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FUNCTIONAL AND HISTOLOGICAL CHANGES IN THE VAGUS NERVE OF THE CAT AFTER DEGENERATIVE SECTION AT VARIOUS LEVELS

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Several workers have suggested that a proportion of the motor fibres in the mammalian vagus nerve have their parent cells in the nodose ganglion. All the evidence is based on experiments in which the vagus nerve was divided intracranially or extracranially above the nodose ganglion and time allowed for nerve fibres separated from their cell bodies to degenerate. In the dog, Morgan & Goland (1932) found that stimulation of the caudal end of the cut cervical vagosympathetic nerve after such operative procedures produced variable effects on the heart rate and blood pressure. It is probable that the effects they obtained were complicated by stimulation of descending fibres in the cervical sympathetic trunk (Foley, 1945; Butson, 1950; I. de B. Daly & Hebb, 1952). In the cat, Heinbecker & O'Leary (1933*a*, *b*) were unable to demonstrate any cardiac effects of stimulation of the cervical vagus, the fibres of which had been allowed to degenerate for 10–20 days after supranodose (extracranial) or intracranial vagotomy. They found, however, that stimulation caused bronchoconstriction and either excitation or inhibition of peristalsis in the duodenum. The absence of any cardiac effects after supranodose vagotomy was confirmed by McSwiney & Spurrell (1933) and Richardson & Hinsey (1933).

On the basis of action-potential studies, Heinbecker & O'Leary (1933*a*, *b*) concluded that there were no synapses in the nodose ganglion and they postulated the presence, within the ganglion, of motor nerve cells with both centrally and peripherally directed processes.

In view of the variability of the results of stimulating the vagus nerve after degenerative section above the level of the nodose ganglion, we have repeated these experiments. The cat has been chosen for this work because the cervical vagosympathetic trunk is readily separable into its two components. As the

sympathetic system contributes few or no fibres to the cervical vagus nerve of the cat (Jones, 1932; Heinbecker & O'Leary, 1933*b*; Ranson, Foley & Alpert, 1933) the effects of stimulation of the latter nerve will not be complicated by concomitant stimulation of sympathetic fibres. Such is not the case in the dog, where intermingling of fibres between the cervical vagus and sympathetic nerves takes place (Braeucker, 1926; I. de B. Daly & Hebb, 1952).

An histological study of the effects of these operative procedures on the thoracic vagus trunk and its cardiac and bronchial branches has also been made.

METHODS

Cats, varying in weight from 1·6 to 4·3 kg, were anaesthetized with either a mixture of chloralose (0·05 g) and urethane (0·5 g/kg body weight, intraperitoneally), or pentobarbitone sodium (nembutal) (45 mg/kg body weight, intraperitoneally).

A cannula was inserted in the trachea, and artificial respiration carried out by means of a Starling 'Ideal' pump. The chest was opened by splitting the sternum in the mid-line. The internal mammary arteries were ligated, and both phrenic nerves were cut. The left and right cervical vagosympathetic nerves were then exposed and separated into their two components, the vagus and sympathetic nerves. The cervical vagus and usually the cervical sympathetic nerves were cut between ligatures at the level of the cricoid cartilage. Blood pressure was recorded from a femoral artery by means of a mercury manometer. Heart rate was measured by the method described by Daly & Schweitzer (1950) using a drop timer (Gaddum & Kwiatkowski, 1938). With this method it is possible to detect changes in rate of five beats per minute over the range found in these experiments.

Small shielded platinum wire electrodes were used for stimulation of the vagus nerves. A square wave electronic stimulator which allowed independent control of the voltage, frequency and the pulse duration of the stimulus was used.

Bronchomotor responses were measured in some experiments by the method of Konzett & Rössler (1940). The constant positive inflationary pressure varied from 5 to 8 cm water in different experiments; the ventilation overflow volume was recorded by means of a piston recorder. In other experiments, the method of recording the tidal air under negative pressure ventilation was used (for details see Daly & Mount, 1951). Occasionally, both methods were used in the same experiment for comparison.

Nerve sections

Three series of experiments involving degenerative section of vagus nerves were carried out under pentobarbitone sodium (45 mg/kg body weight, intraperitoneally) with full aseptic precautions: (1) *Cervical vagotomy* in which 1 cm of the cervical vagus nerve was removed either immediately below the nodose ganglion or at the level of the cricoid cartilage. (2) *Supranodose vagotomy*. The cervical vagus nerve was cut between the skull and the nodose ganglion. In a few experiments, it was found impossible to separate the postganglionic sympathetic trunk from the vagus nerve, and in these, therefore, both nerves were cut. (3) *Intracranial vagotomy*. The vagal rootlets were sectioned as they left the medulla.

All nerve sections were carried out on one side only, and the acute experiments were performed 14–30 days later.

Operation for intracranial vagotomy

Section of the vagal rootlets presented technical difficulties through the inaccessibility of these nerves. Two surgical approaches were used, one through the foramen magnum by a method similar to that described by Brouha & Nowak (1939) for the dog, the other through the postero-lateral

part of the parietal bone and cerebellar fossa. The first method was found unsatisfactory for a number of reasons. Oozing from the bone was sometimes troublesome when nibbling away the dorsal part of the supraoccipital bone. The view of the vagal rootlets obtained was very poor even when the brain was shrunk by intravenous injections of a solution of hypertonic sucrose and when gentle retraction was put on the medulla to the opposite side. Often, the most rostral rootlets could not be seen at all. Section of the rootlets was usually made with a small instrument on the end of which was a curved cutting edge, and damage to nearby vessels occasionally led to uncontrollable bleeding. The second approach was therefore developed with a view to cutting all the rootlets under direct vision.

The head of the cat was held in a Czermak head-holder in a semi-flexed position slightly above the level of its body. No pads were put under its neck as this increased oozing through venous compression. A dorsal mid-line incision was made extending from the level of the lateral processes of the frontal bone caudally for a distance of 7 cm. The group of muscles taking origin from the sagittal and lamdoid sutures and from the eminence of the parietal bone was reflected laterally on one side. A burr-hole was made with a dental drill in the postero-inferior part of the parietal bone about 5 mm medial to the squamous suture and 5 mm rostral to the lamdoid suture. This hole was enlarged to a convenient size, its inferior border being carried to within 2 mm of the squamous suture, which is a useful surface marking for the transverse venous sinus. The exposed dura mater was removed. The cerebellum was then gently retracted medially and the cerebrospinal fluid sucked out. All the vagal rootlets and the spinal accessory nerve could be seen at the lower border of the petrous temporal bone. The vagal rootlets and bulbar portion of the accessory nerve were sectioned by means of an electrocautery. The muscles were then sutured and the skin closed. No special post-operative treatment was given.

Complete section of the vagal rootlets was tested during the later acute experiment by observing any reflex response to stimulation of the cephalic end of the cut cervical vagus on the operated side, the contralateral one being intact. A post-mortem examination for any intact rootlets was also made.

Histological methods

After completing the physiological investigations outlined above, portions of the vagus nerves and their branches on the operated and control sides were removed for subsequent histological examination. The nerves were placed on cardboard frames in a lightly stretched condition and immersed in a fixative. Studies on myelinated fibres were made in nerves fixed for 24 hr in Flemming's fluid (1% chromic acid, 15 ml.; 2% osmic acid, 4 ml.; glacial acetic acid, 1 drop). The nerves were sectioned transversely (5 μ thickness) after paraffin embedding and stained by a modified Weigert technique (Gutmann & Sanders, 1943). The sections were photographed at magnifications of $\times 750$ directly on bromide paper and the outside diameter of the myelinated nerve fibres measured and classified into 2 μ groups. Measurements were made by means of a Perspex sheet on which were imprinted circles in a sequence of increasing diameters (1·5, 3, 4·5 mm, etc.). As each fibre was measured it was pricked with a needle connected to an electric counter. For study of non-myelinated fibres either the Bodian or the Ranson pyridine-silver method was used. In the Ranson method the nerves were threaded through cat spinal cord before fixation to protect them from over-impregnation with the silver nitrate (Ranson & Davenport, 1931). The spinal cord, with its contained nerve, was sectioned transversely at 3 μ thickness. In this investigation observations on the non-myelinated fibre content of the operated and control nerves were purely qualitative as no counts of fibre number in Bodian and Ranson preparations were made.

The composition of control and operated vagus nerves in the upper part of the thorax and of the bronchial and thoracic cardiac branches was investigated. Sections of the vagus trunk were usually taken at a level mid-way between the arch of the aorta and the hilum of the lung.

RESULTS

Effects of stimulation of the cervical vagus nerve

Control tests. In a previous series of experiments on the cat, observations were made on the effects of vagus nerve stimulation on the blood pressure, heart rate and bronchioles (Daly & Mount, 1949, unpublished observations). Bronchomotor responses were measured by recording the tidal air volume under negative pressure ventilation. It was found that in all sixteen experiments stimulation of the caudal end of the cervical vagus nerve on both sides caused a fall in blood pressure, slowing of the heart rate and bronchoconstriction. The magnitude of the effects on the two sides was not always equal nor did the results show that stimulation of either the right or the left nerve was consistently more effective in producing these responses. In most experiments of the present series, therefore, eserine was injected to potentiate the effects of vagus stimulation. The absence of effects observed on the operated side is then unlikely to be due to any cause other than degeneration of motor fibres in the nerve when a pronounced response is obtained to vagus stimulation on the control side.

TABLE 1. The effect upon the bronchioles, blood pressure (B.P.) and heart rate (H.R.) of stimulating the caudal end of the cut cervical vagus nerve, the nerve having been sectioned at the various levels 14–30 days before testing. L (left) and R (right) denote the side on which the section was made. + = response to stimulus; 0 = no response; − = not recorded. Details of the operations are given in the text

		Responses					
		On normal side			On operated side		
Operation	No. of expts.	Bronchioles	B.P.	H.R.	Bronchioles	B.P.	H.R.
Cervical vagotomy	3 (R)	+	+	+	0	0	0
	1 (R)	−	+	+	−	0	0
Cervical vagosympathectomy	1 (L)	+	+	+	0	0	0
	3 (R)	−	+	+	−	0	0
Supranodose vagotomy	1 (L)	+	+	+	0	0	0
	1 (R)	+	+	+	0	0	0
Supranodose vago-sympathectomy	3 (L)	+	+	+	0	0	0
	1 (R)	+	+	+	0	0	0
Intracranial vagotomy	5 (L)	+	+	+	0	0	0
*Intracranial vagotomy	1 (R)	+	+	+	+	0	0

* One vagal rootlet not sectioned.

Cervical vagotomy. In eight experiments, 1 cm of the cervical vagus nerve immediately below the nodose ganglion was removed at a previous operation. In four of these, an adjacent length of the sympathetic nerve was also excised. Stimulation of the caudal end of the cut cervical vagus nerve on the normal side caused a fall in blood pressure and slowing of the heart rate in all these experiments. In four of them, in which the tidal air volume was simultaneously recorded, bronchoconstriction occurred. In none of these experiments was there any effect on blood pressure, heart rate or tidal air on stimulation of the

vagus nerve on the operated side. The results were the same whether the operation was carried out on the left or the right side and are summarized in Table 1.

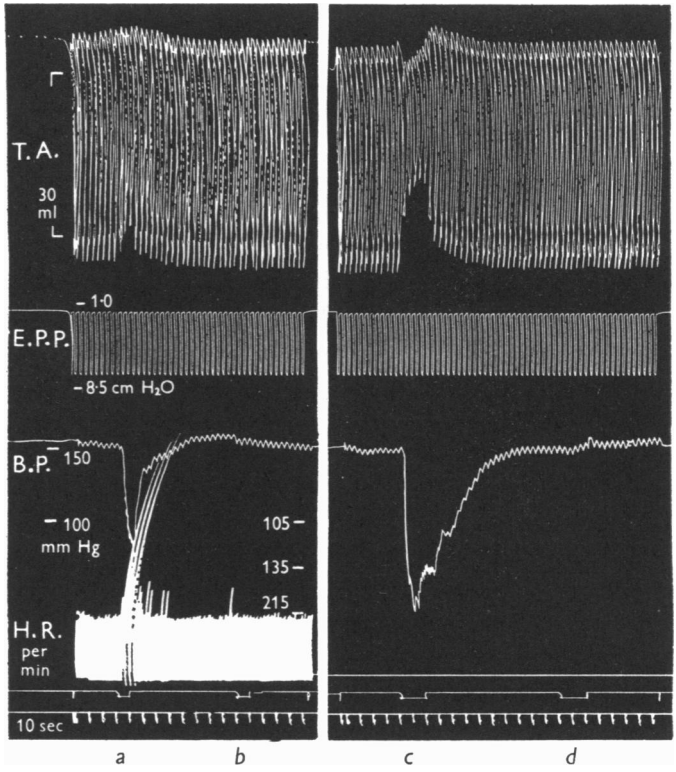
Supranodose (extracranial) vagotomy. The work of McSwiney & Spurrell (1933), Richardson & Hinsey (1933) and Heinbecker & O'Leary (1933*a*, *b*) shows that, in cats, the inhibitory effect of the vagus nerve on the heart cannot be elicited after chronic supranodose vagotomy. Heinbecker & O'Leary found, however, that the motor fibres to the bronchioles and duodenum were unaffected by this operation. In so far as the effects on the bronchioles are concerned, we have been unable to confirm their findings.

In six experiments in which the vagus and sometimes the sympathetic nerves were chronically sectioned above the nodose ganglion, no effect was observed on either the tidal air or ventilation overflow volume when the cervical vagus was stimulated on the operated side (Text-fig. 1*b*, *d* and Table 1). We have confirmed the finding of Heinbecker & O'Leary that there is no change in either blood pressure or heart rate. On the normal side, vagus stimulation caused a fall in blood pressure, slowing of the heart rate and bronchoconstriction (Text-fig. 1*a*, *c*). Similar effects occurred whether the nerves were cut on the left or the right side. In most experiments, eserine was injected to potentiate the effects of vagus nerve stimulation. Further, the electrical stimulus was varied by altering the voltage (1–8 V), frequency (50–100 c/s) and pulse duration (0·05–10 msec) both together and independently of each other. None of these procedures altered the result on the operated side.

Intracranial vagotomy. In six experiments in which the vagal rootlets were sectioned intradurally 14–24 days previously, stimulation of the caudal end of the ipsilateral cervical vagus nerve had no effect on either the blood pressure, heart rate or bronchioles in five of them (Text-fig. 2*b*, *d* and Table 1). Stimulation of the contralateral vagus produced the usual effects (Text-fig. 2*a*, *c*). In each animal, post-mortem examination showed all the rootlets to have been sectioned. The sixth experiment is of interest because stimulation of the vagus on the operated side had no effect on blood pressure and heart rate, but caused bronchoconstriction, the tidal air being reduced by 6%. However, a post-mortem examination of the operation site revealed that the most rostral rootlet was still intact. We believe, therefore, that the response obtained was due to undegenerated bronchomotor fibres in the cervical vagus arising from the dorsal nucleus of the vagus. This experiment was the only one of the series in which the vagal rootlets were sectioned by cutting with a small curved knife; in the other five experiments, an electrocautery was used.

In the five experiments in which all the vagal rootlets had been sectioned we tested the negative response to cervical vagus nerve stimulation after an injection of eserine and with electrical stimuli of different frequencies and pulse durations. On no occasion was any effect elicited.

These results indicate that after chronic section of the vagus nerve above the level of the nodose ganglion, all motor fibres to the heart and bronchial musculature degenerate. Their cells of origin must, therefore, lie within the central nervous system.

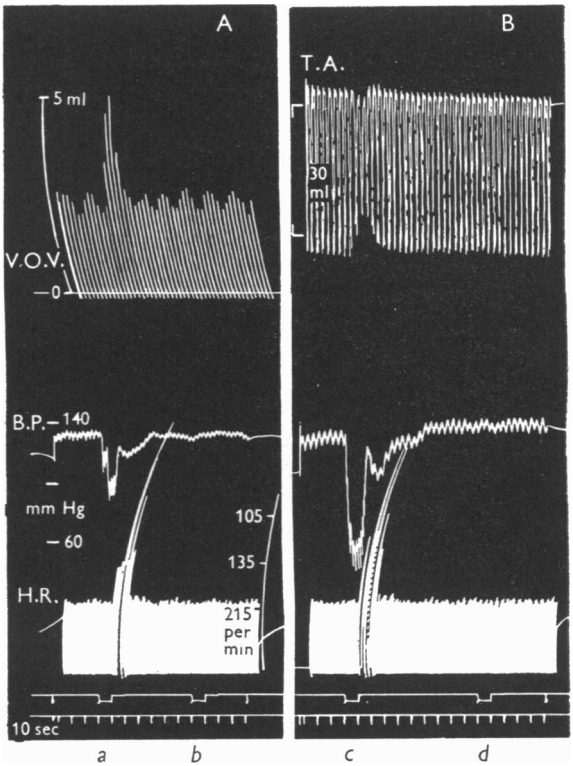


Text-fig. 1. Cat 13, ♂, 2·3 kg. Chloralose-urethane. *Right supranodose vagotomy* 21 days previously. Negative pressure ventilation. Both cervical vagus nerves cut. At *a* and *c*, stimulation of the caudal end of the left cervical vagus, 3 V, 50 c/s, 0·5 msec. The same stimulus was applied to the caudal end of the right cervical vagus at *b* and *d*. Between *b* and *c* eserine (0·1 mg) was injected intravenously. In this and in Text-fig. 2: T.A. = tidal air (inspiration downwards); V.O.V. = ventilation overflow volume; E.P.P. = extrapulmonary pressure; B.P. = blood pressure; H.R. = heart rate.

Histological changes in the thoracic vagus trunk and its cardiac and bronchial branches

Upper thoracic vagus

Normal vagus. The vagus immediately below the origin of the recurrent laryngeal nerve is in the form of a single bundle. Pl. 1, fig. 1, and Pl. 2, fig. 7, show Weigert preparations of a section of the normal vagus trunk taken at a level mid-way between the aortic arch and the hilum of the lung. Medullated

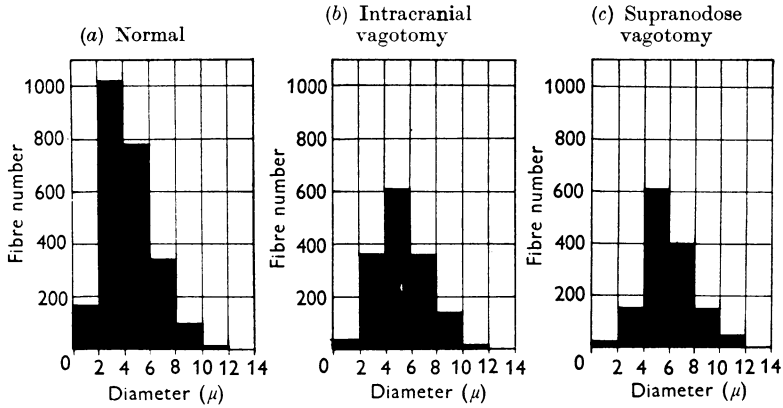


Text-fig. 2. Cat 16, ♂, 2·1 kg. Pentobarbitone. *Left intracranial vagotomy* 20 days previously. Eserine 0·2 mg. Both cervical vagus nerves cut. A: constant positive inflationary pressure. Respiratory pump stroke, 50 ml. At *a* and *b*, stimulation of the caudal end of the right and left cervical vagus nerves respectively, 1·5 V, 50 c/s, 1 msec. B: negative pressure ventilation. At *c* and *d*, stimulation of the caudal end of the right and left cervical vagus nerves respectively, 2 V, 50 c/s, 1 msec.

TABLE 2. Size-frequency distribution of myelinated fibres in the thoracic vagus nerves taken at a level mid-way between the aortic arch and the hilum of the lung

Animal and specimen	No. of fibres in diameter groups of 2μ							
	0–2	2–4	4–6	6–8	8–10	10–12	12–14	Total
				(*a*) Normal				
6*e*	136	2256	645	342	105	10	1	3495
13*b*	168	1028	781	347	101	14	0	2439
17*a*	53	924	808	387	162	23	7	2364
21*d*	43	821	534	297	188	27	4	1914
				(*b*) Intracranial vagotomy				
14*e*	43	526	610	383	248	44	2	1856
17*b*	38	245	631	290	158	8	2	1372
16*d*	42	368	613	361	143	18	3	1548
				(*c*) Supranodose vagotomy				
6*d*	27	154	606	399	151	47	3	1387
9*b*	19	319	390	322	197	43	10	1300
13*c*	28	805	796	315	87	9	1	2041

fibres are present throughout the section, but are somewhat unevenly distributed, being separated by unstained areas. A section of the vagus trunk at the same level stained with the Ranson technique (Pl. 2, fig. 5) shows that these areas are closely packed with non-myelinated fibres which clearly far outnumber the myelinated group. As the nerve descends towards the hilum of the lung there is a progressive decrease in the number of myelinated fibres as these are distributed in its cardiac, tracheal, bronchial and oesophageal branches.



Text-fig. 3. Histograms showing the number of myelinated fibres of different sizes in normal and operated thoracic vagus trunks at a level midway between the aortic arch and the hilum of the lung.

Table 2*a* shows the size-frequency distribution of medullated fibres in four normal vagi taken at comparable levels in the upper part of the thorax. The fibres range from 1 to 14μ in diameter, and considerable variation exists both in the total number of fibres and in the proportion within each diameter group. In all four specimens the distribution of fibre diameter is skew with a single mode at 2–4μ (Text-fig. 3*a*).

Cervical vagotomy. The operation of dividing the cervical vagus caudal to the nodose ganglion was performed in eight cats, and histological data on the resulting nerve fibre degeneration were available in four of them. In three of these the cervical sympathetic trunk was left intact, whilst in the fourth (cat 3) it was cut. Pl. 1, fig. 4, shows a Weigert preparation of the upper thoracic vagus trunk removed 21 days after mid-cervical vagotomy and sympathectomy (cat 3). It will be noted that practically all the myelinated fibres are degenerate; in this instance only twenty-six fibres remained. Most of the myelin of the degenerated fibres has already been absorbed, but here and there droplets of myelin remain, especially in the larger fibres. Pyridine-silver and Bodian preparations of nerves similarly treated show only occasional non-myelinated fibres. In the present study no attempt has been

made to investigate the origin of the few fibres remaining in the upper thoracic vagus trunk following cervical vagotomy.

Intracranial vagotomy. Section of the nerve intracranially, allowing a post-operative period of 14–24 days, produces changes in both the myelinated and non-myelinated fibre content of the vagus trunk in the thorax. Comparison of Weigert preparations of control (Pl. 1, fig. 1) and operated (Pl. 1, fig. 2) nerves at comparable levels in the thorax shows that the myelinated fibres have become reduced in number. Table 2*b* shows the size-frequency distribution of myelinated fibres in three treated nerves and provides quantitative support for this observation. The most striking change produced by the intracranial vagotomy is the considerable reduction in the number of fibres in the 2–4 μ group. In each of the four normal nerves (Table 2*a*) this group contains the largest number of fibres, forming, respectively, 64·5, 42·1, 39·1 and 42·9% of the total. In contrast, the corresponding values in the three treated nerves are, respectively, 28·3, 23·8 and 17·8%. This reduction in the numbers of fibres in the 2–4 μ group is found to be statistically significant ($P < 0{\cdot}01$). This is the case whether the comparisons of the normal and operated nerves are made between: (1) the proportion of the 2–4 μ group to the total number of fibres, or (2) the mean numbers of fibres of 2–4 μ diameter in the two series. Moreover, there is a statistically significant reduction in the 2–4 μ group when the normal nerve showing the smallest proportion of fibres in this group is compared with the nerve showing the largest proportion in the operated series. Some 60% of the fibres in the 2–4 μ group have degenerated and may presumably be considered to be efferent. This figure, however, is not precise, and from the limited number of animals used in this series the number of fibres of this diameter which degenerate may vary from 45 to 75% of the total in the 2–4 μ group. The range of these figures emphasizes the great variability in the composition of the vagus nerve in different cats.

From Table 2*a* and *b* it will be seen that the number of fibres in each of the groups larger than 4 μ in diameter does not differ in thoracic vagi taken from the normal and operated sides, and statistical analysis confirms this. It may be concluded, therefore, that all, or nearly all, the fibres in the 4–14 μ diameter range have their cell bodies in the nodose or jugular ganglion and are presumably sensory in function. Comparison of the spectrum of fibre size in an operated nerve (Text-fig. 3*b*) with that of a normal nerve at the same level shows that the unimodal distribution is retained after intracranial vagotomy, but the skewness of the curve is less marked, the node being at 4–6 μ.

Ranson-stained sections of the thoracic vagus trunk after intracranial vagotomy show that some of the non-myelinated fibres have degenerated. Parts of the nerve section, however, show a fibre density approximately equal to normal (Pl. 2, cf. figs. 5 and 8), whereas in other parts degeneration of

a considerable proportion of the non-myelinated fibres has occurred (Pl. 2, fig. 6). The lack of uniformity in different animals of the effects of intracranial vagotomy upon the myelinated fibre content of the operated nerves was also encountered in sections stained by the Bodian and Ranson methods. The extent of the areas showing apparently normal fibre density and those showing degeneration of some non-myelinated fibres varied considerably in different animals. In view of these variations no quantitative investigations have been made on the non-myelinated fibre content of the control and operated nerves.

Supranodose vagotomy. A study of Table 2*c* and Pl. 1, fig. 3, reveals that the changes produced in the myelinated fibre content of the upper thoracic vagus trunk after supranodose (extracranial) vagotomy are similar to those caused by intracranial vagotomy. Some of the myelinated group degenerate, as indicated by a reduction in total fibre number to a mean of 1576 as compared with 2553 in the normal series (Table 2*a*). Here again, statistical analysis shows that the reduction in the mean proportion of fibres in the 2–4μ group is significant when compared with the corresponding proportion in normal animals but does not differ from the proportion found in the series vagotomized intracranially. Moreover, comparison between the mean number of fibres in the remaining diameter groups in the normal, intracranial and supranodose (extracranial) series shows no significant differences. We conclude, therefore, that either of these operations leads to a reduction in the number of fibres in the 2–4μ group with no significant changes in the remaining groups. A histogram of the fibre-size distribution in one of the operated nerves (Text-fig. 3*c*) shows a unimodal distribution, but the skewness of the curve is reduced as compared with the normal (Text-fig. 3*a*).

A comparison of the calibre spectrum of myelinated fibres in the thoracic vagus trunk after intracranial and supranodose (extracranial) vagotomy shows a close similarity. This is confirmed by statistical analysis which shows no significant difference in the mean numbers of fibres in the 2–4μ group and in the 4–14μ groups following these two types of operation. We conclude, therefore, that the jugular ganglion does not contribute myelinated fibres to the thoracic vagus trunk. This confirms the findings of DuBois & Foley (1937).

Cardiac branches

The thoracic cardiac branches of the vagus are variable in their number, size and level of origin. They normally contain non-myelinated and myelinated fibres, the latter ranging from 1 to 12μ in diameter (Pl. 2, fig. 10). The myelinated fibres show a unimodal size-frequency distribution, the majority being between 2 and 6μ in diameter (Table 3*a*).

After intracranial and supranodose (extracranial) vagotomy, many myelinated and non-myelinated fibres persist in the cardiac branches. Table 3*b*

and *c* shows the size-frequency distribution of myelinated fibres in five nerves obtained from the operated side. The range of diameter (1–12 μ) is similar to normal, but owing to the considerable individual variability no definite conclusions can be drawn about the effect of these operative procedures on the fibre content of the cardiac branches. The reduction in the proportion of fibres in the 2–4 μ group occurring in the thoracic vagus and in the bronchial branches (*vide infra*) is not evident in the cardiac branches.

TABLE 3. Size-frequency distribution of myelinated fibres in cardiac branches of the thoracic vagus nerve. The figures indicate percentages of the total fibre count

Animal and specimen	Fibre diameter (μ)						Total no. of fibres
	0–2	2–4	4–6	6–8	8–10	10–12	
			(*a*) Normal				
6*a*	5·6	39·3	42·3	8·4	4·0	0·4	273
13*a*	2·3	19·4	52·7	20·9	3·9	0·8	129
21*a**	12·5	26·4	53·2	6·4	1·4	—	280
21*b**	32·1	26·8	35·7	2·7	2·7	—	112
21*c**	18·5	38·7	34·7	8·1	—	—	124
18*b*	5·7	31·6	37·3	23·0	2·4	—	209
			(*b*) Intracranial vagotomy				
14*c*	8·4	41·0	34·3	15·7	0·6	—	166
16*b**	6·9	34·5	39·7	19·0	—	—	58
16*c**	8·1	17·1	24·3	33·3	12·6	4·6	111
			(*c*) Supranodose vagotomy				
6*b*	3·9	33·8	40·9	16·3	1·9	3·2	154
7*a*	5·8	35·0	49·6	8·8	0·7	—	137

* These represent different cardiac branches in the same animal.

Bronchial branches

Some of these arise as fine twigs from the vagus rostral to the hilum of the lung, whereas other larger branches, one or two in number, originate from the vagus as it runs on the dorsal aspect of the main bronchus. These branches contain both myelinated and non-myelinated fibres, the former being more compactly arranged than in the thoracic vagus trunk (Pl. 2, fig. 9). Table 4*a* shows the size-frequency distribution of myelinated fibres in normal bronchial branches. The fibres are distributed unimodally and range from 1 to 12 μ in diameter (Text-fig. 4). In one case (5*a*), however, a strict unimodal pattern did not occur.

After intracranial and supranodose (extracranial) vagotomy some myelinated and non-myelinated fibres in the bronchial branches degenerate. The myelinated fibres in the operated nerves have the same range of diameter as in normal ones (Table 4*b*, *c*, and Text-fig. 4). A comparison of the size-frequency distribution of myelinated fibres shows that, after intracranial vagotomy, there is a reduction in the proportion of fibres in the 2–4 μ group. There is no apparent difference between the proportions in the larger fibre groups. Owing to great variability in the proportion of fibres in each group

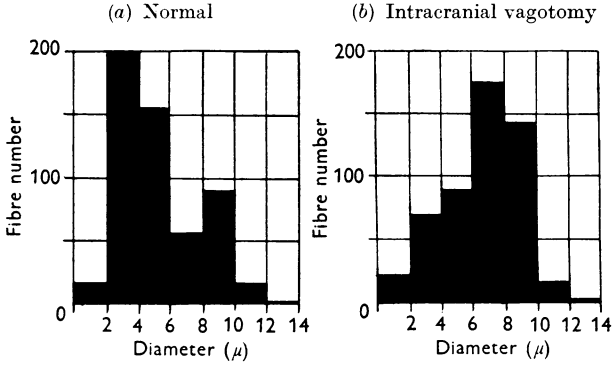
and in the total fibre count even in normal nerves, no statistical analysis has been made of these results. A count of fibre diameter distribution has only been made in one bronchial branch following supranodose vagotomy. As will be seen from Table 4*c*, the diminution in the proportion of fibres in the 2–4 μ group is not evident in this case.

It is probable that a few of the myelinated and non-myelinated fibres in the thoracic vagus and its cardiac and bronchial branches surviving these operative procedures are sympathetic in origin. The number must be small, however, for after chronic cervical vagotomy (below the nodose ganglion) practically all fibres in these nerves degenerate.

TABLE 4. Size-frequency distribution of myelinated fibres in bronchial branches of the thoracic vagus nerve. The figures indicate percentages of the total fibre count

Animal and specimen	Fibre diameter (μ) 0–2	2–4	4–6	6–8	8–10	10–12	12–14	Total no. of fibres
				(*a*) Normal				
4*a*	8·9	44·4	28·3	14·0	4·1	0·3	—	323
5*a*	3·1	37·2	28·6	10·6	17·3	3·0	—	538
18*a*	6·6	32·8	32·1	20·4	5·8	2·2	—	137
19*a**	7·3	32·5	43·7	13·5	2·6	0·4	—	274
19*b**	3·5	30·4	44·9	18·1	3·1	—	—	227
				(*b*) Intracranial vagotomy				
14*a**	5·8	16·2	19·9	26·6	27·0	4·1	0·4	241
14*b**	2·5	11·7	15·9	39·6	27·9	2·1	0·4	283
16*a*	1·6	14·7	51·2	17·8	13·2	1·5	—	129
				(*c*) Supranodose vagotomy				
9*a*	2·6	37·6	48·2	8·4	2·3	1·0	—	311

* These represent different bronchial branches in the same animal.



Text-fig. 4. Histograms showing the number of myelinated fibres of different sizes in bronchial branches of the vagus.

DISCUSSION

The results obtained by previous workers on stimulation of the vagus nerve after chronic degenerative section above the nodose ganglion have been variable. In the dog, Morgan & Goland (1932) found that stimulation of the

cervical vagosympathetic nerve caused a fall in blood pressure and slowing of the heart or occasionally a rise in blood pressure accompanied by a tachycardia. In the cat, McSwiney & Spurrell (1933) found the cardio-inhibitory effects of cervical vagus stimulation to be abolished after degenerative section above the nodose ganglion; in most cases a rise in blood pressure and a tachycardia resulted. They recorded an occasional slight diminution in the amplitude of gastric contraction which was in no way comparable to the effects obtained by stimulation of the vagus on the unoperated side. They suggested that these slight effects were attributable to the concomitant vascular changes. It is not clear whether they were stimulating the cervical vagus or vagosympathetic nerve: in the latter event, their results could be explained as being due to stimulation of descending postganglionic sympathetic fibres (Ranson & Billingsley, 1918; Foley & DuBois, 1940; Foley, 1945; Butson, 1950), or of preganglionic looping fibres (Dixon & Ransom, 1912; Daly & Mount, 1951) running in the cervical sympathetic trunk. In this connexion, Richardson & Hinsey (1933), working on the cat, could find no effect on heart rate or blood pressure on stimulation of the caudal end of the cervical vagus nerves, but a slight rise in blood pressure occurred in two out of five experiments on stimulation of the caudal cut end of the cervical sympathetic nerve. These experiments were carried out after chronic section of the vagus above the nodose ganglion. Similar results were obtained by Daly & Mount (1949 unpublished observations, 1951). Heinbecker & O'Leary (1933*a*, *b*) found that there was no effect upon the heart on stimulation of the cervical vagus after chronic supranodose (extracranial) or intracranial vagotomy. They found, however, that adequate stimulation of the cervical vagus after chronic supranodose (extracranial) vagotomy produced constriction of the bronchi and excitation or inhibition of peristalsis in the duodenum. They do not state whether these motor effects occurred after chronic intracranial vagotomy. They concluded that 'there are fibres in the vagus nerve whose cells of origin are in the nodose ganglia which are efferent in type'. In the present investigation, we have been unable to confirm these findings. From the functional aspect, we can find no evidence for there being motor fibres to the bronchial musculature in the vagus with their cells in the nodose ganglion. In our investigation, the movements of the duodenum were not recorded, so that the possibility of such fibres with their cells in the nodose ganglion innervating the gut cannot be excluded. In this connexion, one of us (Evans & Murray, 1953) found that, in the rabbit, stimulation of the cervical vagus after chronic supranodose (extracranial) vagotomy had no effect on the intragastric pressure; stimulation of the vagus on the normal side produced a marked increase in pressure.

Heinbecker (1930) analysed the action potential waves obtained from the cervical vagus trunk in the cat and demonstrated three potential units which

he correlated with fibre size in preparations stained with osmic acid. He associated the first wave with the activity of the large, heavily myelinated fibres, the second with the small, finely myelinated fibres, and the third with the non-myelinated fibres. This correlation between potential wave form and nerve fibre structure in the cat's cervical vagus was extended by Heinbecker & O'Leary (1933*b*). After section of the vagus above the nodose ganglion these authors found that there was disappearance of the earlier part of the first potential wave and this they correlated with the large motor fibres of the recurrent laryngeal nerve, which degenerate following such a lesion. They found no significant reduction in the amplitude of the later part of the first potential wave, and attributed this to the presence of large myelinated afferent fibres in the cervical vagus which remained intact in their preparations. The second potential wave produced by the small finely myelinated fibres showed a reduction of 30–50%, whilst the third wave, produced by the non-myelinated fibres, was not significantly changed.

Heinbecker & O'Leary also studied the relationship between fibre diameter and function in the cat's cervical vagus by application of gradually increasing pressure to the nerve trunk. Pressure was applied by 'an especially constructed parallel jawed clamp', and they reported that, in this way, it was possible to block the first and second potential complexes, leaving the third complex well developed. With pressure thus applied they found that conduction of reflex respiratory and blood-pressure effects and of pain impulses was effectively blocked. As a result of these observations they concluded that there were no non-myelinated afferent fibres present in the vagus of the cat.

With regard to the efferent fibre-types in the cervical vagus nerve of the cat, Heinbecker & O'Leary (1933*b*) state: 'In normal animals it was demonstrated by a correlation between form and physiological effects in the organism that constriction of the bronchi and intestinal motor excitatory and inhibitory effects are produced by impulses conveyed by the *non-myelinated* fibres of the vagus.' These fibres have their cells of origin in the nodose ganglion. 'Other vagus fibres, certain of those to the heart, are of similar character, but their cells of origin are within the central nervous system.'

Our own histological findings show that after intracranial and supranodose (extracranial) vagotomy both small myelinated and non-myelinated fibres degenerate in the thoracic vagus trunk. With regard to the myelinated fibres degeneration was confined to the 2–4 μ group, of which about 60% disappeared. The extent of this reduction varied from animal to animal. No significant alteration occurred in the 4–14 μ groups. It has not been possible to estimate the proportion of non-myelinated fibres which degenerated. Degeneration of some myelinated fibres of the 2–4 μ group and of a proportion of the non-myelinated fibres also occurred in the bronchial branches of the vagus. In the cardiac branches, however, degeneration of some non-myelinated fibres was

observed but there was no obvious reduction in myelinated fibres. On the basis of our results of electrical stimulation of the cervical vagus nerve showing the absence of motor effects on the heart and bronchial musculature after these operative procedures, we conclude that these motor functions are conveyed essentially by myelinated fibres of the 2–4 μ diameter group and by non-myelinated fibres; these fibres have their cells of origin within the central nervous system. It follows that the large numbers of myelinated and non-myelinated fibres which survive are afferent in function.

SUMMARY

1. The effects of stimulation of the cervical vagus nerve on the heart rate, blood pressure and bronchioles after chronic degenerative section at various levels have been investigated in the anaesthetized cat.

2. After chronic section of the vagus below the nodose ganglion, above the nodose ganglion (extracranial) or intracranially, stimulation of the caudal end of the ipsilateral cervical vagus nerve causes no effect on the heart or bronchioles. Contralateral vagus stimulation produces the usual effects on these structures. It is concluded, therefore, that there are no motor fibres in the vagus supplying the heart and bronchial musculature with their cell bodies in the nodose ganglion.

3. Chronic section of the cervical vagus below the nodose ganglion produces degeneration of nearly all the myelinated and non-myelinated fibres in the thoracic vagus trunk and in its cardiac and bronchial branches.

4. After supranodose (extracranial) or intracranial vagotomy both small myelinated (2–4 μ diameter group) and non-myelinated fibres degenerate in the thoracic vagus trunk. Large numbers of both types of fibres survive. No obvious degeneration of the myelinated fibres in the 4–14 μ groups occurred. Similar effects were observed in the bronchial branches of the vagus. In the cardiac branches, however, there was no obvious reduction in the number of myelinated fibres.

5. Our histological findings indicate that motor functions of the vagus to the heart and bronchial musculature are conveyed essentially by myelinated fibres of the 2–4 μ diameter group and by non-myelinated fibres. Afferent functions are served by myelinated fibres found in all the diameter groups (1–14 μ) and by non-myelinated fibres.

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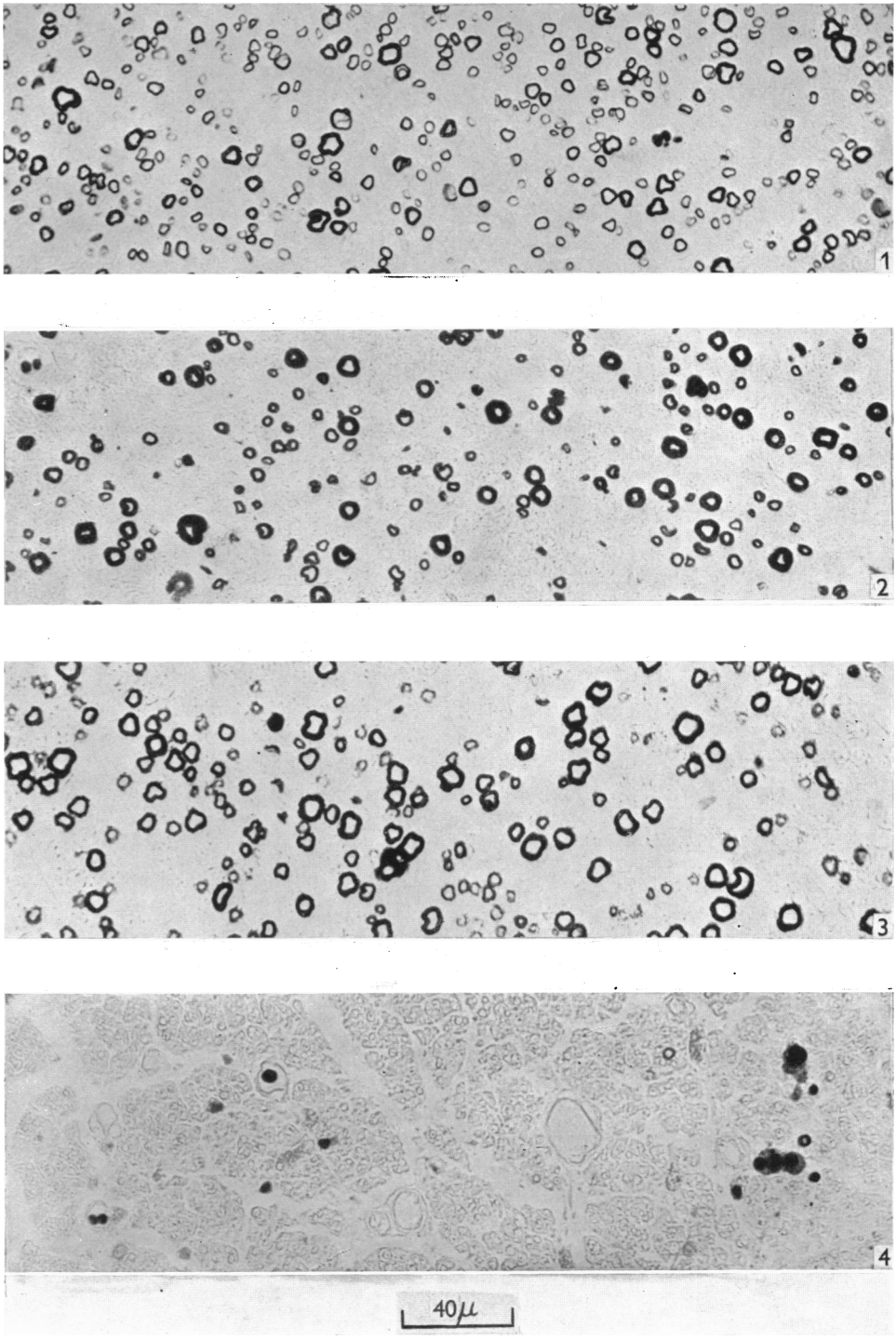

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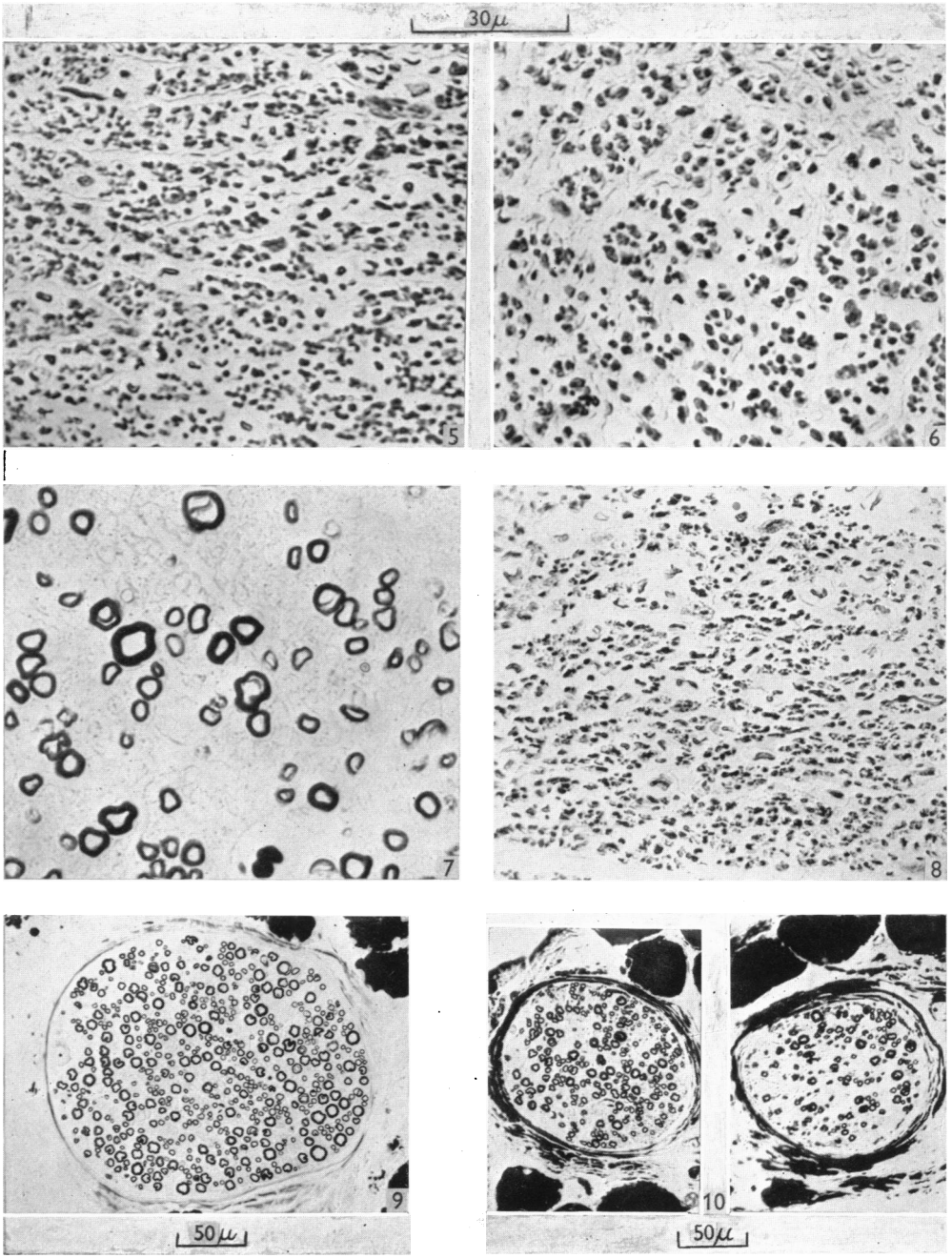
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EXPLANATION OF PLATES

PLATE 1

All photographs of the thoracic vagus trunk were made from transverse section taken at a level mid-way between the level of the aortic arch and the hilum of the lung.

Fig. 1. Myelinated nerve fibres in a portion of a normal thoracic vagus trunk (13*b*). Weigert.

Fig. 2. Myelinated fibres in a portion of the thoracic vagus trunk after intracranial vagotomy (16*d*). Weigert. Note the reduction in the number of small myelinated fibres compared with the normal.

Fig. 3. Myelinated fibres in a thoracic vagus trunk after supranodose vagotomy (6*d*). Weigert. The appearance is similar to that found after intracranial vagotomy.

Fig. 4. Weigert preparation of a thoracic vagus trunk after cervical vagotomy and sympathectomy below the nodose ganglion. Only a few myelinated fibres remain. (3*a*.)

PLATE 2

Fig. 5. Pyridine-silver preparation of a portion of a normal thoracic vagus trunk (16*e*). Both myelinated and non-myelinated fibres are stained, and comparison with Fig. 7, taken at the same magnification, shows that the non-myelinated fibres far outnumber the myelinated fibres.

Fig. 6. Pyridine-silver preparation of a portion of a thoracic vagus trunk after intracranial vagotomy (16*f*). Comparison with Fig. 5 shows that the operation has resulted in a considerable reduction in fibre density in this part of the nerve. This reduction is caused by degeneration of some non-myelinated and small myelinated fibres.

Fig. 7. Weigert preparation of a portion of a normal thoracic vagus trunk (13*c*) taken at the same magnification as Fig. 5.

Fig. 8. Pyridine-silver preparation of a portion of a thoracic vagus trunk after intracranial vagotomy (16*f*). This portion of the nerve shows an approximately normal fibre density.

Fig. 9. Transverse section of a normal bronchial branch of the vagus (5*a*). Weigert.

Fig. 10. Transverse section of two normal cardiac branches of the vagus (21*a* and *c*). Weigert.