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THE EFFECT OF CAROTID BODY DENERVATION UPON THE RESPIRATORY RESPONSE TO HYPOXIA AND HYPERCAPNIA IN THE DUCK

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SUMMARY

1. Respiratory responses to altered P_{a,O_2} at constant P_{a,CO_2} and altered P_{a,CO_2} at constant P_{a,O_2} were measured in fourteen unanaesthetized ducks 5–9 weeks old.

2. All the ducks responded to the inhalation of a few breaths of 100 % O_2 with a fall in $\dot{V}_E$ of between 11 and 17 % of control, and to the reduction in P_{a,O_2} from control levels (93–101 mm Hg) to 38–47 mm Hg with an average increase in $\dot{V}_E$ of 190 % of control which was potentiated by raising the level of CO_2.

3. Ventilation approximately doubled when P_{a,CO_2} was raised to 55 mm Hg, the greatest sensitivity to changes in P_{a,CO_2} being over the range 40–45 mm Hg.

4. Carotid body denervation was carried out in nine ducks and the respiratory responses were modified. The fall in $\dot{V}_E$ with inhalation of 100 % O_2 was abolished in all ducks and the rise in $\dot{V}_E$ with hypoxia was abolished in six. The increase in $\dot{V}_E$ as P_{a,CO_2} was altered in steps was unaffected but the rate at which $\dot{V}_E$ increased in response to 4 % CO_2 was markedly reduced.

5. It is concluded that the chemoreceptor regulation of respiration in ducks is similar to that observed in non-diving animals.

INTRODUCTION

The reflex control of respiration in birds has been studied much less thoroughly than in mammals. Paul Bert (1870) was the first to show that section of the vagi in birds caused respiratory slowing and there seems to be good evidence that the Hering–Breuer reflex is present (Hiestand &

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Randall, 1941; Sina, 1958) though there is some doubt as to its importance (Fedde, Burger & Kitchell, 1961). Chemoreflex activity has never been studied.

Experiments in which the effect of chemoreceptor activity upon the cardiovascular response to immersion of the head in water was being studied in ducks (Jones & Purves, 1970) provided an opportunity to obtain further evidence as to the role of the chemoreceptors. We have therefore measured the respiratory response in the unanaesthetized duck to alterations in blood gas tensions and the modification of these responses after denervation of the carotid bodies.

Some of the results have been presented to the Physiological Society (Jones & Purves, 1969).

METHODS

Tidal volume, respiratory frequency, minute ventilation and heart beat frequency were measured in fourteen unanaesthetized Khaki Campbell and White Aylesbury ducks 5–9 weeks old and weighing 0·75–1·4 kg. The ducks were lightly restrained and an endotracheal cannula made of soft vinyl tubing of the appropriate size, 5–7 mm outside diameter, 1 mm wall thickness, was inserted into the glottis and advanced some 3–4 cm into the trachea. The majority of ducks tolerated this procedure. In those which did not, the trachea was exposed high in the neck under local anaesthesia and was opened and cannulated. The tracheal tube was then attached to a Fleisch pneumotachograph, size OO, air flow was measured with a Statham PM5 differential pressure transducer and the flow signal integrated to give tidal volume. Tidal CO_2 concentration was measured continuously by sampling from a needle inserted into the tracheal cannula at a rate of 25–30 ml./min, or up to 10% of $\dot{V}_E$ (l/kg body weight.min) under control conditions, using a Beckman LB 1 infra red analyser which was calibrated at intervals with CO_2 in air mixtures of accurately known composition. A wing artery was cannulated and as required 0·5 ml. blood samples were removed for immediate analysis. Blood gas tensions were measured at 38° C with appropriate Radiometer electrodes which were frequently calibrated using O_2 in N_2 and CO_2 in air mixtures. Arterial pH was measured with an E.I.L. capillary electrode and Vibron electrometer which was calibrated with standard phosphate buffers.

In order to change the composition of the inspired gas mixture a T-piece was attached to the pneumotachograph and compressed humidified air was passed through its cross arms at a flow rate of between 2 and $2\frac{1}{2}$ l./min. When respiration was stable as judged from the record of tidal volume and CO_2, a series of different O_2 in N_2 or CO_2 in air mixtures was substituted in random order at the same flow rate. After each gas change approximately 7 min was allowed for respiration to become stable at a new level; tidal volume and respiratory frequency were then recorded for 1 min and an arterial sample taken for immediate analysis: two or three such runs and analyses were performed to confirm that a new steady state had been established following a gas change. No attempt was made to control arterial pH. When either P_{a,O_2} or P_{a,CO_2} was altered, the other was held constant at control levels by adjusting the inspired gas mixtures.

Carotid body denervation was carried out as described in the accompanying paper (Jones & Purves, 1970). Following denervation, further respiratory responses were obtained as outlined above after an interval of between 3 days and 6 weeks.

RESULTS

In preliminary experiments, the effect of adding a T-piece to the pneumotachograph and of passing compressed air at different rates of flow through the cross-arms was tested. Fig. 1 (upper records) shows a typical sequence. In *A*, the pneumotachograph only had been added to the endotracheal tube. In *B*, the T-piece had been added and the flow pattern was clearly altered; respiration became irregular and blood gas

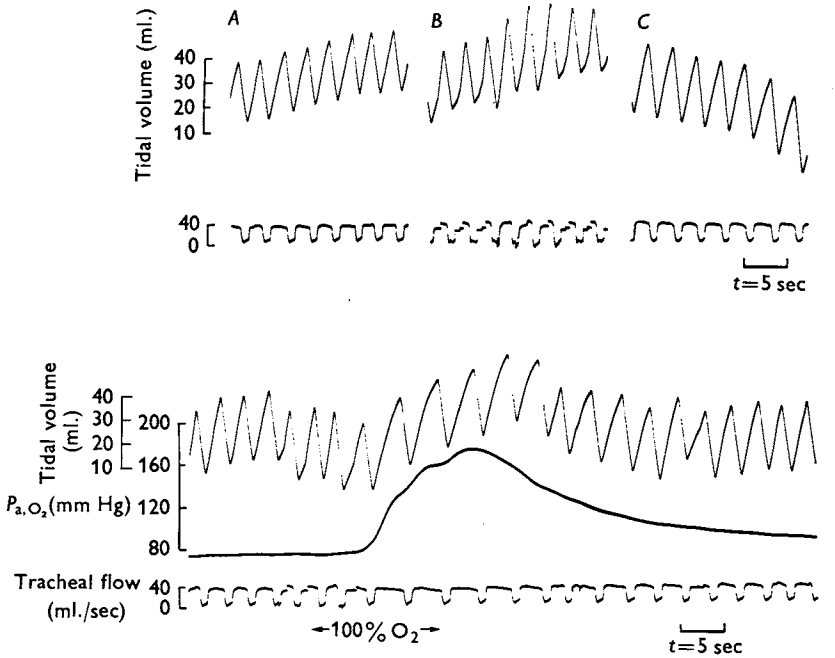

Fig. 1. Upper trace: a series of records in each, above, tidal volume, below, tracheal air flow (ml./sec), taken with *A*, pneumotachograph only attached to endotracheal tube, *B*, a T-piece added to the pneumotachograph and *C*, when compressed, humidified air at a flow rate of 2·5 l./min was passed through the cross-arms of the T-piece. Lower trace: from above down, tidal volume, brachiocephalic arterial P_{O_2} and tracheal air flow. During the period indicated by the extent of the arrows, the duck inhaled 100 % O_2. In all records, the duck was unanaesthetized and lightly restrained. t = 5 sec.

tensions differed from control. When compressed and humidified air was passed through the T-piece (*C*), the flow pattern, tidal volume and blood gas tensions were not obviously different from control.

Artifacts may have been introduced into the respiratory pattern (*a*) by abrupt changes in air flow through the T-piece, or (*b*) by alterations in the CO_2 content of the inspired gas mixture since it has been shown that

the addition of CO_2 causes a fall in ventilation in the duck (Orr & Watson, 1913). We confirmed that changes in airflow of up to approximately 200 ml./min were without effect upon $\dot{V}_E$: larger changes caused a fall in $\dot{V}_E$ and occasionally apnoea. We were unable to confirm that the addition of CO_2 up to 5 % to the inspired gas mixture caused any initial fall in $\dot{V}_E$ provided that the volume of airflow was unchanged. The changes in $\dot{V}_E$ were those illustrated in Fig. 5. Above this level of CO_2, however, ventilation fell transiently for 0·5–1 min and thereafter rose to levels appropriate for the end-tidal and arterial P_{CO_2}.

Responses to changes in P_{a,O_2}

(*a*) 100 % O_2. The respiratory response to 4–6 breaths of 100 % O_2 was tested on thirteen occasions in four ducks which were unanaesthetized and with all nerves intact. On all occasions, $\dot{V}_E$ fell, both tidal volume and frequency being affected. An example of the response is shown in Fig. 1 (lower record). In all these animals an arteriovenous loop, which contained an O_2 electrode, had been inserted under local anaesthesia. The tip of the arterial cannula was in the brachiocephalic artery. The electrode gave an indication of the time of arrival of arterial blood having a changed P_{a,O_2} at the origin of the common carotid artery. However, in view of the time taken for blood to reach the electrode and the small but finite lag of the electrode (0·05 sec), the signal may have lagged behind the stimulus to the carotid bodies by up to 1 sec. If this correction is made, it is clear from the Figure that ventilation started to fall with the first breath after P_{a,O_2} started to rise and that as P_{a,O_2} fell, $\dot{V}_E$ slowly returned to control levels. In the group of thirteen observations, $\dot{V}_E$ fell by between 11 and 17 % of control, a fall between two or three times greater than any variation of respiration seen in the control period.

(*b*) *Step changes in* P_{a,O_2}. Steady-state changes in ventilation in response to alterations of P_{a,O_2} at constant P_{a,CO_2} were studied in nine ducks. Fig. 2 illustrates such a response in a duck in which P_{a,CO_2} was maintained constant at 38 mm Hg. P_{a,O_2} was altered in steps in the order indicated by the Figures. In this experiment as in the others, hypoxia caused an increase in $\dot{V}_E$ which was principally caused by a rise in V_T. The increase in f was +63 % of control and was unusually large. In five other ducks, f increased by < 30 % of control and in three ducks, f actually fell at low P_{a,O_2}.

The changes in $\dot{V}_E$, V_T and f which occurred when P_{a,O_2} was reduced from control levels to 38–47 mm Hg have been summarized for this group of experiments in Table 1. The values for $\dot{V}_E$ in this and succeeding tables take into account the weight of the ducks which at 5–9 weeks (control period) varied between 0·75 and 1·4 kg and have been expressed

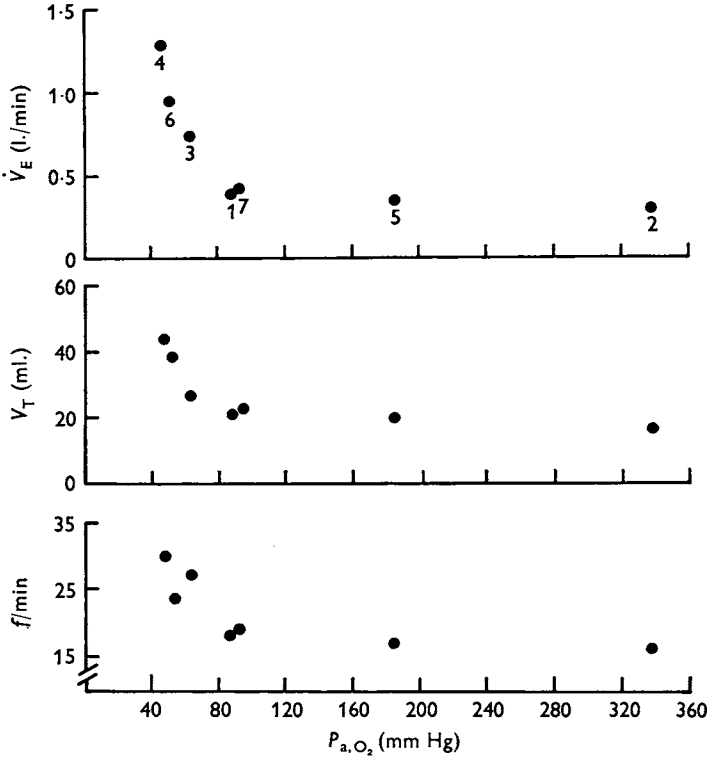

Fig. 2. The relation between minute volume of ventilation ($\dot{V}_E$) upper panel, tidal volume (V_T) middle panel and frequency of breathing (f) and $P_{a,\,o_2}$. Unanaesthetized duck, 8 weeks old. $P_{a,\,co_2}$ maintained at 38 mm Hg. The figures beside values for $\dot{V}_E$ refer to the order in which the readings were made, readings 1 and 7 being control with the duck breathing air.

TABLE 1. Respiratory responses to alterations of $P_{a,\,o_2}$. Twelve tests in nine intact unanaesthetized ducks

$P_{a,\,o_2}$ (mm Hg)		$\dot{V}_E$ (l./kg body wt. min)	V_T (ml.)	f (breaths/min)
93–101	Range	0·29–0·55	17–24	16–22
	Mean	0·403	20	18·8
	S.D. ±	0·024	2·06	4·3
38–47	Range	0·72–1·74	39–58	14–24
	Mean	1·14	45·8	19·8
	S.D. ±	0·036	6·9	3·3
> 300	Range	0·29–0·44	15–21	11–21
	Mean	0·343	17·6	16·6
	S.D. ±	0·037	1·7	3·7

as l./kg body wt.min. Post-operatively, tests were carried out on ducks 10–16 weeks old whose weight varied between 1·25 and 2·6 kg. Over this age range, no change was observed in the ratio $\dot{V}_E$/kg body wt. The results in Table 1 confirm that with hypoxia of this degree, $\dot{V}_E$ approximately trebled and that the mean value for f did not significantly change. Hyperoxia was associated with a small reduction in both V_T and f.

(*c*) *Effect of raised CO_2 upon the response to hypoxia.* The effect of raising P_{a,CO_2} and maintaining it at between 7 and 11 mm Hg above control while the P_{a,O_2} was reduced was tested in four ducks and the

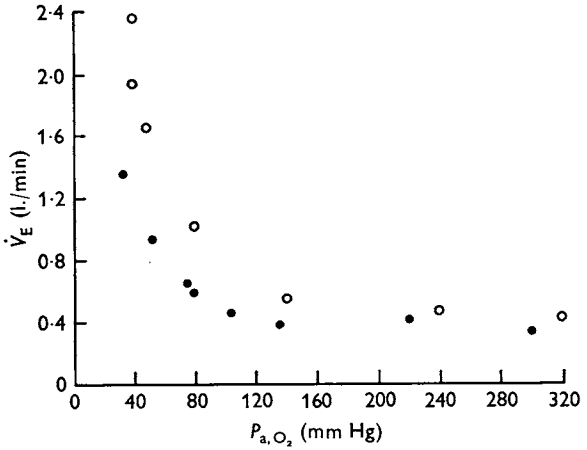

Fig. 3. The effect of alterations of P_{a,O_2} upon $\dot{V}_E$ in an unanaesthetized duck. Filled circles, P_{a,CO_2} maintained at 41 mm Hg; open circles P_{a,CO_2} 52 mm Hg. The reading taken at P_{a,CO_2} 41 mm Hg and P_{a,O_2} 104 mm Hg is control with the duck breathing air.

response for one duck is shown in Fig. 3. This shows first that when CO_2 was raised, $\dot{V}_E$ increased within the physiological range of P_{a,O_2}. As P_{a,O_2} was reduced below *ca.* 60 mm Hg, the increase in $\dot{V}_E$ became more marked. $\dot{V}_E$ at P_{a,O_2} 40 mm Hg was greater than would have been predicted from the sum of the effects of the hypercapnic and hypoxic stimuli. A similar response was seen in the other three ducks and the results have been summarized in Table 2. This confirms that the absolute or percent increase in $\dot{V}_E$ above control at low P_{a,O_2} was significantly higher at high P_{a,CO_2}. These results indicate that in the duck, as in the mammal, CO_2 potentiates the respiratory response to hypoxia.

(*d*) *Heart frequency and hypoxia.* The heart rate was also measured in four ducks, ten tests. When the ducks breathed air, heart frequency varied between 135 and 220 beats/min. When P_{a,O_2} was reduced to 37–45 mm Hg the heart rate increased in one duck (four tests) by an average

of +7% of control. In one duck (two tests), no change occurred and in two ducks (two tests in each), the heart frequency fell by an average of 9 and 14% of control respectively.

Responses to changes in P_{a,CO_2}

(*a*) *Respiratory responses.* The respiratory responses to alterations in P_{a,CO_2} at constant P_{a,O_2} were tested in seven control and in three sham-operated ducks, that is, ducks whose chests had been opened in the usual way but without denervation of the carotid bodies. There was no

TABLE 2. The effect of altering P_{a,CO_2} upon the respiratory response to hypoxia in four unanaesthetized ducks

Duck	P_{a,CO_2} (mm Hg)	$\dot{V}_E$ control (l./kg body wt. min)	$\dot{V}_E$ (P_{a,O_2} 35–40 mm Hg) (l./kg body wt. min)	$\Delta\dot{V}_E$ (l./kg body wt. min)	Change (% control)
1	39	0·37	0·80	0·43	+116
0·9 kg	47	0·65	1·74	1·09	+167
2	41	0·47	1·43	0·96	+204
1·0 kg	49	0·54	1·90	1·35	+245
3	40	0·47	1·52	1·05	+223
1·2 kg	49	0·62	2·25	1·63	+262
4	40	0·51	1·28	0·77	+150
1·1 kg	47	0·77	2·04	1·27	+164

Comparison of the mean increase in $\dot{V}_E$ with hypoxia at control and at high P_{a,CO_2} ($P < 0{\cdot}01$).

consistent difference in the responses of these groups and the results have been considered together. In contrast to the respiratory response to P_{a,O_2}, there was great variation in the pattern of response to CO_2. There was not only the expected quantitative differences between birds but there was considerable variation in the shape of the CO_2 response curves. In Fig. 4, the response typical of that seen in five ducks is shown. It consists of a marked increase in $\dot{V}_E$ with either little or no change in P_{a,CO_2}: indeed in two experiments, although $\dot{V}_E$ approximately doubled, there was a small reduction in P_{a,CO_2}. This is probably of limited physiological significance since these differences in P_{a,CO_2} were within the error of measurement. As P_{a,CO_2} was further raised, however, the rate at which $\dot{V}_E$ increased declined. Fig. 4 also shows a feature common to all ducks tested, namely that the rise in $\dot{V}_E$ was principally due to an increase in V_T and that, as P_{a,CO_2} was raised, f fell although, as is shown in Fig. 4, this fall was irregular.

In the remaining ducks, the response consisted of a curve which was less obviously concave to the P_{a,CO_2} axis or was virtually linear over the

range 38–55 mm Hg P_{a,CO_2}. Above this level and as f started to fall, the increase in $\dot{V}_E$ became much less pronounced. In no duck did we observe a curve which was convex to the P_{a,CO_2} axis.

Since the further changes in $\dot{V}_E$ were small at $P_{a,CO_2} > 55$ mm Hg, the respiratory responses for the group have been summarized by comparing

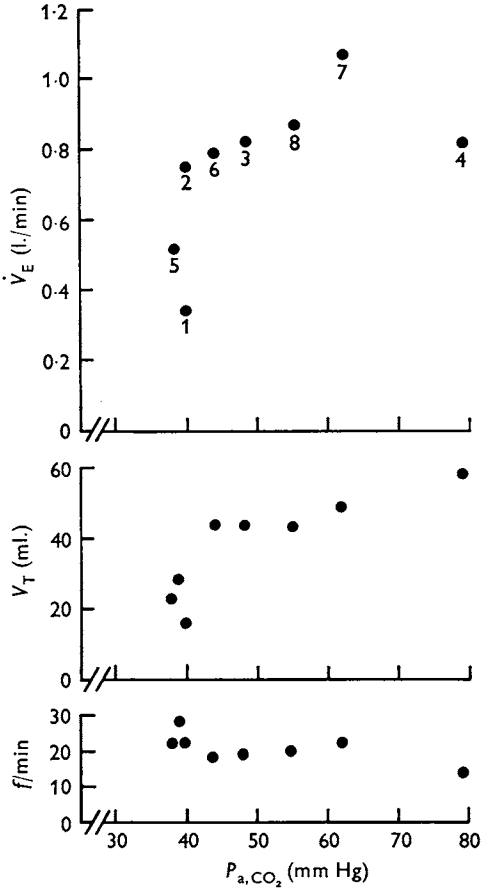

Fig. 4. The relation between, from above down, minute volume of ventilation ($\dot{V}_E$, l./min), tidal volume (V_T, ml.) and frequency of respiration (f, breaths/min) and P_{a,CO_2} (mm Hg). Duck unanaesthetized, P_{a,O_2} 93–95 mm Hg. Reading 1 was control with the duck breathing air.

the values for $\dot{V}_E$ and its components at resting and at P_{a,CO_2} levels of 55 mm Hg or more (Table 3). This confirms that high CO_2 caused an approximate trebling of V_T and a significant reduction in f ($P < 0{\cdot}05$). The changes in $\dot{V}_E$ were therefore less striking than those seen with hypoxia (P_{a,O_2} 38–45 mm Hg).

(*b*) *The rate of change in* $\dot{V}_E$ *in response to* CO_2. Six ducks were given between 3 and 4 % CO_2 in air to inhale for up to 5 min. The compressed air was abruptly replaced by the CO_2 mixture and the changes in $\dot{V}_E$ and its components were measured over 10 sec periods. A response typical of those seen in all the ducks is shown in Fig. 5*A*. The CO_2 mixture replaced air at $t = 0$ and a period of 5 sec elapsed before V_T started

TABLE 3. Respiratory responses to alterations of $P_{a,\,CO_2}$. Seven control and three sham-operated ducks

	$\dot{V}_E$ (l./kg body wt. min)	V_T (ml.)	f (breaths/min)
$P_{a,\,CO_2}$ 39–41 mm Hg			
Range	0·29–0·48	16–26	17–24
Mean	0·375	19·6	20·1
S.D. ±	0·07	3·3	2·65
$P_{a,\,CO_2}$ 55 mm Hg			
Range	0·45–1·46	50–72	9–17
Mean	0·841	60·1	13
S.D. ±	0·18	6·2	3·0

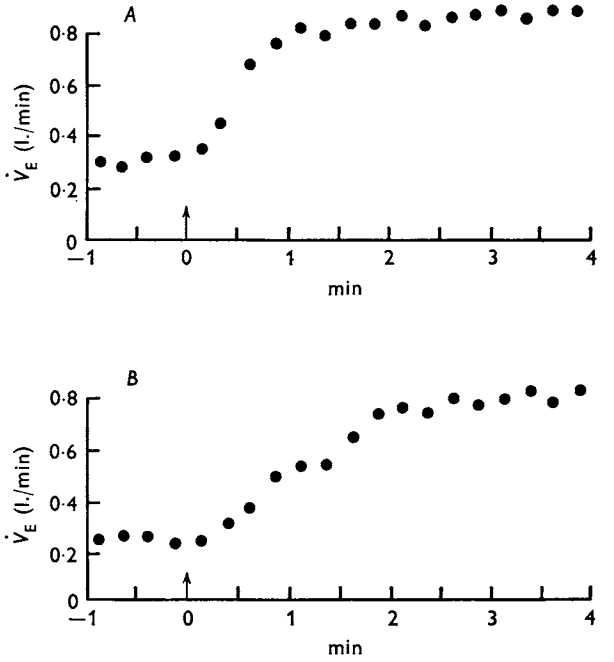

Fig. 5. The changes in respiration (expressed as $\dot{V}_E$, l./min) observed in an unanaesthetized duck 9 weeks old when 4 % CO_2 in air was given at $t = 0$. *A*, with all nerves intact; *B*, the same duck three weeks after the carotid bodies had been denervated.

to rise. Ninety per cent of the final level of $\dot{V}_E$ was achieved in 48 sec. In the group of six ducks, the period before $\dot{V}_E$ was observed to increase following administration of CO_2 varied between 4 and 7 sec and the range of 90 % response times was 40–65 sec.

(*c*) *Changes in heart frequency.* Heart frequency was measured continuously in eight ducks while P_{a,CO_2} was altered. With P_{a,CO_2} in the range 38–41 mm Hg, heart frequency was within the range 150–210 beats/min. As P_{a,CO_2} was raised, heart frequency fell in all ducks. Within the range 50–60 mm Hg P_{a,CO_2}, heart frequency had fallen to between 72 and 168 beats/min and in three ducks in which P_{a,CO_2} was raised to > 65 mm Hg, heart frequency fell to between 48 and 124 beats/min.

Effect of denervation of the carotid bodies

Denervation of the carotid bodies had no effect upon the level of $\dot{V}_E$ or $\dot{V}_E$/kg when these were measured under control conditions in the operated ducks and compared with values in sham-operated ducks of comparable age.

(*a*) *Upon the respiratory responses to changes in* P_{a,O_2}. The respiratory response to inhaling a few breaths of 100 % O_2 was elicited on fourteen occasions in seven ducks after denervation of the carotid bodies and in four of these a wing arteriovenous loop, with O_2 electrode included, was used. Arterial O_2 tension rose on each occasion to > 150 mm Hg but in no experiment was any fall in $\dot{V}_E$ observed which was greater than the variation seen in the control period.

The respiratory response to step changes in P_{a,O_2} was tested in nine ducks after denervation of the carotid bodies, P_{a,CO_2} being held constant within physiological limits, 38–42 mm Hg. A response typical of that seen in six ducks is shown in Fig. 6*A*. This shows that the increase in $\dot{V}_E$ seen before the operation was abolished, $\dot{V}_E$ varying by no more than 7 % of control (when the duck breathed air) over the range of P_{a,O_2} tested.

In the remaining three ducks, as P_{a,O_2} was reduced below 60 mm Hg $\dot{V}_E$ increased so that when P_{a,O_2} was within the range 35–45 mm Hg, it was respectively 35, 63, and 57 % above the level when the duck breathed air. Although this represents a significant response, the changes in $\dot{V}_E$ were substantially less than those seen in any duck before the operation. These birds were sacrificed after the experiments and a careful examination was made of the carotid body region on both sides. Although this was made difficult by the presence of resolving blood clot and fibrous tissue, no obvious intact branch of the nodose ganglion supplying the carotid body area could be seen under the dissecting microscope. The changes in heart frequency during a dive fell within the same range as those of

the whole group of ducks (Jones & Purves, 1970) after denervation of the carotid bodies.

(*b*) *Upon the respiratory responses to changes in* $P_{a,\,CO_2}$. The respiratory response to the inhalation of CO_2 over the range 37–75 mm Hg $P_{a,\,CO_2}$ was tested in eight ducks following denervation of the carotid bodies. The responses were variable but one, typical in most respects, is shown in Fig. 6*B*. This shows that, in contrast to the response seen before the

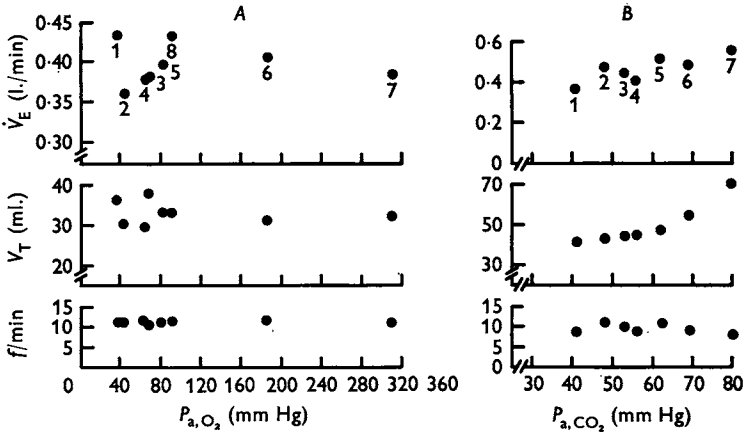

Fig. 6. The relation between, from above down, minute ventilation, tidal volume and frequency of breathing and in *A*, $P_{a,\,O_2}$, $P_{a,\,CO_2}$ being maintained at 39 mm Hg and in *B*, $P_{a,\,CO_2}$, $P_{a,\,O_2}$ being maintained at 95 mm Hg. The ducks were the same as those whose control responses were shown in Figs. 2 and 4 respectively. They were unanaesthetized and the carotid bodies had been denervated 2 and 3 weeks previously. Reading no. 8 in *A* and no. 1 in *B* are control with the duck breathing air.

operation, the increase in $\dot{V}_E$ with step changes in $P_{a,\,CO_2}$ was more nearly linear. In only one duck was the highly sensitive respiratory response shown in Fig. 4 seen. The level of $\dot{V}_E$ achieved at high CO_2 > 55 mm Hg $P_{a,\,CO_2}$ varied between + 85 and + 107 % of control when the duck breathed air. This was not significantly different from the response before denervation (t = 0·89, P > 0·5). Finally, the rate at which $\dot{V}_E$ increased in response to the abrupt administration of 4 % CO_2 in air was tested in six ducks after operation. A representative response is given in Fig. 5*B* and consists of a latent period of between 10 and 15 sec before $\dot{V}_E$ rose after CO_2 was administered. Thereafter the $\dot{V}_E$ increased at a steady rate reaching a final level which was not different from control (before the operation). This level was achieved approximately 120 sec after CO_2 was given. In the group as a whole, the initial latent period varied between 10 and 17 sec and 90 % of the final response was achieved after 120–195 sec.

In each duck these values were more than double those seen before operation.

DISCUSSION

The respiratory responses to hypoxia observed in the present series of experiments are in broad agreement with those reported by Orr & Watson (1913) and by Ray & Fedde (1969). Although in neither case was $\dot{V}_E$ quantitatively related to changes in P_{a,O_2}, it was observed that ventilation increased with hypoxia and that respiratory frequency was virtually unaffected. We have extended these observations to show that $\dot{V}_E$ falls in response to the inhalation of a few breaths of 100% O_2, that $\dot{V}_E$ increases sharply as P_{a,O_2} is reduced below *ca.* 65 mm Hg and that the respiratory responses to hypoxia are potentiated by CO_2. These changes are similar to those reported in mammals and which have been most fully documented in man: they also provide strong evidence that there is a tonic drive to respiration during normoxia (Cormack, Cunningham & Gee, 1958; Dejours, Labrousse, Raynaud & Teillac, 1957). $\dot{V}_E$ diminished by only a small amount when P_{a,O_2} was raised in steps to > 400 mm Hg and this may be due to the effects of more prolonged inhalation of high O_2, e.g. a shift in the CO_2 dissociation curve with a rise in tissue P_{CO_2} and a secondary increase in $\dot{V}_E$. The fact that the changes in $\dot{V}_E$ in response to high or low O_2 were abolished by denervation of the carotid bodies provides further evidence that these effects are mediated principally by this group of peripheral arterial chemoreceptors and also suggests that if other oxygen sensitive receptors do exist in the duck, their effect upon respiration must be small.

The respiratory response to inhaled CO_2 is more complex. Orr & Watson (1913) showed that the administration of CO_2 in air mixtures to the duck caused an early fall in ventilation or apnoea and they concluded that CO_2 inhibited respiration in the duck. Subsequent experiments have shown, however, that these results were almost certainly due to the non-specific stimulation of receptors in the nares, tongue and pharynx for similar responses were obtained when various acids or ammonia were applied locally. Furthermore, if CO_2 was introduced either by low tracheotomy (Johnston & Jukes, 1966; Ray & Fedde, 1969) or via the humeri (Dooley & Koppanyi, 1929; Hiestand & Randall, 1941), thus bypassing the mouth, respiration was invariably stimulated.

More recently, evidence for a further series of receptors has been provided (Peterson & Fedde, 1968). These workers have shown that under their experimental conditions, in which the bird is anaesthetized and the respiratory dead space abolished by a unidirectional flow of gas through the trachea and lungs and out of holes made in the air sacs, an abrupt

fall in inspired CO_2 is followed by a fall in ventilation with a latent period of approximately 0·5 sec. This latent period is unaffected by placing delay coils cephalad or caudad to the heart or by temporarily stopping blood flow in the pulmonary artery and veins. When the sensitive areas, which appear to be either in small bronchioles or lung tissue, are denervated by vagotomy low in the chest, the respiratory response to CO_2 is delayed but not abolished. These results do not define conclusively the physiological function of the CO_2 sensitive areas but they raise the possibility that receptors other than those in the carotid body initiate the respiratory response to CO_2.

The results of the present series of experiments indicate that, in the unanaesthetized duck, the respiratory response to inhaled CO_2 at constant P_{a,O_2} is different from that reported in man (Lloyd, Jukes & Cunningham, 1958) or in the dog (Mitchell, Bainton, Severinghaus & Edelist, 1964) in that the response curve tends to be concave to the CO_2 axis. Further there does not appear to be a range of reduced respiratory sensitivity to changes in CO_2 at or about resting levels (Neilsen & Smith, 1951). Since, in all the present experiments, the nares and pharynx were bypassed by the endotracheal tube, it is unlikely that non-specific receptors in this region were involved. The curves obtained in the present series also differ from those obtained by Johnston & Jukes (1966) and by Ray & Fedde (1969) in the hen. The difference may be attributed to the fact that in the latter series, the hens were anaesthetized with pentobarbitone sodium, 20 and 30 mg/kg respectively.

Although the steady-state respiratory response to step changes in P_{a,CO_2} appeared to be unaffected by carotid body denervation, the rate at which $\dot{V}_E$ increased in response to CO_2 was markedly reduced. This is similar to the response in the new-born lamb (Purves, 1966) and suggests that the peripheral arterial chemoreceptors may be more important in determining the response to small transient changes in P_{a,CO_2}. Further these results do not suggest that the receptors in the lung or bronchioles, proposed by Peterson & Fedde (1968), are of physiological importance in the unanaesthetized duck with a more orthodox type of ventilation, for they should have been unaffected by carotid body denervation and the latent period after administration of CO_2 and before $\dot{V}_E$ started to increase should therefore have been unchanged. Particular care was taken in the present investigation to confirm that vagal conduction was unimpaired post-operatively. It is more probable from a consideration of the lengthening of the latent period and reduction in the rate of rise of $\dot{V}_E$ after carotid body denervation, that the receptors sensitive to CO_2 are placed upstream, probably in the brain. Possibly, they may be similar

to the receptors in the medulla proposed by Mitchell, Loeschke, Massion & Severinghaus (1963) in the cat.

One final point emerges from the present study. We have shown that the chemoreceptor contribution to the respiratory response to hypoxia and probably to hypercapnia in the duck is not inferior to that which has been reported in various non-diving animals. It follows that in response to the asphyxia during a dive, chemoreceptor activity is likely to increase. In strictly terrestrial animals, the increase in the chemoreceptor drive to respiration could be regarded as a protection against excessive breath-holding: in the diving animal, this could be an embarrassment. The question therefore arises: is the reflex inhibition of respiration during a dive so powerful that the chemoreceptor discharge is ignored? Alternatively, is the chemoreceptor sensitivity to changes in blood gas tensions altered in some fashion during a dive? It is known that chemoreceptor sensitivity to changes in blood gas tensions can be altered either by activity in the cervical sympathetic (Eyzaguirre & Lewin, 1961; Biscoe & Purves, 1967) or by activity in efferent fibres to the carotid body running in the sinus nerve of cats (Neil & O'Regan, 1969). It would be of interest to know whether such mechanisms operate in the diving duck or other diving animals.

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