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THE INFLUENCE OF BODY TEMPERATURE ON THE VENTILATORY RESPONSE TO CO_2 IN ANAESTHETIZED RATS

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Abstract. The breathing frequency, tidal volume and partial pressure of CO_2 in arterial blood ($PaCO_2$) were measured continuously in urethan anaesthetized rats at different body temperatures. In urethan anaesthesia the colonic temperature of our rats averaged $33.5 \pm 1.29°$ C, when the ambient temperature was 22–24° C. At this temperature their $PaCO_2$ was the highest, 42 ± 1.2 mm Hg on the average. With decreasing or increasing body temperature the $PaCO_2$ declined. The breathing frequency increased with increasing body temperature. The ventilatory CO_2 response curve in warmed rats was shifted towards higher ventilation. Its relative slope was parallel, in absolute units it was steeper than that of the cooled animals. After vagotomy the rate of breathing averaged 42–48% of the control values, at all body temperatures. The calculated inspirio-inhibitory index (V/V_T) shows a relatively identical decrease (37–39%) after vagotomy in warmed, same as in cooled rats. The results indicate that in urethan anaesthetized rats the sensitivity to CO_2 remains the same in the range of body temperatures from 28 to 38° C. Also the relative role of the vagus nerves does not change within the range of these temperatures.

INTRODUCTION

In our attempt to use the laboratory rat as standard animal for studies in respiratory pathophysiology it soon become apparent that the interdependence of body temperature and breathing needs experimental examination. In anaesthetized dogs maintained sensitivity to CO_2 in hypothermia was reported (Cranston et al. 1955). There was, however, a great quantitative reduction, with body temperature at 28°C (Salzano and Hall 1960). In inhalation anaesthesia the decreased sensitivity to CO_2 may be

due to a relative increase of anaesthesia (Edelist 1970). With increased body temperature Kappey, Albers and Schmidt (1962) found in anaesthetized panting dogs a decrease of the slope of the CO_2 ventilatory response curve (Kappey et al. 1962), whereas Cunningham and O'Riordan (1957) reported a steeper slope in man. A decrease in the CO_2 threshold was reported both in hypo- and hyperthermia in anaesthetized dogs (Pleschka et al. 1965).

METHODS

In our experiments we used 47 male rats of the strain Wistar–Krč, with body weights of 270–340 g. They were anaesthetized with 1.3 g/kg urethan intraperitoneally. Partial pressure of arterial CO_2 ($PaCO_2$) was measured continuously by a technique already described (Hritzová et al. 1970). To obtain the ventilatory measurements, a body plethysmograph was used (Paleček 1969). PCO_2 was increased by rebreathing from an elastic bag, originally filled with 150 ml of oxygen. The room temperature was between 22–24°C during the experiments. The animals were heated — when required — by a metal plate perfused with thermostated water, and/or by radiant heat from an infra-red bulb. The colonic temperature (3 cm deep) was measured by a thermistor sensor, the temperature of the body box by a mercury thermometer. The $PaCO_2$ measured at 38°C was corrected for actual body temperature (Bradley et al. 1956). The applicability of the calculated values for rats was repeatedly checked by adjusting the measuring electrode temperature to that of the animal, and comparing the measured values with the calculated ones.

RESULTS

The colonic temperature of our rats was low; in unanaesthetized animals it was 36.1 ± 0.13°C on the average, and after 30 min of urethan anaesthesia 33.5 ± 1.29°C. The animals were either cooled to an average colonic temperature of 28.3 ± 0.42°C, or warmed to 38.2 ± 0.48°C. The corresponding respiratory values are summarized in Table I. The highest PCO_2 values are found in animals without additional cooling or warming, i.e. with the average colonic temperature of 33.5 ± 1.29°C. To examine the relation of PCO_2 and body temperature, in a separate group of rats, only these two variables were examined. The results are given in Table II. The Table shows average values of the whole group. The highest PCO_2 of each animal was equaled to 100%, and all other values were expressed in per cent of the highest one. The mean of the highest values was

TABLE I

Respiratory values in anaesthetized rats of different body temperature. The values are means ±SE

Colonic temperature (°C)	Rate of breathing (cycles/min)	Tidal volume (ml)	Minute ventilation (ml/min)	$PaCO_2$ (mm Hg)
28.3±0.42	87±4.9	1.4±0.10	118±7.5	36.0±1.9
33.5±1.29	96±3.0	1.4±0.05	138±7.0	39.6±3.6
38.2±0.48	125±7.9	1.8±0.13	236±18.3	25.0±6.5

TABLE II

Average $PaCO_2$ values of anaesthetized rats of different body temperature expressed in per cent of the highest value. 100% = 42±1.2 mm Hg. The $PaCO_2$ per cent values are means ±SE

Colonic temperature (°C)	$PaCO_2$ (%)
24	79.6±3.1
25	83.9±2.7
26	86.0±2.6
27	89.2±2.2
28	88.0±2.3
29	91.9±2.5
30	92.4±2.3
31	95.1±0.3
32	96.3±1.4
33	95.5±0.9
34	96.2±1.7
35	94.4±2.0
36	91.4±4.2
37	(94.2±3.2)[a]
38	(97.4±2.6)[a]

a The values are not representative for the group, being based on three measurements out of 14.

42 ± 1.2 mm Hg. It is obvious that the highest values of PCO_2 (within 5%) were in the range of body temperatures from 31 to 34°C. The PCO_2 values for 37 and 38°C are not representative for the group, as they were measured in 3 rats out of 14 only.

The changes in the rate of breathing followed the changes in body temperature (Table I). The ventilatory response to increasing PCO_2 is demonstrated in Fig. 1. The response curves were measured only at the two extreme body temperatures (28 and 38°C), and their average values are shown. The shape of both curves is similar, with a displacement towards lower PCO_2 and higher ventilation of the curve of the warmed

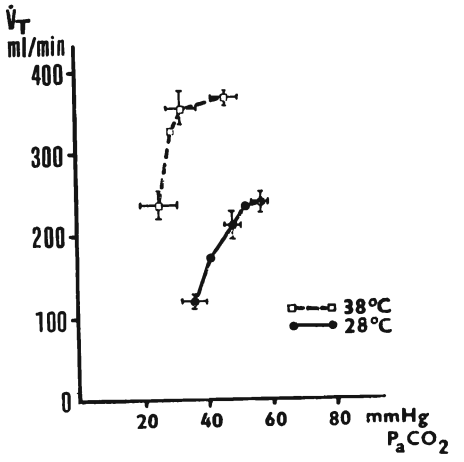

Fig. 1. Ventilatory CO_2 response curves in anaesthetized rats of different body temperature. Ordinate, minute ventilation; abscissa, partial pressure of CO_2 in arterial blood. The bars represent the SE of the means.

animals. The slope of CO_2 response curve of the warmed rats after the first minute of rebreathing is steeper than that of the cooled animals: 25.5 ml/min/mm Hg and 14 ml/min/mm Hg respectively. However, when expressed in per cent of the starting values, the slope is equal under both temperatures, i.e. 10.9%/mm Hg.

Bilateral cervical vagotomy results in a decrease of the breathing frequency to less than 50%; but even in vagotomized rats there is a positive correlation of the rate of breathing and body temperature (Table

TABLE III

Respiratory frequency in anaesthetized rats of different body temperature before and after vagotomy. The values are means ±SE

Control			Vagotomized		
Colonic temperature (°C)	Rate of breathing (cycles/min)	%	Colonic temperature (°C)	Rate of breathing (cycles/min)	%
28.3±0.42	87±4.9	70	27.8±0.48	38±3.7	72
33.5±1.29	96±3.0	77	34.6±0.42	48±3.7	91
38.2±0.48	125±7.9	100	38.3±0.13	53±6.7	100

III). To estimate the relative importance of vagal afferentation during different body temperatures, we calculated an index of inspiratory inhibition. The index is derived on the assumption that the tidal volume is represented by the balance of stimulatory and inhibitory processes: V_T = stimulation/inhibition. If we choose the maximal inspiratory air flow as a quantitative representation of the stimulatory processes, we can

express the inhibition as: inhibition = $\dot{V}_{max}/V_T$. The values of this index are presented on Fig. 2. The higher inhibition with higher body temperature corresponds to the higher rate of breathing. The decrease of inhibition after vagotomy corresponds to the absence of inhibitory impulses, normally transmitted via vagus. The proportion of vagal inhibition is practically the same in cool and warm animals — 39 and 37% respectively.

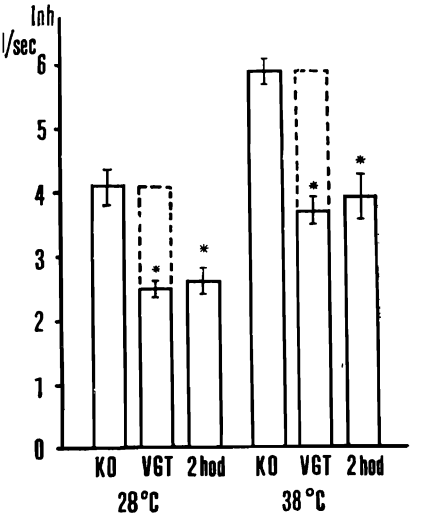

Fig. 2. Inspirio-inhibitory index in anaesthetized rats of different body temperature, before (KO) and after vagotomy (VGT). "2 hod" denotes 2 hr after vagotomy. Description in text. Height of the columns corresponds to mean values, the bars represent SE. The asterisks mark statistical significance of the difference at $p = 0.05$.

DISCUSSION

The decrease of body temperature in urethan anaesthetized rats was measured by Ankermann and Jacobasch (1961), and their results correspond well with ours: the higher rectal temperature (34.6°C) in rats measured by Ankerman and Jacobasch can be explained by the lower dose of the anaesthetic (1 g/kg) and higher ambient temperature (29°C). We have no specific explanation of the relatively low colonic temperature of our unanaesthetized rats, apart from the probable genetic differences of the particular breed.

The highest values of $PaCO_2$ were found in the range of body temperatures which are practically identical with that of the animals without cooling or heating. This observation may be a parallel to the experiments of Pleschka, Albers and Heerd (1965) who observed the highest PCO_2 threshold in anaesthetized dogs during normothermia.

The shift of the CO_2 response curve in warmed animals towards higher ventilation values supports the concept that the increased body temperature provides an extra drive to ventilation, even at lowered PCO_2. The slope of the curves indicates that the increased ventilatory drive is

not combined with decreased sensitivity to CO_2. In absolute units the slope of the CO_2 response curve in warmed animals is higher; however, in relative units it is the same as in cooled rats. The importance of vagus function does not change within the range of temperatures studied; its relative proportion to the ventilatory drive remains the same, as is indicated by the calculated index of inspiratory inhibition. Intact vagal function is one of the determinants of the slope of the CO_2 response curve (Richardson and Widdicombe 1969, Chválová et al. 1970). In our experiments, vagotomized rats did not survive an increase of body temperature. Euler, Herrero and Wexler (1970) found in decerebrate cats no increase in breathing frequency in the ventilatory response to CO_2 at the given body temperature after vagotomy (Euler et al. 1970), similarly as Richardson and Widdicombe (1969) in anaesthetized rabbits. This is in accord with our earlier observations on urethan anaesthetized rats (Chválová et al. 1970).

We conclude that (i) the colonic temperature decreases several centigrades in urethan anaesthetized rats; (ii) at this temperature their $PaCO_2$ is the highest, and warming or cooling the animals causes its lowering; (iii) the sensitivity to increasing CO_2 is maintained in the range of colonic temperatures from 28 to 38°C; (iv) the role of vagal transmission is relatively the same in the studied range of temperatures.

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ERRATA

Page 155, line 11 of Abstract:
instead of (V/V_T) *should be* $(\dot{V}/V_T)$

Page 173 first line from bottom should read:
use $\dot{V}$-PCO_2 curves.

Page 191, line 19 from top:
instead of bandpass 8–1,0000 cycle/sec *should be* bandpass 8–1,000 cycle/sec