units which were primarily affected by lung inflation rather than by retching. Horizontal solid lines under traces indicate lung inflation periods. See the text for further explanations.

A inspiratory units **B expiratory units**

Fig. 5. Graphs showing correlations between the respiratory groups of units and their discharge types observed during retching. Groups of respiratory units are shown on the left side: DRG, dorsal respiratory group; VRG, ventral respiratory group; Others, the group of respiratory units existing outside the dorsal and ventral respiratory areas. C but not to Th: bulbospinal neurons antidromically activated by C2 stimulation but not by Th2 stimulation. Th: bulbospinal neurons antidromically activated by C2 and Th2 stimulation. The discharge types of the respiratory units during retching are represented by the patterns shown at the bottom of the figure. The numerals in the bands indicate the number of units showing the discharge type represented by the pattern. The numerals in parentheses outside of the bands indicate the total numbers of the units in the respiratory group. *Significant difference between the ratios of the neurons of both groups showing these discharge patterns ($p < 0.05$, Wilcoxon test).

About half (7/13) of the units that were antidromically activated by C2 but not by Th2 stimulation fired with SH-type discharge, while many of those activated by Th2 stimulation fired with BL- (27/69) and SH-type discharge (20/69). None of the low-frequency and constant units were activated by spinal stimulation. The ratio of constant units exhibiting SH-type discharge was significantly larger than the ratios of the augmenting and decrementing units ($p < 0.05$, Wilcoxon test, Table 1, *). In addition, all late units, which were bulbospinal, fired synchronously with retches (SH-type).

Depressed discharge (DT-type) was observed in more than one-third (12/35) of the propriobulbar inspiratory units in the DRG. Conversely, this type was observed in only one of 31 units in the VRG. There were significant differences between the ratio of DRG propriobulbar units exhibiting the seven types of retching discharge and that of VRG propriobulbar units (Fig. 5A, *), but not between DRG and VRG bulbospinal units. An example of AV-type discharge is shown in Fig. 4F. This unit mainly fired during lung deflation periods of artificial ventilation, but its discharge during deflation was inhibited simultaneously with each retch, as indicated by broken lines in Fig. 4F. Four neurons in DRG and two neurons in VRG has discharge almost restricted within lung deflation periods even when retching was elicited (Fig. 5A).

During the vomiting phase, most of the inspiratory units (14/16) did not fire, but two units which exhibited SH-type discharge during retching also fired concomitantly with vomiting.

Expiratory units. All of the seven types of retching discharge found in inspiratory units were also noted in expiratory units, and 40% of these units displayed SH-type discharge (Fig. 5B). All the expiratory units of TH-type were propriobulbar, whereas all inspiratory units of this type were bulbospinal. BH-type discharge was found only in bulbospinal early and late units (Fig. 5B, Table 1). However, there was no significant difference between the ratio of the expiratory bulbospinal units exhibiting the seven types of retching discharge and that of expiratory propriobulbar units, as was the case for the inspiratory bulbospinal and propriobulbar units. Half (4/8) of the units activated by C2 but not by Th2 stimulation strongly fired with retches (SH-type), while only one of the units fired with a high frequency between retches (BH-type). Forty-one percent (9/22) of the units activated by Th2 stimulation also fired with SH-type discharge. The latter type of discharge was found in half (21/42) of the expiratory propriobulbar units in VRG, but in only one of 10 DRG expiratory propriobulbar units. Therefore, a significant difference also existed between the ratio of propriobulbar DRG expiratory units exhibiting the seven types of retching discharge and that of propriobulbar units of the VRG (Fig. 5B, *). Examples of AV-type discharge are shown in Fig. 4B and D. The DRG propriobulbar unit in A was inhibited continuously during retching, but discharge during lung inflation periods remained (B). The VRG bulbospinal unit in C was also inhibited during retching, but excited strongly only when retches occurred during inflation, as indicated by the filled circles in D.

The AV-type discharge, which increased during lung inflation, were observed in two DRG units and six VRG units (Fig. 5B). One of two DRG units fired within lung inflation periods during retching, and its basic firing pattern was almost similar to that during respiration. Thus, the unit may be excited only by lung inflation. This unit seems to correspond to P or pump cell described by BERGER (1977), and BONHAM and MCCRIMMON (1990). However, the other DRG unit seemed not to be categorized as the P cell, since the unit fired during lung deflation periods as well as lung inflation periods.

The behavior of only five expiratory units was observed during the vomiting phase. Three units discharged concomitantly with vomiting, while the remaining two units did not fire.

DISCUSSION

Although MILLER *et al.* (1987, 1990) and MILLER and NONAKA (1990) elucidated the behavior of respiratory bulbospinal neurons during retching and vomiting in cats, this study is the first one to describe the retching behavior of bulbar respiratory neurons (including the propriobulbar neurons) in dogs. In this study, all respiratory propriobulbar neurons and bulbospinal neurons in the caudal bulb in the dorsal and ventral respiratory groups in the dogs exhibited diverse patterns of discharge during retching. On the other hand, excitatory synaptic interconnections of bulbospinal inspiratory neurons on both sides of the VRG in cats are well established (MERRILL, 1974; EZURE and MANABE, 1989). In addition, augmenting inspiratory neurons of the VRG project to the contralateral VRG (SASAKI *et al.*, 1989) and make monosynaptic excitatory connections to other augmenting inspiratory bulbospinal neurons (EZURE and MANABE, 1989) in cats. In spite of these interconnections, all of the seven types of retching discharge were also found in augmenting inspiratory neurons. These results thus seem to support the assumption that neuronal retching activity is not formed by alternating activity of the respiratory pattern generator. The results of the present study, therefore, were analyzed from the standpoint that a vomiting center exists outside the respiratory pattern generator (BORISON and WANG, 1949; BORISON, 1986).

Based on the present results showing that respiratory activity was changed to retching discharge in all the respiratory neurons observed, the vomiting center may excite and/or inhibit various respiratory neurons including neurons generating respiratory rhythm and, as a result, the seven types of retching discharge might be formed. Therefore, it is speculated that the discharge synchronous with retches (SH- and SL-type) and the discharge between retches (BH- and BL-type) in respiratory neurons are produced, respectively, by the excitatory and inhibitory effects of rhythmic inputs from the vomiting center. In addition, discharge of TH- and DT-types might be produced, respectively, by convergent excitatory and inhibitory inputs from units firing with both SH- and BH-type discharge.

Bulbospinal units. In this study, respiratory bulbospinal neurons exhibited

SH-, BH-, TH-, SL-, BL-, DT-, and AV-type discharge during retching (Fig. 5). KOGA and FUKUDA (1990) observed the behavior of nerves to the thoracic respiratory muscles during retching in decerebrated and paralyzed dogs and indicated that these nerves produced various types of retching discharge and that the same kind of nerve (e.g., the external intercostal nerve) includes motor fibers which fire with various discharge types (e.g., BH-, SL-, BL-, and DT-types). Figure 6 shows the correlation between the retching discharge types of the bulbospinal units and those of motor nerves to the respiratory muscles. All of the various discharge types found in nerve strands and single active fibers to the respiratory muscles during retching (KOGA and FUKUDA, 1990) were demonstrated in the respiratory bulbospinal units. These findings suggest that the various patterns of retching activity in respiratory muscles are essentially formed in the medulla oblongata and that the respiratory bulbospinal neurons relay the patterns to the motor neurons of the respiratory muscles.

In anesthetized cats, MERRILL and LIPSKI (1987), however, showed that monosynaptic connections between the respiratory neurons in the nucleus retroambiguus and intercostal motoneurons are rare and segmental interneurons are interposed between the majority of descending respiratory axons and intercostal motoneurons. Similarly, as has been pointed out by MILLER *et al.* (1985), monosynaptic connections between brain stem respiratory neurons and abdominal motoneurons are scarce. Therefore, the spinal interneurons which are interposed between the respiratory bulbospinal neurons and respiratory motoneurons may play a crucial role in determination of the activity patterns of the respiratory muscles

Fig. 6. Correlations between retching discharge types of the bulbospinal units and those of nerves or motor fibers innervating respiratory muscles. The discharge types of the bulbospinal units are schematically shown at the top of this figure. The filled circles indicate which discharge types were found in the muscle nerves.

during retching.

Inspiratory bulbospinal units: About half (7/13) of the inspiratory bulbospinal units having exclusive projection to the cervical cord were active with SH-type discharge (Fig. 5A). These inspiratory bulbospinal units seem to contribute to the diaphragmatic contraction for retching. SH-type discharge (20/69) of the inspiratory neurons projecting to the thoracic cord may contribute to contraction of the serratus dorsalis cranialis, scalenus, rectus thoracis, intercartilagineus, and the internal intercostal muscle (Fig. 6). However, MILLER *et al.* (1990) observed SH-type discharge in only one of 51 inspiratory bulbospinal neurons of cats, and concluded that inspiratory bulbospinal neurons do not make a major contribution to activation of the diaphragm and the external intercostal muscles during retching. However, the results of the present study indicate that a considerable number of the inspiratory bulbospinal neurons (one-third) exhibited sufficient activity to contribute to retching contractions of the inspiratory muscles. Furthermore, in this study, discharge between retches (BH- and BL-types) was found in 36 of 82 inspiratory bulbospinal units. These neurons may contribute to the complicated behavior of the intercartilagineus and the external and internal intercostal muscles during retching (Fig. 6, KOGA and FUKUDA, 1990). In cats, however, MILLER *et al.* (1990) reported that only one of 51 inspiratory bulbospinal neurons discharged between retches. Moreover, they showed that about half (23/53) of the inspiratory bulbospinal neurons fired near the end of the phrenic discharge during retching and classified these neurons as "End" neurons. Surprisingly, the "End" neuron was not recognized in the 82 bulbospinal and 92 propriobulbar inspiratory neurons of dogs in this study. Such fundamental differences were not found in retching discharge of expiratory bulbospinal neurons of cats (MILLER *et al.*, 1987) and dogs (this study). Consequently, the differences in the retching discharge of inspiratory bulbospinal neurons do not seem to be caused by differences in the experimental conditions. Therefore, these differences in retching activity of inspiratory neurons may suggest that the inspiratory neurons and muscles are differently organized during retching in cats and dogs.

The phrenic nerve did not exhibit a stereotyped pattern of retching discharge in all dogs. In some dogs, the onset of retching discharge of the phrenic nerve preceded that of the nerve to the rectus abdominis, as shown in Figs. 3J and 4D, while, in many others, retching discharge of both nerves started concomitantly (Figs. 2B and 3B). In addition, the nerve innervating the intercartilagineus (an inspiratory muscle) showed larger variations in its retching discharge, i.e., SH-, SL-, BL-, and DT-types (Fig. 6). These findings suggest that the neuronal process coordinating inspiratory motor neurons is not always the same in the retching of individual dogs. Therefore, the large differences in the retching activity of the inspiratory neurons of cats and dogs seem to be a natural consequence.

Expiratory bulbospinal units: MILLER *et al.* (1987) reported that about one-third (9/27) of the expiratory bulbospinal neurons in cats discharged synchronously with retches. In the present study, similar types of retching discharge (SH-

and SL-types) were also found in the expiratory bulbospinal units projecting to the thoracic cord with a comparable ratio (9/22). These neurons seem to contribute to the emetic contractions of the internal intercostal muscle, obliquus externus abdominis and rectus abdominis (Fig. 6).

MILLER *et al.* (1987) observed that about two-thirds of expiratory bulbospinal neurons discharged between retches and that these neurons decreased their firing frequency as compared with those during respiration. Similar low frequency discharge (BL-type) was observed in the expiratory bulbospinal neurons projecting to Th2 in this study, but the ratio (5/22) was much smaller. However, some expiratory bulbospinal units (3/22) increased their frequency during periods between retches (BH-type) as compared with those during respiration. The BH-type of discharge may contribute to the retching contractions of the expiratory motor units comprising the external and internal intercostal muscles and the thoracic part of the rectus abdominis, since this type of discharge was observed in all expiratory motor fibers in the external intercostal nerves, in some (10/52) of the expiratory fibers in the internal intercostal nerves and in the nerve innervating the thoracic part of the rectus abdominis in some dogs (3/11) (KOGA and FUKUDA, 1990).

It seems rather curious that six of the eight expiratory bulbospinal neurons which were antidromically activated by C2 but not by Th2 stimulation concomitantly discharged with retches, since the expiratory neurons are known to inhibit phrenic motor neurons (GILL and KUNO, 1963) and the cervical phrenic nerve is always active synchronously with retches. However, the periesophageal crural region of the diaphragm in cats is known to contract concomitantly with retches but not with vomiting (expulsion) in contrast to the costal region which contracts in association with retching and vomiting (MONGES *et al.*, 1978; TAN and MILLER, 1986). Moreover, the retching discharge of the crural branch was apparently different from that of the costal branch in dogs, i.e., the retching discharge of the crural branch reached a maximum in its firing frequency at the early phase of each retch, thereafter promptly decreased, and ceased at the end of the retch (MONGES *et al.*, 1978; MILLER, 1990; Fukuda and Koga, unpublished results). Thus, some motor neurons innervating the periesophageal crural region of the diaphragm seem to be inhibited during each retch except during the initial phase. The phrenic motor neurons innervating the periesophageal crural region, therefore, seem to be inhibited with each retch by SH-type discharge from the expiratory bulbospinal neurons, which exclusively project to the phrenic nucleus.

Respiratory propriobulbar units. Thirty-four percent of the inspiratory propriobulbar neurons in the DRG were depressed during retching (DT-type), but only 3% of those in the VRG were. In addition, only one of 10 expiratory propriobulbar neurons in the DRG exhibited SH-type discharge, while half of those (21/42) in the VRG strongly fired with retches. Thus, there were significant differences between the ratios of the inspiratory propriobulbar units in the DRG and VRG exhibiting the seven types of retching discharge, and between the expiratory propriobulbar units in the DRG and VRG (Fig. 5, *). In the present

study, the propriobulbar units in the DRG and VRG, therefore, seem to have played different roles during retching.

BH-type discharge was not found among the discharge of 63 expiratory propriobulbar units, whereas it was observed in 4 out of 30 expiratory bulbospinal units in this study. MILLER and NONAKA (1990) showed that all 20 augmenting expiratory neurons in the Bötzing complex in cats discharged between retches and the firing frequency was higher than respiratory firings in four neurons. FEDORKO and MERRILL (1984) suggested that there is an excitatory synaptic connection from the expiratory neurons in the Bötzing complex to the same kind of neurons in the nucleus retroambiguus. If so, the BH-type discharge from the expiratory bulbospinal neurons in the caudal bulb could possibly be caused by the same type of discharge from the expiratory neurons in the Bötzing complex.

Comparison of behavior of the bulbar neurons during retching and straining. During straining, whose essential force for expulsion of rectal, vesical, and uterine contents is known to involve simultaneous contraction of the diaphragm and abdominal muscles (MENDELOFF, 1968; FUKUDA and FUKAI, 1986) which is also true for retching and vomiting, almost all of inspiratory bulbospinal neurons are silent and most of the expiratory bulbospinal neurons are active (FUKUDA and FUKAI, 1988). FUKUDA and FUKAI (1988) suggested that expiratory neurons relay commands for straining from the pontine straining reflex center to the motor neurons of the expiratory muscles, but that bulbar inspiratory neurons do not relay commands to the inspiratory motor neurons. The present study, however, clarified that both inspiratory and expiratory bulbar neurons exhibit appropriate discharge to contribute to retching contractions of the respiratory muscles. Therefore, the neurons of the vomiting center neighboring the DRG (BORISON, 1986) may directly or by interposing propriobulbar neurons, control the respiratory bulbospinal neurons for the formation of all of the various retching activities of the respiratory muscles.

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