Functional anatomy of the vagal innervation of the cervical trachea of the dog

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Coon, Robert L., Patrick J. Mueller, and Philip S. Clifford. Functional anatomy of the vagal innervation of the cervical trachea of the dog. J Appl Physiol 89: 139–142, 2000.—The canine cervical trachea has been used for numerous studies regarding the neural control of tracheal smooth muscle. The purpose of the present study was to determine whether there is lateral dominance by either the left or right vagal innervation of the canine cervical trachea. In anesthetized dogs, pressure in the cuff of the endotracheal tube was used as an index of smooth muscle tone in the trachea. After establishment of tracheal tone, as indicated by increased cuff pressure, either the right or left vagus nerve was sectioned followed by section of the contralateral vagus. Sectioning the right vagus first resulted in total loss of tone in the cervical trachea, whereas sectioning the left vagus first produced either a partial or no decrease in tracheal tone. After bilateral section of the vagi, cuff pressure was recorded during electrical stimulation of the rostral end of the right or left vagus. At the maximum current strength used, stimulation of the left vagus produced tracheal constriction that averaged 28.5% of the response to stimulation of the right vagus (9.0 ± 1.8 and 31.6 ± 2.5 mmHg, respectively). In conclusion, the musculature of cervical trachea in the dog appears to be predominantly controlled by vagal efferents in the right vagus nerve.

smooth muscle; lung; autonomic nervous system; airway; vagus nerve; parasympathetic control; bronchoconstriction

THE MEASUREMENT OF THE TRACHEAL dynamics of the extrathoracic, or cervical, trachea has often been used as a model to demonstrate reflex vagal effects on airway smooth muscle (1–4, 6, 7, 10, 12, 13). Recently, our laboratory used this model to investigate the effects of several central mediators applied to an area of the ventral medulla believed to be important in the control of tracheal muscle in the dog (10). During the course of the experiments, it was observed that microinjection of glutamate-receptor antagonists into the right rostral ventrolateral medulla abolished the reflex constrictor effects of increased systemic arterial CO2 on the tracheal musculature of the cervical trachea. Preliminary experiments suggested that this phenomenon resulted from a disproportionate innervation of the cervical trachea by the right vagus. This would not be unprecedented. The innervation to porcine cervical trachea, although bilateral, is derived predominantly from the left vagus nerve (11). The purpose of this paper was to determine whether there is lateral dominance of either the left or right vagal innervation of the canine cervical trachea.

METHODS

All experimental procedures were approved by the Institutional Animal Care and Use Committee and conducted in accordance with the American Physiological Society’s Guiding Principles in the Care and Use of Animals. Twelve mongrel dogs (12–35 kg) were anesthetized with intravenous pentobarbital sodium (30 mg/kg), with supplemental doses administered as required, intubated, and placed on positive-pressure ventilation. Arterial and venous catheters were placed in a femoral artery and vein for blood pressure measurement and administration of additional anesthetic and intravenous fluids, respectively. Because these studies were conducted before but in conjunction with another set of experiments, a midsternal thoracotomy was also produced. Pressure recorded from the fluid-filled endotracheal tube cuff placed in the trachea, rostral to the sternal notch, was used as an index of tracheal tone (2). Cuff pressure and systemic arterial pressure were monitored by using Statham transducers and recorded on a Grass Instruments polygraph. A baseline cuff pressure was achieved by increasing ventilator output until cuff pressure reached a minimum level. Fluid volume in the cuff was then adjusted to the minimum level required to prevent air from leaking around the cuff during lung inflation. Vagally mediated tracheal tone was produced by either decreasing the level of ventilation or adding CO2 to the ventilatory gas mixture. Once tracheal tone was established, either the right (n = 5) or left (n = 7) cervical vagus nerve was sectioned, followed by section of the contralateral vagus. Measurements of cuff pressure were made after establishment of tracheal tone, after section of either the right or left vagus nerve, and after both vagi had been sectioned. In each instance, cuff pressure after bilateral denervation was subtracted from the recorded pressure. The response after denervation was analyzed as the percentage of the control response before denervation.

To further investigate the functional anatomy of the vagal innervation of the cervical trachea, the vagi were electrically stimulated. In five of the dogs, after section of the vagi, the rostral end of either the right or left cervical vagus nerve was stimulated followed by stimulation of the contralateral vagus.

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nerve. Stimulation parameters were 30 Hz and 3 ms at current strengths of 0.1, 0.3, 0.5, 1.0, 2.0, 3.0, and 6.0 mA. Cuff pressure recorded at each stimulation level was measured as the increase in pressure from the baseline pressure before stimulation. The data were then analyzed as the percentage of the response observed when the right vagus was stimulated at 6.0 mA. Group data are expressed as means ± SE with differences in group data being considered significant, by using a t-test, at $P$ values ≤ 0.05.

RESULTS

The dominance of the right vagus in its effect on the cervical trachea is apparent in the polygraph tracings shown in Fig. 1. When the left vagus was sectioned first, only a small transient effect was observed. A greater effect was observed when the right vagus was then sectioned. However, in another animal, when the right vagus was sectioned first followed by section of the left vagus, section of the right vagus produced a maximum loss of cuff pressure with no further effect when the left vagus was sectioned. Similarly, in five dogs in which the right vagus was sectioned first (Fig. 2A), cuff pressure decreased to baseline levels, and no further decrease in cuff pressure was observed when the left vagus was sectioned. However, in three of the seven animals in which the left vagus was sectioned first (Fig. 2B), cuff pressure was not affected. In the remaining four animals, only a partial return toward baseline cuff pressure was observed. After section of the right vagus, cuff pressure decreased approximately to the level at which the pressure in the cuff had been set originally. The decrease in cuff pressure after section of both vagi was not significantly different in the two groups of animals (24.3 ± 2.2 and 26.2 ± 4.8 mmHg when the left vs. the right vagus was sectioned first, respectively).

The dominance of the effect of a supramaximal electrical stimulation (6.0 mA) of the right vagus vs. the left vagus on cuff pressure in the cervical trachea is evident in the polygraph tracing shown in Fig. 3. However, the tracing also gives evidence that the left vagus, although less dominant, may affect the tone of the cervical trachea. The individual results of graded stimulation of the left vs. the right vagus in five dogs are shown in Fig. 4. At 6.0 mA, stimulation of either the left or right vagus produced bronchoconstriction [9.0 ± 1.8 ($n = 5$) and 31.6 ± 2.5 ($n = 5$) mmHg, respectively]. However, the response to stimulation of the right vagus was significantly greater than the response to stimulation of the left vagus. The response to supra-

Fig. 1. Polygraph tracing of effect of section of left vagus (L vagus) followed by section of right vagus (R vagus; A) and section of vagi in the reverse order on cuff pressure (Cuff pres; B).

Fig. 2. Individual data from 5 animals in which right vagus was sectioned first (A) and from 7 animals in which left vagus was sectioned first (B). To allow individual animal's data to be distinguishable, lines for 5 animals in which right vagus was sectioned first are offset slightly from 100% at control.

Fig. 3. Polygraph tracing of effect of stimulating left and right vagus nerves on cuff pressure (B) with stimulation parameters of 30 Hz and 3 ms at a current strength of 6 mA. A: blood pressure (BP).
maximal stimulation of the left vagus averaged 28.5% of that of the right vagus.

**DISCUSSION**

Electrical stimulation of the right or left vagus demonstrated that vagal innervation of the cervical trachea of the dog appears to be predominantly, but not exclusively, from the right vagus. When a right or left vagus nerve was sectioned in the presence of existing vagal tone, the right was also shown to have a disproportionate effect on the vagal control of the cervical trachea. The left vagus was ineffective in producing vagally mediated tone in the cervical trachea in the absence of the right vagus. Thus the physiological role of the left vagus in developing tone in the cervical trachea appears to be limited. Because reflex activation of parasympathetic activity would be expected to be less effective in producing tracheal constriction than direct electrical stimulation, it is likely that increases in left vagal nerve activity alone would be insufficient to elicit tone in the cervical trachea.

As a model for the study of vagal control of tracheal muscle, the cervical trachea is particularly useful because it can be exposed without opening the chest (1, 2). When changes in pressure in an endotracheal tube cuff are used to record changes in tracheal tone, the cuff is often placed in the cervical trachea, partially because of the length of the endotracheal tube and partially because the cuff can be located outside the thorax so that the cuff is not directly exposed to intrathoracic pressure. For a preponderance of the studies that have used this model to study the vagal control of tracheal muscle, the laterality of the functional anatomy of the vagal innervation was irrelevant. However, when unilateral central blockade or stimulation of efferent output to the trachea is conducted by using this model, the functional anatomy of the vagal innervation, with respect to right vs. left vagal innervation of the cervical trachea, may become relevant. If the vagal innervation of the trachea is predominantly unilaterally distributed, right medulla to right vagus and left to left, then results of unilateral studies of medullary control of tracheal muscle by using the cervical trachea would depend on the side studied. Furthermore, if the number of efferent neurons is related to the relative responses to unilateral stimulation of the right or left vagus nerves, the number of efferents to the left would be ~28% of those to the right. This may also suggest that tracer studies in which the tracer was applied to the cervical trachea would be distributed centrally with a much greater labeling on the right than on the left. Actually, with incomplete labeling, there may be little, if any, label located on the left. Additionally, although it was not investigated in this study, a similar finding may be observed with regard to the vagal control of mucus secretion.

Species variation in the functional anatomy of the vagal innervation of the cervical trachea evidently exists. The functional innervation of the musculature of the cervical trachea of the dog appears to be predominantly from the right vagus. However, tone in the cervical trachea of the pig reportedly is predominantly controlled by the left vagus (11). The cervical trachea of the cat has also been used in a number of studies concerning the medullary control of tracheal smooth muscle (5, 8, 9); however, the possible lateral dominance of either the left or right vagus in control of the musculature of the cervical trachea of this species does not appear to have been investigated.

In conclusion, the musculature of cervical trachea in the dog appears to be predominantly controlled by vagal efferents in the right vagus nerve. The more complete understanding of the functional anatomy of the vagal innervation of the musculature of the cervical trachea produced by the results of this study may be useful in the design of future experiments to study the central nervous system pathways in the control of tracheal tone and may also be important in the interpretation of the data obtained.

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