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ON THE DIRECT AND CROSSED COMPONENTS OF REFLEX RESPONSES TO UNILATERAL STIMULATION OF THE CAROTID BODY CHEMORECEPTORS IN THE DOG

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SUMMARY

1. In dogs under chloralose-urethane anaesthesia the chemoreceptors of the two carotid bodies were separately stimulated.

2. The distribution of three primary reflex responses to carotid body stimulation was studied: parasympathetic bradycardia, sympathetic vasoconstriction, and increase in somatic phrenic nerve activity.

3. The reflex bradycardia evoked by either carotid body was mediated by both vagus nerves, but when either vagus was blocked a greater response could be obtained from the contralateral than from the ipsilateral carotid body.

4. The reflex vasoconstriction evoked by either carotid body was seen in both hind limbs, with no predominance in either limb.

5. The reflex increase in phrenic nerve activity evoked by either carotid body was seen in both phrenic nerves, with no predominance in either nerve.

INTRODUCTION

Among the primary reflex responses to carotid body chemoreceptor stimulation in the dog are hyperpnoea, bradycardia due mainly to increased vagal tone, and systemic vasoconstriction due entirely to increased sympathetic tone (Daly & Scott, 1958; Bernthal, Motley, Schwind & Weeks, 1945). In spontaneously breathing dogs the primary bradycardia and vasoconstriction may be masked by secondary effects of the increase in pulmonary ventilation (Daly & Scott, 1962, 1963). A similar situation is found in the cat (Scott, 1966) and in the rabbit (Korner & Edwards, 1960).

Fedorchuk (1957) found that, after ablation of one carotid body in decerebrate cats, intravenous injections of chemoreceptor stimulant

drugs caused an increase in impulse traffic in the phrenic nerve on the side of the intact carotid body and no increase on the side of the ablated carotid body. Fedorchuk (1954) also found that stimulation of one carotid body caused a reflex release of catecholamines predominantly or solely from the adrenal gland on the same side. Nazarenko (1958) studying the reflex bradycardia on carotid body stimulation in decerebrate cats concluded that the right carotid body exerts its effect entirely through the right vagus nerve, while the left carotid body acts through both vagi.

We have studied the distribution between the two sides of the body of the somatic respiratory, the parasympathetic cardiac and the sympathetic vascular effects of the stimulation of one carotid body at a time in dogs. Our results indicate that the parasympathetic effect is mainly ipsilateral, while the sympathetic and somatic effects are evenly distributed on the two sides.

Preliminary accounts of this work have been published (McQueen & Ungar, 1969*a*, *b*, *c*).

METHODS

Mongrel dogs of either sex weighing between 6·8 and 21·5 kg, and two cats weighing 3·0 and 3·5 kg respectively were used.

Anaesthesia. Dogs were premedicated with morphine sulphate (1 mg/kg subcutaneously) and anaesthetized 30 min later with a mixture of α-chloralose (55 mg/kg) and urethane (550 mg/kg) injected intravenously as a solution containing 2·5 % α-chloralose and 25 % urethane in a mixture of equal volumes of 0·9 % aqueous sodium chloride and polyethylene glycol 200. To maintain anaesthesia a 2 % solution of α-chloralose was infused at a rate adjusted according to the state of the animal's reflexes.

One cat was anaesthetized by an intraperitoneal injection of pentobarbitone (25 mg/kg) and the other was decerebrated at the intercollicular level under ether anaesthesia.

Respiration. In all animals the trachea was cannulated in the neck.

The lungs of eight dogs were artificially ventilated with a 60 % oxygen 40 % nitrogen mixture by a Starling 'Ideal' pump. Their chests were opened by splitting the sternum in the mid line, and held open by a self-retaining retractor after ligature of the internal thoracic vessels.

In twenty dogs under artificial ventilation decamethonium iodide (0·25 mg/kg) was given intravenously to prevent respiratory movements when the chemoreceptors were stimulated.

Blood from a cannulated femoral artery was sampled at 15 min intervals throughout the experiment. The P_{a,CO_2}, P_{a,O_2} and pH were estimated by means of a Radiometer PA 927 gas monitor. Arterial P_{CO_2} was held between 30 and 35 torr by adjustment of the stroke of the respiratory pump which ran at 20 rev/min. The plasma bicarbonate concentration was held between 20 and 25 mM by intravenous injections of molar sodium bicarbonate solution, the base deficit being calculated from the nomogram of Singer & Hastings (1948).

The P_{a,O_2} was always above 150 torr. Under these conditions we assumed that there was no resting chemoreceptor tone, so that the results should not have been com-

plicated by withdrawal of resting tone when the vagi or carotid sinus nerves were cut or blocked.

Elimination of secondary reflexes from the lungs. In the animals with open chests the thoracic vagal trunks were cut, on the left side between the aorta and the left pulmonary artery, and on the right side at the level of the azygos vein. This procedure eliminates the pulmonary branches of the vagi but does not affect the cardiac branches (Daly & Scott, 1963).

In animals with intact chests, where cardiac reflexes were not being studied, both vagosympathetic trunks were cut in the neck.

Elimination of reflexes from the bladder. Each animal's bladder was catheterized to prevent progressive filling with the resulting influence on autonomic reflexes (Oberholzer, 1963).

Blood pressure compensation. In five dogs with open chests a blood pressure compensator was connected to the left subclavian artery in order to reduce fluctuations in arterial pressure on chemoreceptor stimulation. The compensator consisted of an inverted conical flask of 1 litre capacity containing about 200 ml. 0·9% sodium chloride solution. The outlet was connected to the artery by wide bore silicone rubber tubing, and the air space in the flask connected to a source of compressed air set to the animal's resting arterial pressure.

Temperature control. A thermistor probe (Standard Telephones & Cables type F23) was inserted into the animal's rectum, and connected through an A.E.I. 'Sunvette' temperature controller to an infra-red heater. The animal's temperature was held at $37 \pm 0{\cdot}5°$ C.

Stimulation of the carotid body chemoreceptors. Nylon catheters (0·75 mm o.d.) were inserted through both superior thyroid arteries, their tips lying in the common carotid arteries about 3 cm upstream of the origins of the superior thyroid arteries. Each carotid body was independently stimulated by infusion through the appropriate catheter, with a Watson Marlow MHRE pump, of a solution of suberyl dicholine di-iodide (83 μM) in a phosphate buffer at pH 7·4. The infusions lasted 10 sec, and were separated by intervals of 5 min, the two carotid bodies being stimulated alternately. The amount of suberyl dicholine di-iodide (SDC) infused during a stimulus varied from 3 to 58 n-mole (2–35 μg), the usual effective dose being 30 n-mole (18 μg).

SDC has peripheral nicotinic actions but no central nervous effects at the dosage used. It is rapidly metabolized by pseudocholinesterase (Anichkov & Belen'kii, 1963). We have found that this time cycle of dosage can be followed for several hours without tachyphylaxis in the reflex responses. This confirms similar findings in the cat (Mikhel'son, Rybovlev, Gorelik & Dardymov, 1957).

Block of conduction in the vagi. Each vagosympathetic trunk in the neck was dissected and placed on a cooling device (Daly, Hazzledine & Ungar, 1967). The two nerves were cooled in turn to between 0 and $-2°$ C during cycles of alternate carotid body stimulation.

The bradycardia obtained by electrical stimulation of the cut vagus nerve was abolished on cooling to 5° C, and returned to its previous magnitude on rewarming even after cooling to $-4°$ C.

Recording procedure. A Honeywell 2106 twelve channel ultra-violet oscillograph was used. Honeywell M400/350 galvanometers gave a frequency response flat to 320 Hz. Kodak Linagraph 1843 paper was used.

Arterial pressure. Arterial pressure was measured by means of a Bell and Howell L222 transducer from a catheter (2 mm o.d.) in either a femoral or a radial artery. The output from the transducer was amplified by a Fenlow AD2000 amplifier and recorded on a channel of the oscillograph.

Measurement of changes in limb vascular resistance. A nylon catheter (2 mm o.d.) was inserted through each femoral artery just below the inguinal ligament so that its tip lay in the abdominal aorta. The catheter was connected by a loop of silicone rubber tubing, which passed through a Watson Marlow MHRE pump, to a cannula inserted caudally into the same femoral artery. A tape was tied tightly around the limb between the catheter and the cannula, avoiding the femoral vein. This perfusion system provided a constant flow against arterial pressures up to 250 mm Hg.

The time taken for blood to traverse the perfusion tube was about 12 sec at the pump speed usually used.

The perfusion pressure in each limb was recorded from a 'Y' piece in the perfusion tubing in a similar way to that described for systemic arterial pressure. As the limbs were perfused at constant flow, pressure changes were taken to be proportional to changes in vascular resistance.

Cardiac period (R–R interval). The electrocardiogram was recorded from chest leads chosen to give prominent R waves. A trigger circuit was set so that each R wave reset a linear ramp generator (Computing Techniques SA 6). The height of each ramp, recorded on a channel of the oscillograph, was proportional to the R–R interval. The mean cardiac period during the first 10 sec of each test of carotid body stimulation was compared with the mean cardiac period before, and after stimulation.

Electrical activity in the phrenic nerves. Each phrenic nerve was cut between ligatures at the level of the seventh cervical transverse process, and placed on bipolar platinum electrodes in a pool of mineral oil. Impulses were amplified by a differential input FET amplifier passing a band of frequencies between 10 and 1 KHz.

Activity above a threshold set to exclude the resting noise was averaged with a time constant of 20 msec, and recorded on a channel of the oscillograph.

The amplitude of the averaged record was taken as a measure of the impulse traffic in an inspiratory burst. Changes during carotid body stimulation were calculated as the mean increase in amplitude of inspiratory peaks expressed as a percentage of the mean resting amplitude before and after stimulation.

Drugs. The following drugs were used: α-chloralose (B.D.H. or Koch Light Laboratories Ltd), polyethylene glycol 200 (B.D.H.), ethyl carbamate (urethane) (B.D.H. or May and Baker Ltd.), decamethonium iodide (K and K Labs Inc., New York), morphine sulphate (Macarthys Ltd), atropine sulphate (B.D.H.), suberyl dicholine di-iodide (kindly prepared by Dr J. N. T. Gilbert, Department of Pharmaceutical Chemistry, School of Pharmacy, London University) and guanethidine sulphate (Ciba).

RESULTS

Reflex bradycardia. We carried out preliminary experiments in order to establish

(i) whether the changes in heart rate recorded were due entirely to stimulation of receptors on the side into which the stimulant was infused.

(ii) whether the changes in heart rate were mediated entirely by parasympathetic fibres in the two vagus nerves.

In two dogs tests of carotid body stimulation were carried out on both sides before and after section of one carotid sinus nerve. In both animals the cardiac response to stimulation on the denervated side was abolished, while the response to stimulation on the intact side was unaffected.

In two dogs tests of carotid body stimulation were carried out before and after intravenous administration of atropine sulphate (180 n-mole/kg or 125 μg/kg and 360 n-mole/kg or 250 μg/kg). The reflex bradycardia was abolished, while the concomitant vasoconstriction in the hind limbs was unaffected.

In five dogs tests of carotid body stimulation were carried out before and after division of both vagosympathetic trunks in the neck. Reflex bradycardia was abolished in all of these.

Twenty-eight tests of carotid body stimulation were carried out on six dogs with intact chests artificially ventilated and paralysed with decamethonium iodide. In four out of thirteen tests the reflex slowing of the heart was potentiated by cooling the left vagus, and in six out of fifteen tests it was potentiated by cooling the right vagus. We attributed this effect, which invalidates any quantitative comparison between the two sides, to blocked sensory fibres in the vagi from pulmonary stretch receptors, and possibly also from aortic baroreceptors (see Discussion).

Forty-three tests of carotid body stimulation were carried out on seven dogs with open chests after cutting both vagi between the origins of their cardiac and pulmonary branches (see Methods). A typical record of a set of responses is shown in Fig. 1. The results are shown in Table 1. While both vagi were intact, stimulation of either carotid body gave rise to a similar degree of slowing of the heart. While the left vagus was blocked, stimulation of the right carotid body gave rise to greater slowing than did stimulation of the left carotid body in six out of seven dogs. Conversely, while the right vagus was blocked, stimulation of the left carotid body gave rise to greater slowing than did stimulation of the right carotid body in all of the seven dogs. These differences are statistically significant ($P < 0{\cdot}01$). Whichever vagus was blocked, the degree of slowing produced by stimulation of the ipsilateral carotid body was about half that produced by stimulation of the contralateral carotid body. While the left vagus was blocked both the ipsilateral and contralateral responses were about twice the size of the corresponding ipsilateral and contralateral responses obtained while the right vagus was blocked.

Reflex vasoconstriction. As with the reflex bradycardia we carried out preliminary experiments in order to establish

(i) whether the changes in hind limb resistance recorded were due entirely to stimulation of receptors on the side into which the SDC was infused.

(ii) whether the changes were mediated entirely by sympathetic adrenergic fibres.

In three dogs stimulation of each carotid body gave rise to reflex vasoconstriction. After section of one carotid sinus nerve in each dog

vasoconstriction was only seen when the innervated carotid body was stimulated.

In three dogs guanethidine sulphate (3·5 μmole/kg) was injected close-arterially into one hind limb while both hind limbs were perfused at constant flow. A test of chemoreceptor stimulation was carried out before the guanethidine had time to circulate. In each experiment the reflex vasoconstriction previously observed in that limb was abolished, with no effect on the vasoconstriction in the other hind limb.

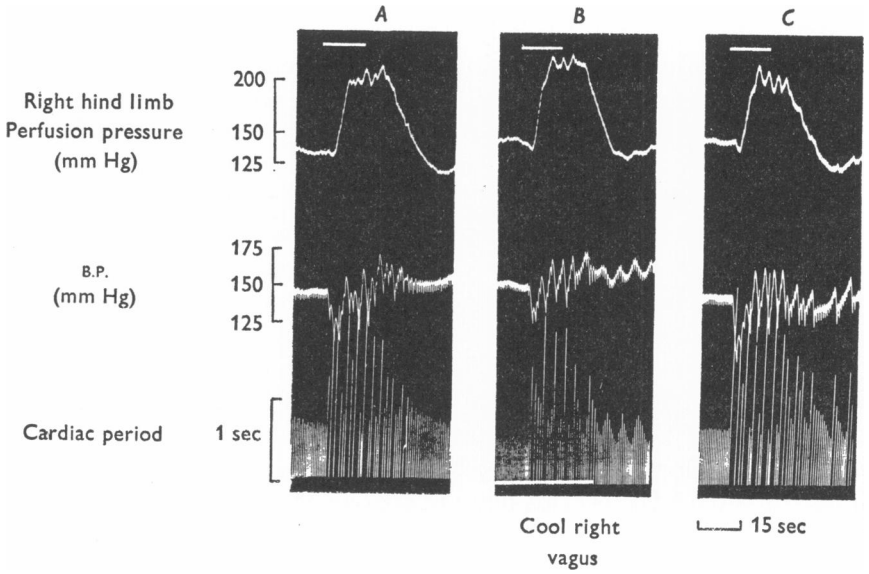

Fig. 1. Reflex responses to stimulation of the right carotid body of a dog. The records from above downwards show arterial pressure in the right hind limb, perfused at constant flow, mean systemic arterial pressure, and cardiac period (R–R interval). The marker at the top indicates the period of stimulation by infusion of SDC into the right common carotid artery. The responses before, during and after cold block of the right vagosympathetic trunk in the neck are shown in blocks *A*, *B* and *C* respectively.

Sixty-six tests of carotid body stimulation were carried out in eight dogs, artificially ventilated and paralysed with decamethonium iodide, after cutting both vagosympathetic nerves in the neck. The results are shown in Table 2. Whichever carotid body was stimulated, the difference between the means of the responses in the two hind limbs is smaller than their standard errors.

In two dogs both forelimbs were similarly perfused at constant flow. Whichever carotid body was stimulated, a balanced vasoconstriction was seen in both forelimbs.

TABLE 1. The effect of stimulation of each carotid body on the cardiac period (R–R interval). Experiments on dogs with open chests, artificially ventilated, the cervical vagi being cooled in turn

A

	Both vagi intact. Cardiac period (msec)			Left vagus cooled. Cardiac period (msec)			Right vagus cooled. Cardiac period (msec)		
		CB stimulated			CB stimulated			CB stimulated	
Experiment	Control	Left	Right	Control	Left	Right	Control	Left	Right
1	400	830	750	470	750	1280	350	470	450
2	360	2000	1840	320	1020	1460	340	1220	720
3	560	710	830	450	490	520	360	380	360
4	500	1460	1920	480	1080	1680	540	1410	960
5	730	1180	1280	540	630	1090	740	1060	810
6	380	710	730	340	620	800	350	430	400
7	530	910	840	460	610	610	430	500	460
Means ± S.E.	490 ± 50	1110 ± 180	1170 ± 190	440 ± 30	740 ± 80	1060 ± 170	440 ± 60	780 ± 160	590 ± 80

B

	Animal		Both vagi intact. Increase in cardiac period (msec). CB stimulated		Left vagus cooled. Increase in cardiac period (msec). CB stimulated		Right vagus cooled. Increase in cardiac period (msec). CB stimulated	
Experiment	Sex	Weight (kg)	Left	Right	Left	Right	Left	Right
1	F	11	430	360	280	810	120	110
2	M	8	1640	1500	700	1140	870	370
3	M	12·8	150	270	40	70	20	0
4	F	14	960	1440	600	1200	870	420
5	M	14·4	280	550	90	550	320	70
6	F	8·2	330	360	280	460	80	50
7	M	14	380	310	150	150	70	30
		Means ± S.E.	590 ± 200	680 ± 210	310 ± 100	630 ± 170	340 ± 140	150 ± 80

TABLE 2. The effect of stimulation of each carotid body on the vascular resistance of both hind limbs perfused at constant flow. Sixty-six tests in eight dogs, artificially ventilated and paralysed with decamethonium iodide, after cutting both vagosympathetic trunks in the neck

Animals		Control			Mean % increase in resistance			
					Left carotid body stimulated		Right carotid body stimulated	
Sex	Weight (kg)	Mean B.P. (mm Hg)	Left leg mean perfusion pressure (mm Hg)	Right leg mean perfusion pressure (mm Hg)	Left left	Right leg	Left leg	Right leg
F	9·5	123	108	122	18·5	22·6	22·5	23·2
F	8·5	140	146	153	9·7	9·3	12·8	9·9
M	9·6	140	160	136	9·8	6·4	6·5	9·5
M	11·8	140	148	142	9·3	12·5	14·0	10·7
M	12·2	115	132	120	75·7	40·9	41·4	51·2
F	11·0	140	129	158	55·9	39·5	22·4	40·9
M	10·2	142	144	151	15·6	18·3	19·3	14·1
M	14·4	113	117	124	19·9	22·7	42·8	30·1
				Means ± S.E.	23·8 ± 3·5	22·1 ± 2·6	25·4 ± 3·7	24·7 ± 3·0

Phrenic neurogram. As in the previous sections, we carried out a preliminary experiment to establish whether the changes in phrenic activity recorded were due entirely to stimulation of receptors on the side into which SDC was infused.

In one dog tests of carotid body stimulation were carried out on both sides before and after section of one carotid sinus nerve while electrical activity was recorded from both phrenic nerves. The reflex increase in activity in both prenic nerves previously evoked from the denervated side was abolished, but the response from the other side was unaffected.

TABLE 3. The effect of stimulation of each carotid body on the averaged electrical activities of both phrenic nerves. One hundred tests in six dogs, artificially ventilated and paralysed with decamethonium iodide, after cutting both vagosympathetic trunks in the neck

Animals		Control		Mean % increase in phrenic activity			
				Left carotid body stimulated		Right carotid body stimulated	
Sex	Weight (kg)	Mean B.P. (mm Hg)	Mean P_{a,CO_2} (torr)	Left phrenic nerve	Right phrenic nerve	Left phrenic nerve	Right phrenic nerve
F	17·5	138	35	86	51	115	70
M	11·8	143	39	62	56	36	37
M	13·4	169	48	53	53	51	50
M	21·5	126	40	39	35	21	21
F	12·6	158	38	24	21	30	26
M	16·0	106	49	36	40	45	63
		Means ± S.E.		48 ± 7	44 ± 4	49 ± 6	45 ± 5

One hundred tests of carotid body stimulation were carried out in six dogs, artificially ventilated and paralysed with decamethonium iodide, after cutting both vagosympathetic nerves in the neck. The results are shown in Table 3. Whichever carotid body was stimulated, the difference between the means of the responses in the phrenic nerves is smaller than their standard errors.

In view of the disparity between our results and those of Fedorchuk (1957), who worked on cats, we repeated our experiments on one anaesthetized and one decerebrate cat. In both of these experiments we obtained uniform increases in activity in the two phrenic nerves, whichever carotid body was stimulated. A record of a pair of tests in the decerebrate cat is shown in Fig. 2.

Systemic arterial pressure. The responses to carotid body stimulation that we studied were accompanied by variable changes in systemic arterial pressure, and these can give rise to secondary reflex changes in heart rate,

vascular tone and respiratory drive by affecting the baroreceptors of the carotid sinuses and aortic arch (Heymans & Neil, 1958).

In the experiments on reflex bradycardia the changes in systemic pressure were biphasic (see Fig. 1) and our measurements of reflex slowing were made before the onset of the sustained rise in pressure. In the other two series of experiments there were simple rises in pressure, as the vagi were

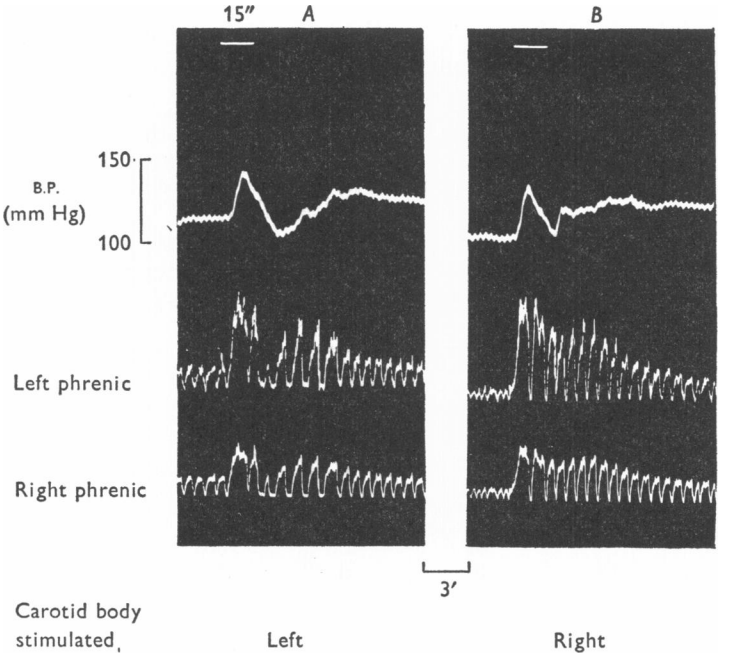

Fig. 2. Reflex responses to stimulation of the left carotid body (*A*) and the right carotid body (*B*) of a decerebrate cat. The records from above downwards show mean systemic arterial pressure, averaged electrical activity in the left phrenic nerve, and averaged electrical activity in the right phrenic nerve.

cut (see Fig. 2). Here our measurements, made in the first ten seconds of the response, should not have been affected by reflex changes secondary to the pressure rise.

In order to establish whether such changes were altering the size of our primary responses, we carried out tests of carotid body stimulation with and without a blood pressure compensator.

In three animals tests of reflex bradycardia, in three animals tests of reflex vasoconstriction, and in one animal tests of reflex increase in phrenic activity were carried out with and without the blood pressure compensator. In none of these experiments did we see any change in the size of the primary reflex responses.

DISCUSSION

The methods used in these experiments have enabled us to study three primary reflex responses to chemoreceptor stimulation, and to stimulate the chemoreceptors of the two carotid bodies separately.

Acetylcholine-like drugs, if used at much higher concentrations than those affecting chemoreceptors, have been shown to stimulate baroreceptor endings in the cat (Diamond, 1955). We exclude the possibility that SDC stimulated the baroreceptors in our experiments for the following reasons:

(i) Jarisch, Landgren, Neil & Zotterman (1952) gave intracarotid injections to cats and dogs of drugs that stimulate both chemoreceptors and baroreceptors. They found that stimulation of chemoreceptor fibres occurred immediately, whereas impulse traffic in baroreceptor fibres increased after delays of at least 15 sec. There would thus be no stimulation of baroreceptors in our experiments during the time when reflex responses were recorded.

(ii) McQueen (1970) studied the problem under similar conditions to those of the present experiments. One carotid body was embolized with lycopodium, using the technique of Heymans & Bouckaert (1933). This procedure did not affect either the cardiac or the vascular reflex responses to occlusion of the common carotid artery, showing that the baroreceptor reflex was intact, nor did it affect the reflex responses to infusion of SDC into the contralateral common carotid artery. The responses to infusion of SDC into the ipsilateral common carotid artery were totally abolished, even at twenty times the greatest dosage used in these experiments.

(iii) Supporting evidence was provided by the observation that intracarotid injections of SDC and sodium cyanide that evoked equal respiratory responses also evoked equal increases in hind limb resistance and cardiac period. Any stimulation of the baroreceptors would have been expected to potentiate the bradycardia, but to counteract the vasoconstriction.

Reflex bradycardia. Pagano (1900) working before the discovery of the sensory function of the carotid bodies, described the bradycardia following the injection of nicotine or of prussic acid into the common carotid artery of a dog. He found that the bradycardia could be much reduced or even abolished by cutting the vagus nerve on the side on which the injection was given. Nazarenko (1958) injected potassium cyanide intravenously into decerebrate cats having one carotid body excised and one vagus nerve cut in the neck, and made a non-parametric comparison of the incidence of bradycardia in the four combinations of unilateral carotid body excision and unilateral vagotomy. He concluded from his results that the reflex

evoked by the right carotid body is mediated only by the right vagus, while the reflex from the left carotid body is mediated by both vagi.

Our results indicate that the reflex from either carotid body is mediated by both vagi, as shown in Fig. 3. Each vagus nerve, however, predominantly mediates the reflex from the carotid body on the same side. We thus seem to agree with Pagano, but not with Nazarenko. This conflict could be due to a species difference between dogs and cats, but it could also be due to two differences in technique:

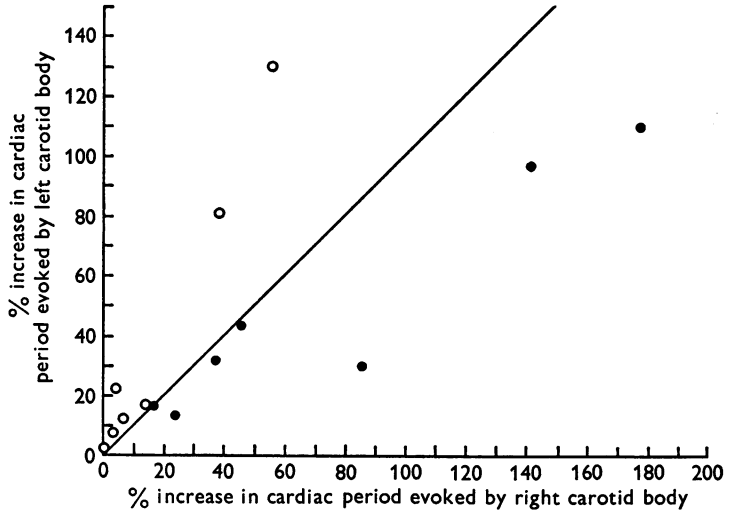

Fig. 3. Spot diagram of ipsilateral against contralateral responses: reflex bradycardia. Graphical representation of the results in Table 1. The percentage increase in cardiac period evoked by stimulation of the left carotid body is plotted against that evoked by stimulation of the right carotid body in each experimental situation. Open circles represent tests in which the right vagosympathetic trunk was cooled; filled circles represent tests in which the left vagosympathetic trunk was cooled. The line of equality is indicated.

(i) Intravenous injections of potassium cyanide would stimulate the aortic bodies as well as the carotid bodies, but sensory inpulses would only reach the brain on the side of the intact vagus.

(ii) The pulmonary inflation reflex, which modifies the response to chemoreceptor stimulation (Daly & Scott, 1962, 1963) would have been active though only on the side of the intact vagus in Nazarenko's experiments, whereas in our experiments it was totally eliminated.

A factor common to our experiments and Nazarenko's is the withdrawal of sensory influence from the heart and great vessels when one or the other vagus nerve is blocked or cut. There are thus different backgrounds of reflex activity in the three situations with one or the other or both

vagi conducting. It is impossible to make quantitative comparisons among the reflexes elicited against these different backgrounds. We have therefore only compared the effects of stimulating the two carotid bodies, in each state of the vagi.

Another possible factor is a component of withdrawal of sympathetic tone in the reflex bradycardia. We studied the reflex bradycardia during only the first ten seconds of the response and found it to be abolished by atropine or bilateral vagotomy. Our results are not incompatible with a sympathetic component in the steady state, as found by Daly & Scott (1962).

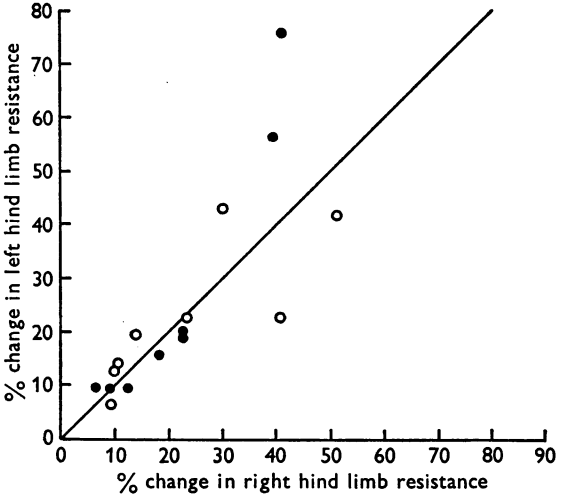

Fig. 4. Spot diagram of ipsilateral against contralateral responses: reflex vasoconstriction. Graphical representation of the results in Table 2. Open circles represent effects of stimulation of the right carotid body (RCB) and filled circles represent the effects of stimulation of the left carotid body (LCB). Percentage changes in right hind limb resistance are plotted on the abscissa and percentage changes in left hind limb resistance on the ordinate. The line of equality is indicated.

Reflex vasoconstriction. Our results confirm the findings of Daly & Scott (1962) that a primary reflex response to carotid body stimulation is vasoconstriction, mediated entirely by sympathetic adrenergic nerves.

It is evident from Fig. 4 that whichever carotid body we stimulated, we saw a reflex vasoconstriction in both hind limbs, and that the response on neither side was consistently larger than that on the other. This sympathetically mediated reflex thus differs in its pattern of distribution from the parasympathetically mediated bradycardia.

The only previous work of which we are aware on the distribution of a sympathetically mediated reflex from the carotid bodies is that of

Fedorchuk (1954), who found that the reflex release of catecholamines occurred solely or predominantly from the adrenal gland on the same side as a stimulated carotid body in the cat. McQueen & Ungar (1970) did not find such a predominance in the dog.

Reflex increase in phrenic activity. Our results, illustrated in Fig. 5, indicate that stimulation of either carotid body gives rise to uniform increases in activity in both phrenic nerves in the dog. Our two experiments in cats suggest that the pattern is similar.

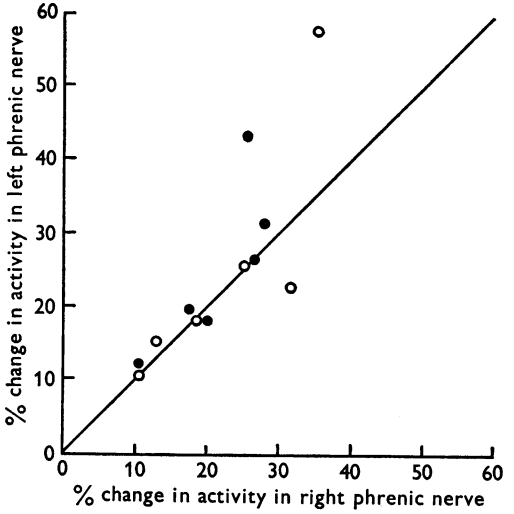

Fig. 5. Spot diagram of ipsilateral against contralateral responses: reflex increase in phrenic nerve activity. Open circles represent the effects of stimulation of the right carotid body (RCB), and closed circles the effects of stimulation of the left carotid body (LCB). Percentage changes in activity in the right phrenic nerve are plotted on the abscissa, and percentage changes in the left phrenic nerve on the ordinate. The line of equality is indicated.

We thus differ from Fedorchuk (1957) who found that after ablation of one carotid body, an intravenous injection of cytisine only increased activity in the phrenic nerve on the side of the intact carotid body. Having excluded the possibility of a species difference between dogs and cats, the possibility remains that denervation of one group of receptors may alter the pattern of responses to stimulation of the remaining receptors.

We conclude from our results that the central pathways from chemoreceptor afferent fibres to cardio-inhibitor fibres in the vagi must be different from their pathways both to the sympathetic fibres to the limbs and to phrenic motoneurones. Pathways to the first are predominantly ipsilateral, but with the last two there seems to be a balanced influence on the two sides.

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