STUDIES ON THE NERVE PATHWAYS INVOLVED IN THE
LARYNGEAL REFLEX (LARYNGOSPASM) IN THE CAT

BY
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SUMMARY
The receptor sites and nerve pathways involved in the reflex production of laryngospasm have been investigated in the cat. The trigeminal nerves and the internal branch of the superior laryngeal nerves were shown to provide an afferent pathway for the reflex when the nasopharynx and larynx were exposed to ether vapour. Evidence was obtained suggesting that the recurrent laryngeal nerves may form part of the afferent innervation of the trachea involved in this reflex response. The vagus nerves provide an afferent pathway from receptors in the trachea and lungs.

The literature on laryngeal structure and function reviewed previously (Rex, 1970a) indicated the nerve pathways which are probably involved in the stimulation of laryngospasm. Murtagh and Campbell (1954), in particular, considered that the afferent pathways involved are those from the surface of the pharynx and larynx (trigeminal, hypoglossal and vagus nerves). However, they drew attention to the possibility that stimulation of receptors in many areas of the body may produce laryngospasm. They considered the motor pathways to be in the vagus nerve and its branches, including the superior laryngeal nerves and recurrent laryngeal nerves. They stated that the external branch of the superior laryngeal nerve provides the motor innervation to the cricothyroid muscle and that the recurrent laryngeal nerve has motor branches to the other intrinsic laryngeal muscles.

In a previous paper (Rex, 1970b) evidence was provided for the existence of receptors which are stimulated by volatile anaesthetic agents not only in the nasopharynx and larynx, but also in the trachea and lungs. Stimulation of these receptors when they are exposed to ether vapour may result in laryngospasm and apnoea or other changes in the respiratory rhythm.

The work reported here is a series of experiments carried out to determine the effect of exposure of regions of the respiratory tract to ether after cutting nerves from them which were thought to form part of the afferent pathway for the laryngeal reflex. In other experiments the effects of electrical stimulation of intact nerves and of the central and peripheral ends of cut nerves were also recorded.

METHODS
The preparations used were 8 cats anaesthetized with chloralose (65 mg/kg) and 38 decerebrate cats. The techniques of anaesthesia, decerebration, and electromyography have been described previously (Rex, 1970b). An electromyographic record of the activity of the cricothyroid muscle (an adductor of the larynx) and the diaphragm was obtained during quiet respiration at the start of each series of observations in each experiment. Different sections of the respiratory tract were then exposed to 10–20 per cent ether, and the resulting spasm of the cricothyroid muscle and apnoea or change in diaphragmatic rhythm recorded. After cutting the nerve whose activity was being investigated, the area of the respiratory tract was again exposed to ether to see whether nerve section had abolished or modified the response.

Experimental Manipulations
Bilateral section of the internal branch of the superior laryngeal nerves.
In 8 cats under chloralose anaesthesia in which the respiratory tract was intact, the internal branches of the superior laryngeal nerves were cut and in 28 decerebrate cats the internal...
branches of both superior laryngeal nerves were
cut. In these experiments the respiratory tract
was exposed to ether as a spray or to ether vapour
(10–20 per cent) and oxygen. Records of the
activity of the cricothyroid muscle and the dia-
phragm during exposure of the respiratory tract
to ether were obtained both before and after cut-
ting the nerves. These nerve sections and other
combinations of sectioned nerves have been sum-
marized in table I.

<table>
<thead>
<tr>
<th>No. of expts</th>
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</tr>
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<tbody>
<tr>
<td>12</td>
<td>Internal branches of both superior laryngeal nerves</td>
</tr>
<tr>
<td>4</td>
<td>Both vagus nerves</td>
</tr>
<tr>
<td>10</td>
<td>Internal branches of both superior laryngeal nerves and both vagus nerves</td>
</tr>
<tr>
<td>1</td>
<td>Both recurrent laryngeal nerves</td>
</tr>
<tr>
<td>5</td>
<td>Both vagus nerves and both recurrent laryngeal nerves</td>
</tr>
<tr>
<td>4</td>
<td>Internal branches of both superior laryngeal nerves, both vagus nerves and both recurrent laryngeal nerves</td>
</tr>
<tr>
<td>6</td>
<td>Internal branches of both superior laryngeal nerves and local analgesic block of trigeminal nerves</td>
</tr>
<tr>
<td>2</td>
<td>Internal branches of both superior laryngeal nerves, both vagus nerves and local analgesic block of trigeminal nerves</td>
</tr>
<tr>
<td>1</td>
<td>Internal branches of both superior laryngeal nerves, both recurrent laryngeal nerves and local analgesic block of trigeminal nerves</td>
</tr>
<tr>
<td>1</td>
<td>Internal branches of both superior laryngeal nerves, both vagus nerves, both recurrent laryngeal nerves and local analgesic block of trigeminal nerves</td>
</tr>
</tbody>
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Recurrent laryngeal nerve section.

The recurrent laryngeal nerves were cut in the
mid-cervical region in 10 decerebrate prepara-
tions. Ether vapour was then passed through the
trachea in 9 and through the nasopharynx and
larynx in 1 and the activity of the diaphragm and
intrinsic laryngeal muscles recorded.

Perineural block of the trigeminal nerves
with local analgesic solution.

In 8 decerebrate cats the trigeminal nerves were
blocked within the cranial cavity immediately
peripheral to the Gasserian ganglia, using 2 per
cent lignocaine hydrochloride (Xylocaine; Astra)
solution injected around the nerve. (This proved

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the only practicable technique of "sectioning"
this nerve.) In these preparations the internal
branches of the superior laryngeal nerves had
already been cut. Ether vapour (10–20 per cent)
and oxygen were then administered through the
nasopharynx and larynx by means of a latex
rubber face mask (Hall, 1957).

Section of the cervical vagus nerves.

In experiments on 26 cats the respiratory tract
was exposed to 10–20 per cent ether before and
after cutting the cervical vagus nerves. In 4 pre-
parations the vagi were the only nerves cut, but
in the rest of the experiments other nerves were
cut or blocked as indicated in table I.

Nerve stimulation.

In 4 cats under chloralose anaesthesia and 4
decerebrate preparations, electrical stimulation of
intact or cut nerves was carried out using a
Palmer (London) student stimulator. The nerves
stimulated were the internal and external
branches of the superior laryngeal nerves, and the
recurrent laryngeal nerves.

RESULTS

Inhalation of ether, as has been reported pre-
viously (Rex, 1970b), stimulated laryngospasm in
the cat (fig. 1a).

Laryngospasm was first evident within 0.2 sec
of the administration of ether and frequently had
two phases, the second phase being apparent as
an exacerbation of the previous response and
occurring up to 5 sec after the first application
of ether. The effects of nerve sections on the
production of laryngospasm were examined in the
experiments described below, which were aimed
at elucidation of the sensory nerve pathways
involved in the reflex.

Section of the internal branch of the superior
laryngeal nerves reduced but did not abolish the
laryngospasm and respiratory changes produced
when the nasopharynx and larynx were exposed
to ether (fig. 1b). That the reduction of laryngo-
spasm by section of the internal branch of the
superior laryngeal nerves was due to sensory
denervation and not motor insufficiency was
indicated by the observation that a vigorous con-
traction of the cricothyroid muscle still followed
immediately after stimulation of the intact
nerve pathways involved in the laryngeal reflex

Decerebrate cat, prepared under halothane anaesthesia. From above down traces show time marker 0.2 sec (interruptions of the time trace E indicate that ether administration had started), (1) electromyogram from cricothyroid muscle, and (2) electromyogram from diaphragm. (Spikes retouched.)

(a) Shows the stimulation of increased activity of the cricothyroid muscle (biphasic pattern) and apnoea when 10-20 per cent ether is passed through the isolated nasopharynx and larynx.

(b) Laryngospasm and apnoea are still stimulated when ether vapour is passed through the nasopharynx and larynx after cutting the internal branch of both superior laryngeal nerves.

(c) After perineural block of the trigeminal nerves in the same cat, ether vapour passed through the nasopharynx and larynx produced neither laryngospasm nor apnoea.

The importance of the internal branches of the superior laryngeal nerves was also indicated by the results of experiments in which the vagus nerves and recurrent laryngeal nerves were cut at the laryngotracheal junction and the respiratory tract transected cranial to the first tracheal ring.

Under these conditions, the internal branches of the superior laryngeal nerves were intact, laryngospasm was produced by exposure of the nasopharynx and larynx to ether. The possibility was examined that laryngospasm and changes in respiratory rhythm produced when ether was passed through the nasopharynx and larynx were due to stimulation of receptors with their afferent pathways in the trigeminal nerves.

Triangular nerve block produced by perineural injection of local analgesic solution affected the development of laryngospasm. Whereas laryngospasm and interruptions in respiratory rhythm were consistently produced after either the external (motor) branch of the nerve, the internal branches of the superior laryngeal nerves were cut or the trigeminal nerves were blocked, when the transmission of afferent impulses via both pathways was abolished, laryngospasm and associated respiratory changes did not occur. Figure 1a shows the production of laryngospasm when 10-20 per cent ether vapour and oxygen were passed through the isolated nasopharynx and larynx with all nerves intact. Figure 1b shows that 30 min after cutting the internal branches of both superior laryngeal nerves the effects of ether were reduced, but laryngospasm and apnoea were still stimulated. These effects were abolished when, in addition, a perineural block of the trigeminal nerves was carried out (fig. 1c).

The effect of section of the cervical vagus nerves was to abolish laryngospasm in response to the passage of 10-20 per cent ether through the distal trachea and into the lungs. Ether vapour administered by tracheal cannula to an isolated segment of trachea in such a manner as not to enter the larynx (fig. 2c) or its administration to the distal trachea and lungs (fig. 2a) still stimulated laryngospasm and apnoea when the internal branch of both superior laryngeal nerves had been cut and the trigeminal nerves blocked. Afferent pathways from the trachea could be expected to be in the recurrent laryngeal or vagus nerves. When both vagus nerves were cut at the level of the first tracheal ring, laryngospasm was not stimulated when ether was passed through the distal trachea and into the lungs in 22 of 26 experiments (fig. 2b). In the other 4 experiments the effect on respiratory rhythm and stimulation of cricothyroid activity was delayed for between 5 and 10 sec.

The effect of electrical stimulation of nerves possibly forming part of the laryngeal reflex pathways was examined in 2 cats under chloralose anaesthesia and 1 decerebrate preparation in which stimulation of the intact recurrent laryngeal nerve was found to cause movement of the ipsilateral vocal cord and arytenoid to a position midway between adduction and abduction. The cord stayed in this position for the duration of the stimulus. The rapidity of the response to stimulation of the external branch of the superior laryngeal nerve and its restriction to the side on which the nerve was stimulated indicated that it was due to efferent motor nerve fibre stimulation.
Decerebrate cats prepared under halothane (a) and (b), and halothane/ether anaesthesia (c). From above down traces show time marker 0.2 sec (interruptions of the time trace E indicate that ether administration had started), (1) electromyogram from cricothyroid muscle, and (2) electromyogram from diaphragm. (Spikes retouched.)

(a) A response to passage of ether into the distal cervical trachea and lungs (in this preparation the internal branches of both superior laryngeal nerves had been cut and the trigeminal nerves blocked earlier). Passage of ether vapour into the distal trachea and lungs produced laryngospasm (shown by increased cricothyroid muscle activity) and an alteration in respiratory rhythm following a burst of increased activity recorded from the diaphragm after a latency of 8 sec.

(b) Same preparation as (a). Both vagus nerves had been cut, and passing ether into the distal trachea and lungs had no effect on the cricothyroid muscle or on respiratory rhythm.

(c) A delayed response to passing ether vapour through an isolated tracheal segment with its nerve and blood supply intact stimulated a burst of activity (transient laryngospasm) from the cricothyroid muscle about 9 sec after the start of ether administration.

Note the increased inspiratory activity recorded at the same time from the diaphragm, which was followed by apnoea. The internal branches of both superior laryngeal nerves had been cut and the trigeminal nerves blocked.

In contrast, stimulation of the internal branch of the superior laryngeal nerve led, after a perceptible delay, to a bilateral response—indicative of a reflex response to afferent nerve fibre stimulation.

DISCUSSION

The present work confirms that of Allen (1929, 1936) and that of Murtagh and Campbell (1954) in which it was indicated that the trigeminal nerves and the superior laryngeal nerves provide important afferent pathways involved in the production of laryngospasm by anaesthetic agents. The finding that cutting the internal branch of the superior laryngeal nerves and blocking the trigeminal nerves prevented the occurrence of laryngospasm when the nasopharynx and larynx were exposed to 10–20 per cent ether vapour also confirmed the suggestions that these nerves contain afferent nerve fibres from the nasopharynx and larynx concerned in the laryngeal reflex (Allen, 1929, 1936; Faaborg-Andersen, 1957; Murtagh and Campbell, 1954; and a number of other workers cited by Rex, 1970a). It must be emphasized, however, that laryngospasm can be stimulated from the respiratory tract at sites below the larynx and the present experiments show that afferents contained in the vagus nerve trunks are involved in these effects. The vagus nerve afferents are responsible for mediating the effects of stimulation by ether of receptors in the distal trachea and lungs. Although it appears that afferent pathways in the recurrent laryngeal nerves have little part in the responses to the inhalation of volatile anaesthetic agents mediated by stimulation of afferent receptors in the nasopharynx and larynx, the possibility remains that the recurrent laryngeal nerves are part of the afferent pathway involved in the reflex stimulation of laryngospasm when anaesthetic agents stimulate tracheal receptors. It is possible that afferent impulses from the trachea may travel in the recurrent laryngeal nerves to the vagus through the anastomotic branches which Lemere (1932) found in the dog between the superior and recurrent laryngeal nerves. This point has not been investigated in the present experiments.

The inhalation of ether vapour into the distal trachea and lungs failed to stimulate laryngospasm and the rhythm of the diaphragm remained regular in most cases when the vagus nerves were cut at the level of the laryngotracheal junction. The latency between the start of ether administration into the trachea and the onset of increased activity in the cricothyroid muscle was from 0.4 to 10.0 sec. The shorter latencies are consistent with stimulation of receptors in the tracheal mucosa and lungs and the involvement of an afferent pathway in the vagus nerves. The existence of such a pathway is in accord with Comroe's
view that chemoreceptors are present in the lung bed (Comroe, 1965). The longer latencies and the time of onset of a second phase in the biphasic responses are consistent with the possibility that chemoreceptors in the aortic and carotid bodies may have been stimulated by ether absorbed into the bloodstream. This would account for those observations in which laryngospasm and interruptions of diaphragmatic rhythm occurred with administration of ether into the distal trachea even after the section of both vagus nerves. Evidence for chemoreceptor stimulation of laryngospasm has been obtained in other unpublished work.

ACKNOWLEDGEMENTS
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REFERENCES
Allen, W. F. (1929). Effect on respiration, blood pressure and carotid pulse of various inhaled and insufflated vapors when stimulating one cranial nerve and various combinations of cranial nerves. III: Olfactory and trigeminals stimulated. Amer. J. Physiol., 88, 117.


