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THE EFFECTS OF STIMULATION OF AUTONOMIC NERVES ON CAROTID BODY BLOOD FLOW IN THE CAT

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SUMMARY

1. The effects of electrical stimulation of the distal ends of cut preganglionic cervical sympathetic trunks and cut sinus nerves on carotid body total blood flow, local blood flow and tissue P_{O_2} (P_{t,O_2}) were studied in anaesthetized cats.

2. Sympathetic stimulation caused reductions, often marked, of the total blood flow through the carotid body, yet did not influence local flow or P_{t,O_2} recorded by electrodes whose tips lay in deep locations within the carotid body. Intraglomeral electrodes did respond to reductions of perfusion pressure and to perfusions of the carotid body with saline solutions.

3. Values of P_{t,O_2} recorded from superficial tissues of the carotid body were higher than those from deeper locations and were increased by blowing oxygen over the surface of the organ. In these locations, sympathetic stimulation increased P_{t,O_2}.

4. An increase in the frequency of sinus nerve chemosensory discharges during sympathetic stimulation was obtained in the presence of an unchanged P_{t,O_2} recorded from deep glomeral locations.

5. Stimulation of the distal end of the sinus nerve increased the total blood flow through the carotid body but did not affect local flow or P_{t,O_2} recorded from deep glomeral locations.

6. It is concluded that autonomic nerves supplying the carotid body mainly influence arteriovenous anastomotic and/or other shunt vessels, with little control being exerted on vessels regulating the flow through the capillary network of the specific tissue. This investigation also indicates that the flow in the capillary network of the specific tissue is a small proportion of the total flow. Support is given to the view that autonomic nerves can influence chemoreceptor activity by non-vascular mechanisms.

INTRODUCTION

Activation of sympathetic and parasympathetic fibres supplying the carotid body (glomus caroticum) can cause changes of blood flow through the organ (Daly, Lambertsen & Schweitzer, 1954; Purves, 1970*b*; Neil & O'Regan, 1971) and can also alter the frequency of sinus nerve chemosensory discharges (Floyd & Neil, 1952;

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Eyzaguirre & Lewin, 1961; Neil & O'Regan, 1971). The view that the modifications of chemosensory discharges are solely the consequence of changes of blood flow in the vicinity of chemosensitive elements in the glomus (Eyzaguirre & Lewin, 1961; Goodman, 1973; Belmonte & Eyzaguirre, 1974; McCloskey, 1975) is disputed by reports indicating the existence of non-vascular mechanisms of modulation by both parasympathetic (Neil & O'Regan, 1971; Sampson, 1972; O'Regan, 1975; Willshaw, 1975) and sympathetic (O'Regan, 1977, 1981) fibres.

Measurements of changes of local flow and P_{O_2} within the specific tissue of the glomus during activation of autonomic nerves could provide a greater insight into how these nerves control glomeral blood flow and influence chemosensory activity. In this paper we report on the effects of autonomic nerves on both local flow and tissue P_{O_2} recorded from within the glomus and compare these effects with those exerted on the total blood flow through the carotid body and on sinus nerve chemosensory discharges. Some of the results have been briefly reported in a Communication to the Physiological Society (Acker & O'Regan, 1979).

METHODS

General procedures. Twenty-four cats of either sex weighing 2–3 kg were anaesthetized by pentobarbitone sodium (Nembutal, Abbott, 42–48 mg/kg I.P.). Cannulae were inserted into a femoral vein, a femoral artery and the trachea low in the neck. Heparin (Liquemin, 1000 i.u./kg at 2 hr intervals) and supplemental doses of pentobarbitone (6–12 mg) were given I.V. The arterial cannula was used for the measurement of systemic arterial blood pressure (Statham transducer) and for withdrawing samples of blood for determination of arterial P_{O_2}, P_{CO_2}, pH (Radiometer, Copenhagen), oxygen content (LEX-O_2-Con) and haematocrit (Yellow Springs Instruments). The expired concentrations of oxygen and carbon dioxide were continuously monitored using a mass spectrometer (Perkin–Elmer). Four cats, which required artificial ventilation either because of respiratory insufficiency or because cervical muscular movements interfered with chemosensory recordings, were given gallamine triethiodide (Flaxedil, May & Baker, 4–12 mg/kg) and pentobarbitone (6–12 mg) at hourly intervals I.V., and the stroke of the ventilator set to maintain arterial P_{O_2}, P_{CO_2} and pH at physiological levels.

The trachea, larynx, pharynx and oesophagus were reflected cranially to expose the carotid bifurcations. The ventromedial surface of the carotid body (usually left) was cleared of overlying fat and connective tissue, great care being taken to avoid damage to the blood supply and autonomic innervation of the organ. The venous drainage of the carotid body was vascularly isolated using a technique described in detail elsewhere (Neil & O'Regan, 1971). A lingual arterial cannula was used for intracarotid (I.C.) injection of drugs.

Measurements of carotid body total flow, local flow and tissue P_{O_2}. The vascularly isolated venous segment (usually the transverse pharyngeal vein), which received only the venous outflow from the carotid body, was cannulated with polyethylene tubing. Total flow through the carotid body was obtained by measuring the weight of the outflowing blood over periods of between 5 and 20 sec and appropriate calculations were then carried out so as to express the flow rates in μl./min.

Oxygen tension within the glomus (P_{t,O_2}) was measured polarographically using needle electrodes inserted into the organ through its ventromedial surface (Acker, Lübbers & Purves, 1971). The electrodes were elastically suspended with copper wire so as to follow the movements of the glomus without causing undue tissue compression. In four cats electrodes of a more rigid structure were driven into the glomus at varying distances from its surface and these electrodes allowed a systematic study of the effects of sympathetic stimulation on P_{t,O_2} recorded at different locations within the organ. The situation of the electrodes was tested by blowing oxygen over the surface of the carotid body. In superficial situations, as distinct from deep locations, P_{t,O_2} increased during this test. Electrodes were calibrated before and after insertion.

Elastically suspended electrode assemblies, described by Acker, Lübbers & Durst (1977), utilized hydrogen clearance to measure flow changes from small localized volumes within the carotid body.

Two platinum electrodes with tip diameters of about 1 μm were glued together. With one electrode small quantities of hydrogen gas were electrolytically generated using a constant current between 6 and 10 nA while the other electrode measured the hydrogen concentration in its immediate vicinity. Changes of blood flow in the vicinity of the tip of the hydrogen-sensing electrode caused a greater or lesser dissipation of hydrogen. This electrode gave only qualitative information on local flow changes.

It was usual to withdraw and re-insert both P_{O_2} and hydrogen clearance electrodes on several occasions during an experiment. The presence of multiple electrode tracks in the glomus made it impossible to correlate by histological means the location of the electrode tips with the physiologial findings. However, P_{O_2} values recorded from deep glomeral locations in the present investigation were in the same range as those reported in another study where histological evidence showed that the measurements were made from the specific tissue of the glomus (Weigelt, Seidl, Acker & Lübbers, 1976).

The output of the electrodes (in nA current) was continuously monitored and recorded together with blood pressure (B.P.) and respired gas concentrations on separate channels of a direct-writing ink recorder (Rikadenki). Signals were also stored using a four-channel FM tape recorder (Precision Instruments at 30 IPS).

Tests of electrode responses. Animals were periodically ventilated with 5% oxygen in nitrogen to produce hypoxic hypoxia, a condition known to cause decreases not only of P_{t,O_2} but also of the rate of hydrogen clearance (Acker *et al.* 1977). Additionally, in four cats the area of the carotid bifurcation was so prepared as to permit the perfusion pressure to be reduced to zero, thereby abolishing glomeral blood flow. The preparation also allowed the glomus to be artificially perfused with saline solutions. All arteries arising from the common and external carotid arteries in the vicinity of the carotid bifurcation were tied, with the exception of those supplying the carotid body and the superior cervical ganglion. Polyethylene tubing containing a three-way tap was used as a connecting pathway for the diversion of blood from the external carotid artery distal to the origin of the lingual artery and the external jugular vein. A lingual arterial cannula was used to monitor pressure levels in the prepared segment of the common and external carotid arteries. To produce carotid body ischaemia, the common carotid artery was clamped just below the bifurcation and the perfusion pressure reduced to zero by appropriate adjustment of the tap in the polyethylene connecting tubing. The carotid body was artificially perfused for periods of between 0·5 and 2·5 min with saline equilibrated with air (P_{O_2}, 138–156 mmHg; pH, 7·38–7·43; temperature, 37–38 °C) from a syringe connected to the three-way tap. The prepared segment of artery was first cleared of blood and perfusion was then carried out using a perfusing pressure of between 120 and 160 mmHg.

Reductions of perfusion pressure and saline perfusions should be reliable tests of the ability of the electrodes to respond to flow changes within the glomus, as both procedures are known to cause not only changes in total flow through the organ (Daly *et al.* 1954; Joels & Neil, 1963) but also alterations of carotid chemosensory discharges (Landgren & Neil, 1951; Joels & Neil, 1963; McCloskey, 1975). In the present investigation, P_{t,O_2} and the rate of hydrogen clearance decreased at low perfusion pressures and showed opposite changes during saline perfusion. In the example shown in Fig. 1, total flow fell from 40 μl./min to zero and P_{t,O_2} decreased from 10 mmHg to zero during a reduction of the perfusion pressure (Fig. 1*A*). These changes were associated with an elevation of hydrogen concentration consequent on a reduced clearance of the gas. All values recovered on re-establishing perfusion pressure. When saline replaced blood perfusion, P_{t,O_2} and the rate of hydrogen clearance increased, and these changes were accompanied by an elevation of carotid body total flow (Fig. 1*B*).

Recording of chemosensory potentials. Fine filaments were peeled off the cut sinus nerve and placed on bipolar stainless steel electrodes in a pool of warm mineral oil. Potentials, obtained from single or a few active chemosensory units, were led to an amplifier and from thence to an oscilloscope and audiomonitor for preliminary examination. Activity was considered to be of chemoreceptor origin if it showed appropriate responses during alterations in the oxygen content of the inspired air. The output of the amplifier was also led to an electronic integrator for measurement of impulse frequency and from thence to the ink-writing recorder. Stimulus artifacts during electrical stimulation of the ipsilateral preganglionic cervical sympathetic trunk were gated out of the chemosensory recordings.

Stimulation of autonomic nerves supplying the carotid body. The preganglionic cervical sympathetic trunk was cut low in the neck, dissected free from the vagus, and placed on bipolar stainless steel

electrodes. The electrodes were either covered by a pledget soaked in warm mineral oil or immersed in a pool of the same liquid. Square-wave pulses (20 Hz, 300 μA, 1 msec), delivered from a constant current stimulator (Tekronix 2601), were sufficient during sympathetic stimulation to cause a maximal dilatation of the ipsilateral pupil. The same method was used electrically to stimulate the distal end of the cut sinus nerve and the efficacy of this stimulation was assessed by noting hyperaemic responses of carotid body flow (Neil & O'Regan, 1971).

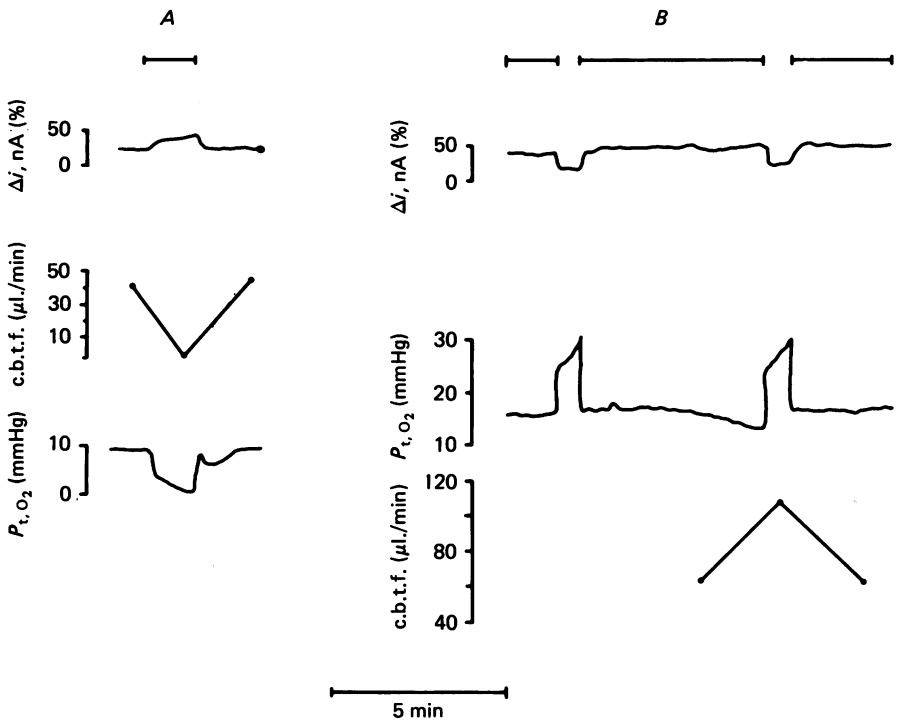

Fig. 1. Responses of intraglomeral electrodes monitoring local flow and tissue P_{O_2} during stoppage of flow and saline perfusions of the carotid body. *A*, responses during a reduced perfusion pressure. Period of stopped-flow indicated by horizontal bar above recordings. *B*, responses during saline perfusion. Spaces between horizontal bars indicate when saline replaced blood perfusion. Measurements shown are current as recorded by the hydrogen-sensitive electrode (Δi, nA), carotid body total flow (c.b.t.f.) and tissue P_{O_2} (P_{t,O_2}). Calibration of hydrogen-sensitive electrode here and in the subsequent Figure refers to a 50% change of current (in nA) from initial levels; an increase of current indicates a local flow decrease and *vice versa* (non-qualitative). (Consult text for further explanation.)

RESULTS

Responses of carotid body total flow, local flow and tissue P_{O_2} during stimulation of autonomic nerves

Stimulation of cut preganglionic cervical sympathetic trunks and cut sinus nerves caused changes, often marked, of carotid body total blood flow. It was most unusual, however, for these changes of total flow to be accompanied by any alterations of either P_{t,O_2} or the rate of hydrogen clearance measured by elastically suspended electrodes inserted into the glomus. Fig. 2 shows a typical example of responses observed in these experiments. During hypoxic hypoxia, total flow increased from 30 to 40 μl./min

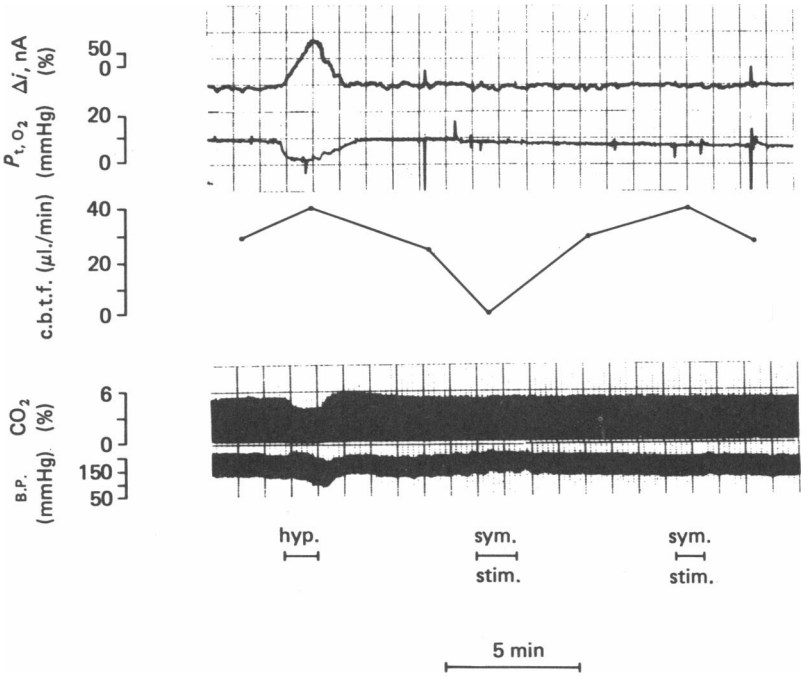

Fig. 2. Responses of carotid body total flow, local flow and tissue P_{O_2} during stimulation of autonomic nerves and during hypoxic hypoxia. Measurements shown from above downwards are hydrogen electrode current (Δi, nA), tissue P_{O_2} (P_{t,O_2}), carotid body total flow (c.b.t.f.), carbon dioxide concentration of gases sampled from the tracheal cannula (CO_2) and systemic arterial blood pressure (B.P.). Durations of various procedures are indicated by horizontal bars below the records: hyp., inspiring 5% oxygen in nitrogen; sym. stim., electrical stimulation of the distal end of the cat ipsilateral preganglionic cervical sympathetic trunk; s.n. stim., electrical stimulation of the distal end of the cut ipsilateral sinus nerve. Artifacts on electrode recordings are due to mechanical interference during weighing of carotid body venous outflow.

while both P_{t,O_2} and the rate of hydrogen clearance decreased. Hypoxic excitation of innervated arterial chemoreceptors reflexly increased ventilation sufficient to reduce end-tidal carbon dioxide concentration. There was a gradual fall of B.P. during hypoxia. The venous outflow from the carotid body decreased from 25 to 2 μl./min during electrical stimulation of the preganglionic sympathetic trunk, but this marked change of total flow was not associated with any alterations in the rate of hydrogen clearance, P_{t,O_2}, B.P. or end-tidal concentration of carbon dioxide. Stimulation of the distal end of the cut sinus nerve increased total flow from 30 to 40 μl./min but did not influence the other measurements.

Fig. 3 is a compilation of the results. The first readings refer to measurements obtained 60 sec before stimulation of the nerves and represent steady-state values. The second readings are those values recorded 60 sec after the onset of nerve stimulation indicated by the arrows. For technical reasons it was not possible in a small number of experiments to measure all values simultaneously. Sympathetic stimulation always reduced the total blood flow of the carotid body, although the magnitude of this effect varied considerably between experiments (Fig. 3*A*). Except in two cats, these changes of blood flow were unaccompanied by any modifications

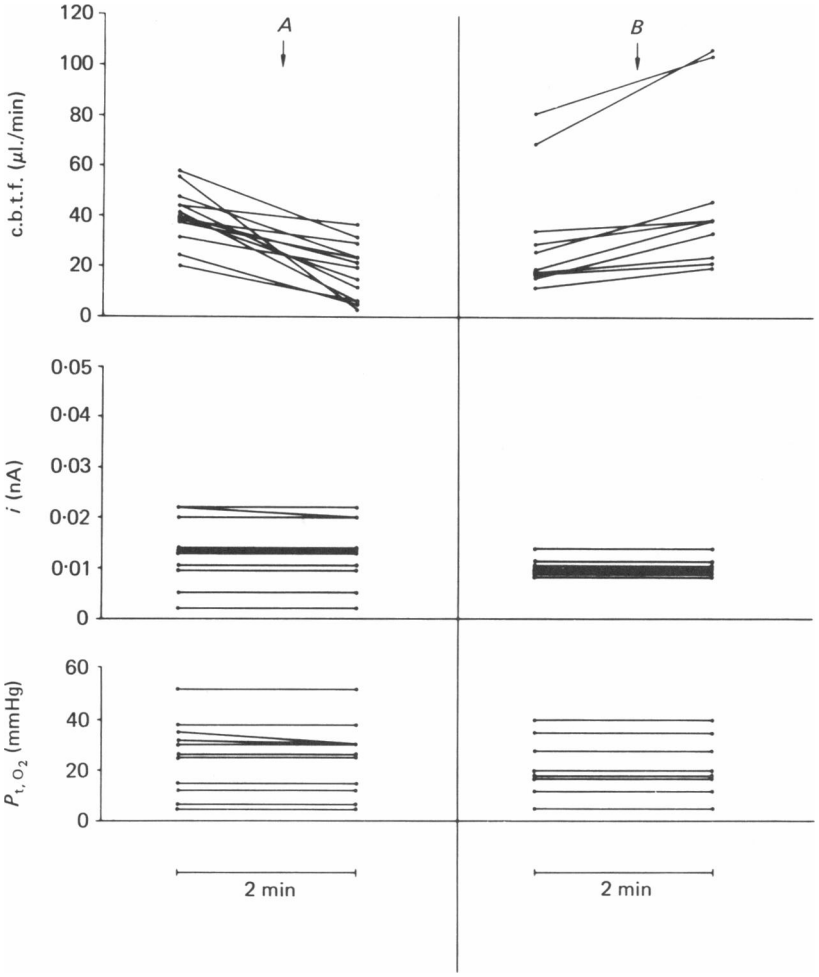

Fig. 3. Effects of autonomic nerve stimulation on carotid body total flow (c.b.t.f.), local flow and tissue P_{O_2} (P_{t,O_2}) in spontaneously breathing anaesthetized cats. *A*, effects during preganglionic sympathetic stimulation ($n = 13$). *B*, effects during sinus nerve stimulation ($n = 11$). First readings refer to measurements obtained 60 sec before stimulations (indicated by the arrows); second readings were recorded 60 sec after the onset of stimulations. *i* (nA), hydrogen electrode current.

of either P_{t,O_2} or local flow. In one cat, sympathetic stimulation increased the rate of hydrogen clearance while in another cat P_{t,O_2} decreased by approximately 4 mmHg during stimulation. Following administration of the α-adrenoceptor antagonist, phentolamine (Regitin, Ciba, 0·3–0·5 mg I.C.) in five cats, sympathetic stimulation no longer reduced total blood flow. Stimulation of the distal end of the sinus nerve increased total flow although to a variable extent (Fig. 3*B*) but did not affect either P_{t,O_2} or local flow in any experiment in which these measurements were carried out.

Effects of sympathetic stimulation on tissue P_{O_2} recorded at varying depths from the surface of the glomus

The wide scatter of P_{t,O_2} values (5–50 mmHg) recorded by elastically suspended electrodes (Fig. 3) may have arisen from different placements of the electrode tips within the glomus (Acker *et al.* 1971). In four cats a systematic study of the effects of sympathetic stimulation on P_{t,O_2} recorded at varying depths from the surface of

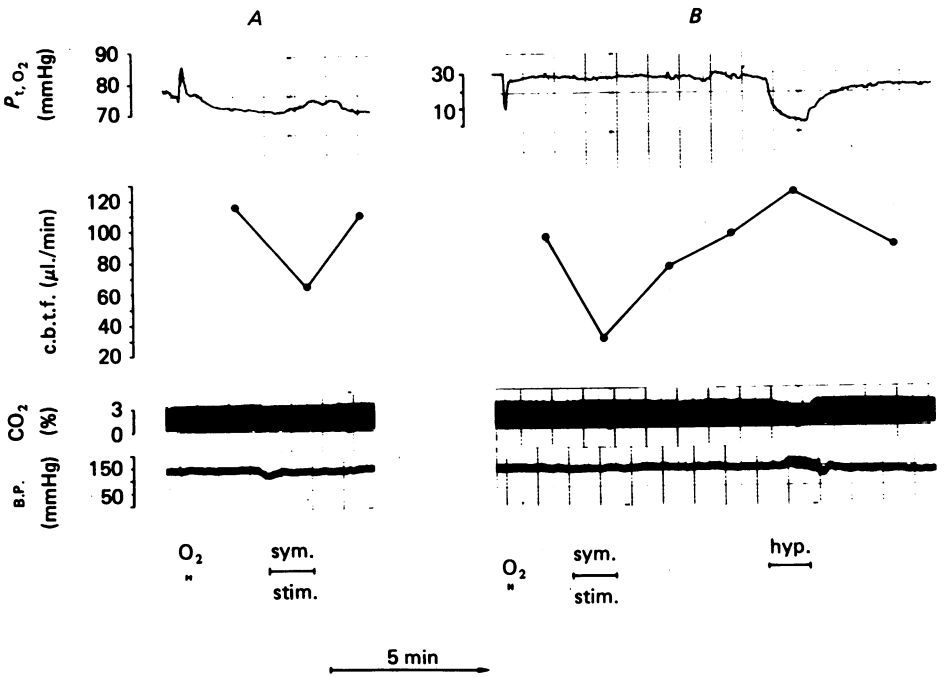

Fig. 4. Effects of sympathetic stimulation on tissue P_{O_2} recorded at different depths from the surface of the carotid body. *A*, electrode tip in superficial location. *B*, electrode tip 400 μm within carotid body. P_{t,O_2}, c.b.t.f., CO_2, B.P., hyp. and sym. stim. have same meanings as in Fig. 2. Durations of different procedures are indicated by horizontal bars below the records. O_2, blowing oxygen over surface of the carotid body. (Consult text for further explanation.)

the glomus was carried out. Fig. 4 shows a typical example of the results obtained. In superficial locations, P_{t,O_2} values ranged between 70 and 90 mmHg (Fig. 4*A*). Blowing oxygen over the surface of the glomus was usually associated with an initial short-lasting reduction of current output from the electrodes which probably arose from the cooling effects of the passage of gas on the extraglomeral part of the electrode or its electrical connexions. Thereafter, P_{t,O_2} rose steeply due to diffusion of oxygen inwards from the surface. A rapid recovery ensued on cessation of exposure to external oxygen. In these locations stimulation of the preganglionic sympathetic trunk caused an accentuation of P_{t,O_2} of between 5 and 10 mmHg, but this effect took some time (30–50 sec) to manifest itself. On cessation of stimulation P_{t,O_2} remained elevated for periods of between 30 and 120 sec before gradually recovering to prestimulation values (Fig. 4*A*). These changes of P_{t,O_2} during sympathetic stimulation occurred in the presence of reductions, sometimes considerable, of the total flow through the carotid body.

In deeper locations (Fig. 4*B*), with the electrode tips located at depths between 100 and 600 μm from the surface of the glomus, P_{t,O_2} values were lower (10–50 mmHg). An initial reduction of current output from the electrode occurred on blowing oxygen over the surface of the organ but there was no subsequent elevation of P_{t,O_2}. In deeper locations, P_{t,O_2} was unaffected by stimulations of the preganglionic sympathetic trunk adequate to cause marked reductions in carotid body total blood flow (Fig. 4*B*). Hypoxic hypoxia caused reductions of P_{t,O_2}, decreases of end-tidal carbon dioxide concentration and elevations of total flow (Fig. 4*B*). Systemic arterial B.P. showed a slight increase during hypoxia but was unaffected by sympathetic stimulation. Thus, the responses recorded from deeper locations in these experiments were closely similar to those obtained in investigations where elastically suspended electrodes were used to monitor P_{t,O_2} levels within the glomus (Figs. 2 and 3).

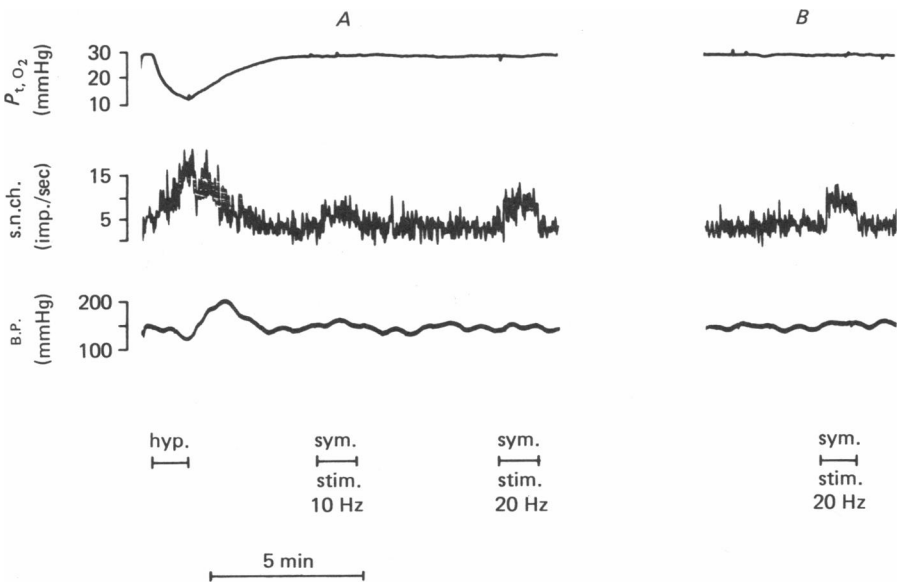

Fig. 5. Effects of sympathetic stimulation and hypoxic hypoxia on carotid body tissue P_{O_2} and sinus nerve chemosensory activity in an artificially ventilated anaesthetized cat. Recordings in *B* were obtained 20 min after an I.C. injection of phentolamine (0·3 mg). Records shown from above downwards are P_{t,O_2}, chemosensory impulse (imp.) frequency as obtained by a ratemeter (s.n.ch.) and B.P. Durations of different procedures are indicated by horizontal bars below the record. P_{t,O_2}, B.P., hyp. and sym. stim. have same meanings as in Fig. 2. Stimulus artifacts were gated out of the chemosensory recordings.

Responses of sinus nerve chemosensory discharges and carotid body tissue P_{O_2} during preganglionic sympathetic stimulation

In four cats electrical stimulation of the distal ends of preganglionic cervical sympathetic trunks increased the frequency of chemosensory potentials recorded from fine filaments of ipsilateral sinus nerves. Except in one experiment, however, these alterations of chemosensory discharges occurred in the presence of an unchanged P_{t,O_2} recorded from within the glomus by means of elastically suspended electrodes. The excitatory effects of sympathetic stimulation on chemosensory discharges which occurred without changes of P_{t,O_2} were still elicited after administration of phentolamine (0·3–0·5 mg I.C.). Fig. 5 shows an example of these responses. During artificial

ventilation of the cat with 5% oxygen in nitrogen, P_{t,O_2} fell from 30 to 12 mmHg and the frequency of chemosensory potentials as measured by the ratemeter increased fourfold. These changes were accompanied by a fall of B.P. On re-ventilation with air, both P_{t,O_2} and chemosensory discharges gradually recovered to prehypoxic values, as did the level of B.P. after an accentuation in the period immediately following the hypoxic episode. Electrical stimulation of the preganglionic trunk at 10 Hz caused a small but definite increase of chemosensory discharges, an effect which became more marked on increasing the frequency of stimulation to 20 Hz. Sympathetic stimulation did not affect P_{t,O_2} (Fig. 5*A*) and still caused an increase of chemosensory activity after an I.C. injection of 0·3 mg phentolamine (Fig. 5*B*).

In one cat sympathetic stimulation doubled the discharge rate of chemosensory potentials and this change was associated with a decrease of P_{t,O_2} of 5 mmHg. Both effects were no longer elicited after administration of phentolamine (0·3 mg I.C.). This animal had a haematocrit of 18 and a B.P. of 80 mmHg which could have influenced this finding. However, we were unable to reproduce these effects of sympathetic stimulation in two animals rendered anaemic and/or hypotensive.

DISCUSSION

The most outstanding, if unexpected, finding in this investigation was that stimulation of autonomic nerves supplying the carotid body caused changes, often considerable, of total blood flow through the organ yet had little influence upon either tissue P_{O_2} or local flow recorded by electrodes whose tips were located in deep positions within the glomus.

Intraglomeral electrodes did respond, however, to flow changes induced by reducing perfusion pressures or by perfusing the carotid body with saline solutions. Apart from the increases of P_{t,O_2} during saline perfusions, the electrode responses are readily explained. These increases of P_{t,O_2} could have arisen from an enhanced delivery of oxygen to or a reduced demand for oxygen by respiring tissues in the glomus. Marked reductions of oxygen usage by the carotid body do occur during cell-free perfusions of the organ (O'Regan, 1979*a*) but such reductions are not a feature during periods of perfusion as short as those carried out in the present investigation. It is likely, therefore, that the elevated P_{t,O_2} during saline perfusions resulted from an enhanced delivery of oxygen. Because the oxygen content of saline solution is considerably less than arterial blood, this increased oxygen delivery must have arisen from a marked increase of flow in the vicinity of the P_{O_2} electrode, presumably in the capillary circulation of the specific tissue. To give the changes of P_{t,O_2} observed, this flow must have increased to a much greater extent than would be expected from the elevations of total blood flow in the carotid body, and as such indicates that, during saline perfusions, flow is distributed in favour of the capillary bed of the specific tissue. This circumstance could not be verified in the present investigation owing to the non-quantitative measurements given by the electrode monitoring local flow. However, marked changes of flow and, presumably, pressure in the capillary vessels of the glomus, could be an important factor contributing to the declines of both oxygen usage by and chemosensory responsiveness of the carotid body during cell-free perfusions of the organ (Joels & Neil, 1968; Whalen & Nair, 1977; O'Regan, 1979*a*, *b*). Histological studies have shown that cellular damage occurs

during prolonged perfusion of the glomus with blood having haematocrit values less than 15 (Seidl, Heinrich, Schäfer & Acker, 1978).

Tissue P_{O_2} values recorded by electrodes whose tips lay just beneath the surface of the carotid body were high (70–90 mmHg) and increased further on blowing oxygen over the surface of the organ. The responses during exposure to external oxygen indicate the likelihood that the electrode tips in these circumstances were located not within the specific tissue of the carotid body but rather in the surrounding connective tissue capsule (Weigelt *et al.* 1976). The elevations of P_{t,O_2} recorded from superficial locations during sympathetic stimulation are difficult to explain. It is possible that sympathetic stimulation caused stagnation of blood in the capillaries of the superficial tissues and that the P_{O_2} of the stagnant blood increased due to an inward diffusion of oxygen from the atmosphere; the increased P_{O_2} of the blood then affected the surrounding tissues. With electrode tips located deeper within the carotid body, P_{t,O_2} values were lower (10–50 mmHg), did not increase on exposure to external oxygen and were unaffected by sympathetic stimulation. From the range of P_{t,O_2} recorded from these deep locations and the lack of response to external oxygen it is likely that the measurements were obtained from the specific tissue of the glomus (Weigelt *et al.* 1976).

Alterations of carotid body total flow during autonomic nerve stimulation unaccompanied by any changes of P_{t,O_2} or local flow recorded from deep locations in the glomus indicate that the major control by these nerves is exerted on vessels other than those regulating the flow through the capillary network of the specific tissue. An obvious candidate for such control is the arteriovenous anastomoses which are a feature of the vascular architecture of the carotid body (Goormaghtigh & Pannier, 1939; de Castro, 1940; Schäfer, Seidl, Acker, Keller & Lübbers, 1973). It is also possible that some of the capillaries of the specific tissue act as thoroughfare or preferential channels as in other tissues (Chambers & Zweifach, 1944). The effects of autonomic nerve stimulation found in the present investigation resemble the influences exerted by changes of B.P. on carotid body blood flow. Under steady-state conditions, changes in the mean values of B.P. between 60 and 160 mmHg cause alterations of carotid body total flow (Daly *et al.* 1954; Purves, 1970*a*) but do not affect capillary flow; chemosensory discharges and local flow remain unchanged despite changes in perfusion pressure (Biscoe, Bradley & Purves, 1970; Acker *et al.* 1977).

The enormous blood supply which the carotid body receives in relation to its weight (20 ml./g per min) is so far in excess of that needed to satisfy the oxygen needs of the organ that a trivial arteriovenous oxygen difference exists (Daly *et al.* 1954; Purves, 1970*a*). The P_{O_2} of carotid body venous blood considerably exceeds P_{O_2} values recorded by intraglomeral electrodes (Acker *et al.* 1971; Whalen, Savoca & Nair, 1973). In the absence of a counter-current exchange system for oxygen between carotid body arterial and venous vessels this discrepancy between venous and tissue P_{O_2} indicates that a considerable proportion of the venous outflow is derived from shunted blood. High values for shunt flow receive considerable confirmation in the present investigation. In three experiments sympathetic stimulation reduced carotid body total flow to values of 5 μl./min or less without changing either P_{t,O_2} or local flow recorded from deep glomeral locations.

The findings that local flow and P_{t,O_2} remain unchanged with deep electrode placements in the glomus during autonomic nerve stimulation provide cogent evidence in favour of a non-vascular mechanism of control of these nerves. The excitatory effects on chemosensory activity mediated by sympathetic stimulation which were elicited in the absence of any changes of P_{t,O_2} and which resisted doses of phentolamine sufficient in themselves to abolish the alterations of carotid body total flow during sympathetic activation resemble the type I responses reported in another paper (O'Regan, 1981). Possible non-vascular mechanisms which could be involved in the generation of these responses are discussed in that paper.

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