J. Physiol. (1976), **258**, *pp.* 157–171
With 9 text-figures
Printed in Great Britain

THE REGULATION OF RESPIRATORY EVAPORATIVE HEAT LOSS IN THE RABBIT

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(*Received 11 November 1975*)

SUMMARY

1. Respiratory evaporative heat loss in the rabbit has a minimum value of 0·2–0·3 W/kg and a maximum value of about 1·1 W/kg in non-evaporatively limited environments.

2. Both skin temperature and hypothalamic temperature influence respiratory evaporative heat loss, and they do so in a multiplicative fashion. Thus, at low skin temperature the hypothalamic temperature threshold for the onset of panting is above normal hypothalamic temperature and hypothalamic thermosensitivity is high. On the other hand, at high skin temperatures, the hypothalamic temperature threshold for the onset of panting is well below normal hypothalamic temperature, but hypothalamic thermosensitivity is greatly reduced.

3. The influence of mean skin temperature ($\bar{T}_{sk}$) and hypothalamic temperature on respiratory evaporative heat loss (E_{res}) in the rabbit can be described by the equation:

$$E_{res} = 1{\cdot}1 - 0{\cdot}08\ (\bar{T}_{sk} - 39{\cdot}7)\ (T_{hy} - 42{\cdot}9) \geqslant 0{\cdot}3\ \text{W/kg}.$$

4. Thus, the ability of a lowered mean skin temperature to increase the thermosensitivity of the hypothalamus in response to local temperature changes applies to heat loss mechanisms as well as heat production mechanisms. It is suggested that the characteristics of this peripheral input into the C.N.S. are fulfilled by tonic cold fibre input originating from the peripheral cold receptors on the body surface.

INTRODUCTION

A recently proposed model for the regulation of metabolic heat production in the rabbit (Stitt, Hardy & Stolwijk, 1974) is based on a multiplicative interaction between $\bar{T}_{sk}$ and T_{hy}. The model is described by the equation:

$$MR = 0{\cdot}094\ (\bar{T}_{sk} - 39{\cdot}6)\ (T_{hy} - 45{\cdot}0) \geqslant 3{\cdot}0\ \text{W/g} \qquad (1)$$

and is characterized by both a changing T_{hy} threshold for the onset of shivering *and* a changing hypothalamic thermosensitivity in response to changes in skin temperature. This was presented as a possible resolution of the apparent conflict between the additive 'adjustable set point' model proposed by Hammel, Jackson, Stolwijk, Hardy & Strømme (1963) and the multiplicative 'variable gain' model of Stolwijk & Hardy (1966) and Jacobson & Squires (1970), since it contains the major feature of both models. Studies which have attempted to analyse thermoregulatory effector outputs in terms of skin and hypothalamic temperatures have tended to concentrate on metabolic heat production, since it is easy and relatively precise to measure. Descriptions of the regulation of evaporative heat loss, on the other hand, are not as definitive. For example, Hellstrøm & Hammel (1967) while demonstrating changes in the hypothalamic threshold temperature for the onset of panting with different ambient temperatures, left open the question of whether there were changes in the slope of hypothalamic sensitivity at different ambient temperatures. Jacobson & Squires (1970) on the other hand, also demonstrated changes in the hypothalamic temperature threshold for the onset of panting but maintained that hypothalamic thermosensitivity in the control of panting was unaffected by changes in ambient temperature. The major problem encountered when attempting to describe the regulation of panting is the narrow range of ambient temperature over which it can be studied. Under normal conditions, panting does not appear spontaneously in most domestic animals until the ambient temperature reaches 30° C. By the same token, most of these animals cannot maintain thermal equilibrium in ambient temperatures much in excess of 35° C. This limited range of ambient temperature makes it extremely difficult to distinguish the relative contributions of the different body temperatures to the panting mechanism.

The influence of skin and hypothalamic temperatures in the regulation of respiratory evaporative heat loss in the New Zealand white rabbit was studied. The rabbit is not well able to withstand thermal stress; in fact, it is difficult for these animals to maintain thermal equilibrium in ambient temperatures of 35° C. Consequently, it was necessary to devise a method to assist animals in maintaining thermal equilibrium at the upper extreme of range of ambient temperatures used in this study, namely 39° C. This was accomplished by taking advantage of the ability of the rabbit's ears to dissipate large quantities of heat. A specially constructed heat sink (see Methods) was fitted over the ear when exposing the animal to ambients of 39° C and the excess heat necessary to keep the animal in thermal balance was removed from the body through the ear by the water perfused heat sink. In this manner, one was able to observe the influence of skin temperature and hypothalamic temperature in the regulation of respiratory evaporative heat loss in ambient temperatures of 20, 29 and 39° C.

METHODS

The study was performed on four male New Zealand white rabbits weighing between 3·0 and 4·0 kg. The animals were previously implanted with thermodes and thermocouple re-entrant tubes under general anaesthesia, but the actual experiments were conducted on the unanaesthetized animals minimally restrained in conventional rabbit stocks within a partitional calorimeter. Between experiments the animals were housed individually in cages in an ambient temperature of 20–23° C with a normal night and day cycle and allowed rabbit chow and water *ad libitum*.

Thermode implantation

The thermodes and thermocouple re-entrant tubes were implanted in the preoptic-anterior hypothalamic area using the stereotaxic atlas and co-ordinates of Sawyer, Everett & Green (1954). Thermodes were located at co-ordinates A 4·0, L1·5, V3·0 and A1·0, L1·5, V3·0 to one side of the mid line and a thermocouple re-entrant tube was located at A2·5, L4·5, V3·0 on the same side. The rabbits were anaesthetized with Diabutal (30 mg/kg I.V.) and placed in a Kopf stereotaxic frame. After the appropriately located craniotomy holes had been trephined in the skull, two stainless-steel self-tapping screws were attached to the parietal bones and the thermode tubes (1 mm o.d.) were inserted into the brain to the required depth. They were anchored with fast drying acrylic dental cement to the screws in the calvaria. The reflected muscles and skin were replaced around the acrylic mound containing the tubes and were sutured with chromic gut (000). The wound was dressed with antibiotic ointment and 300,000 units (I.M.) penicillin were administered. The animals were allowed a period of two weeks to recover before experiments were begun.

Construction of the ear heat sink

Due to its large surface area and ample vasculature, the rabbit's ear is a good thermal radiator. However, at ambient temperatures in excess of 35° C, the small thermal gradient between the ear and the environment limits its usefulness as a thermoregulatory organ at high temperatures. It was found that by placing a water perfused heat sink over one ear, it was possible to remove sufficient heat from the body to keep rabbits in thermal balance in ambient temperatures equal to their rectal temperature. An illustration of the heat sink is shown in Fig. 1. It was constructed within a hollow lucite cylinder measuring 130 mm in length and 50 mm in diameter and consisted of a manifold at each end of the tube, connected by twelve thin walled stainless steel tubes (5 mm o.d.) in a circular fashion against the inner wall of the cylinder. The twelve steel tubes acted as heat exchangers. The manifold at the upper end was divided into two parts, one serving as an inlet and the other as an outlet. Each half of the upper manifold fed six of the heat exchangers. The manifold at the other end of the sink accepted all twelve steel tubes and was ring-shaped. The hole in the middle admitted the rabbit's ear to the inside of the heat sink. Thus, water perfusing the sink entered the inlet manifold, passed down six of the heat exchangers to the ring manifold and then returned via the remaining six heat exchangers to the outlet manifold at the top. In this manner large volumes of water under considerable pressure could perfuse the heat sink without raising the hydrostatic pressure within the chamber containing the rabbit's ear. Thermal contact between the heat exchangers and the ear was produced by filling the heat sink with water. A thin latex sheath was attached to the outer surface of the open end of the heat sink and entered through the middle of the ring manifold to form a blind sac within the heat sink. This allowed the ear to be placed inside the sink without

being wetted and prevented water from escaping from the heat sink where the ear entered. The pressure within the heat sink could be adjusted through a syringe connected to the water inside the sink by a steel tube in the sink wall. This permitted a good thermal contact with the ear without occlusion of venous return from the ear. Water was perfused through the heat exchanger portion of the sink at rates of up to 100 l./min.

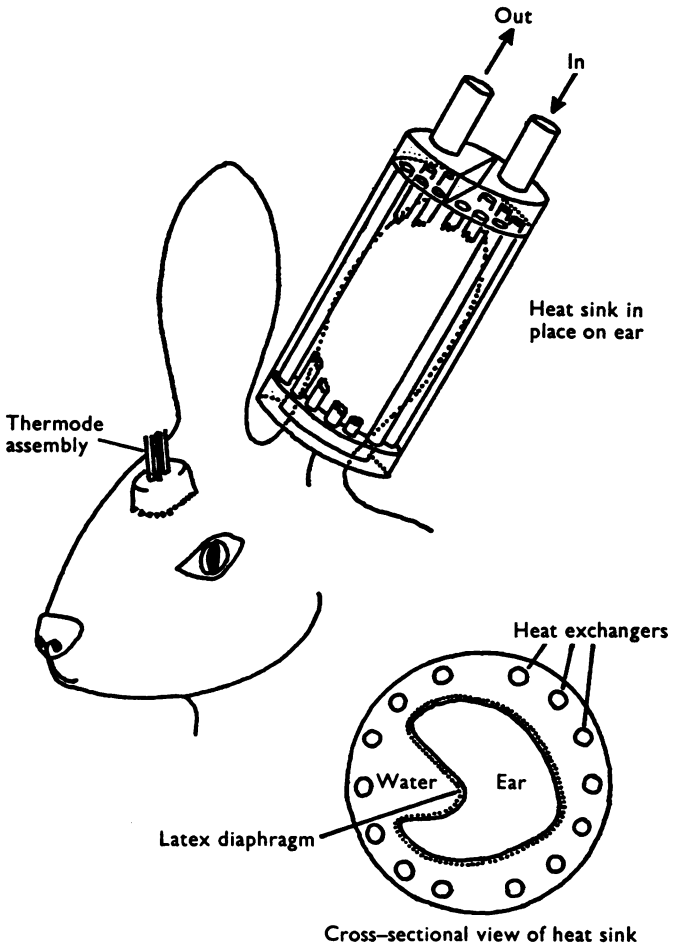

Fig. 1. Details of the construction and placement of the ear heat sink.

Measurement of respiratory evaporative heat loss

The experiments were conducted in a partitional calorimeter (Fig. 2) which was described previously (Stitt & Hardy, 1971), and respiratory evaporative heat loss was measured by hygrometry. A pair of wet and dry bulb thermocouples placed in an airstream which sampled the ambient air within the chamber, enabled one to calculate the water content of the ambient air. The head of the rabbit was enclosed in a loose fitting plexiglass hood which was evacuated at the rate of about 9 l./min

by a pump outside the chamber. This open draw system ensured that all of the animal's expired air was collected in the effluent tube leaving the hood, thus permitting the measurement of both oxygen consumption and respiratory water loss. A second pair of wet and dry bulb thermocouples was located within the airstream of the mask effluent. These measured the water content of the air containing water evaporated from the rabbit. The amount of evaporating water produced by the animal was calculated by the equation

$$\text{Water loss} = (\text{water content (circuit air)} - \text{Water content (ambient air)}) \times \text{airflow}.$$

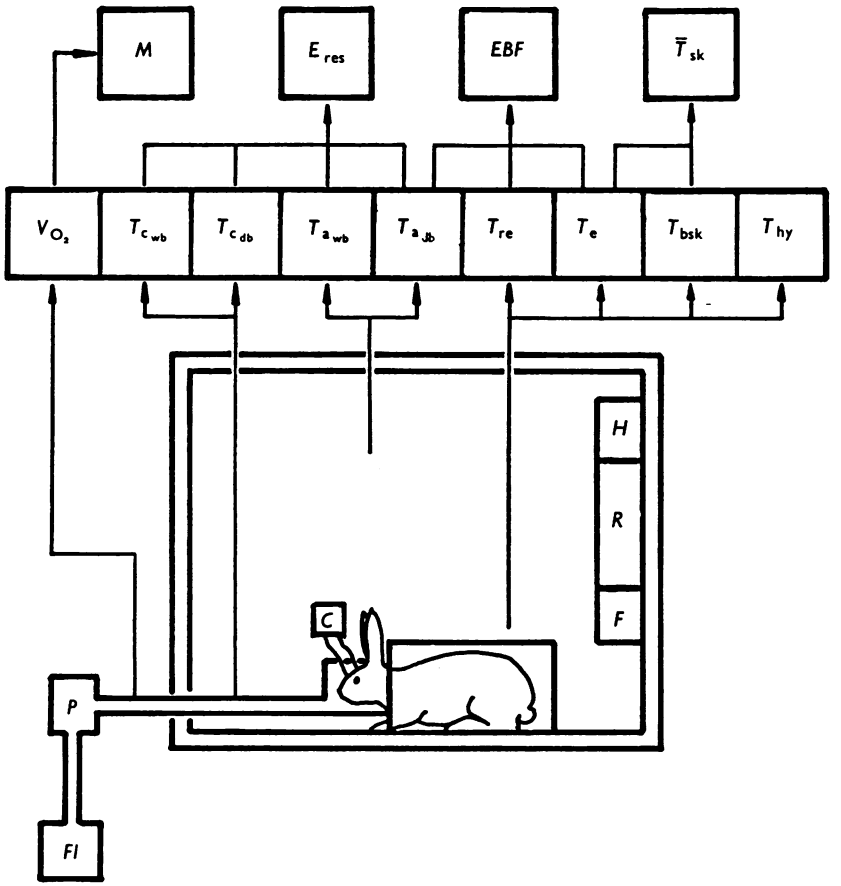

Fig. 2. The partitional calorimeter used to conduct the experiments. M, metabolic rate; E_{res}, respiratory evaporative heat loss; EBF, ear blood flow; $\bar{T}_{sk}$, mean skin temperature; V_{O_2}, oxygen uptake; $T_{c_{wb}}$, circuit wet bulb temperature; $T_{c_{db}}$, circuit dry bulb temperature; $T_{a_{wb}}$, ambient wet bulb temperature; $T_{a_{db}}$, ambient dry bulb temperature; T_{re}, rectal temperature; T_e, ear temperature; T_{bsk}, back skin temperature; T_{hy}, hypothalamic temperature; H, chamber heaters; R, refrigeration unit; F, fans; P, draw pump; Fl, flow meter; C, thermode circulator.

Respiratory evaporative heat loss was then calculated assuming that 1 g water evaporated = 0·70 Whr.

Experimental protocol

The animals were randomly exposed to ambient temperatures of 20, 29 and 39° C. After being placed in the chamber, they were allowed to come to thermal equilibrium with their environment for a period of 90 min before the experiments were started. When a rabbit was to be exposed to T_a = 39° C, the heat sink was attached to one ear, and a flow rate and perfusion temperature were established so as to maintain the animal's rectal temperature between 39 and 39·5° C. Thermocouples were attached to the ears to measure ear blood flow (Stitt, 1973) and two thermocouples were attached to the back skin under the fur using a thin film of beeswax to preserve the natural thermal insulation of the skin. Mean skin temperature, when used, was calculated using the formula $\bar{T}_{sk} = 0{\cdot}12T_c + 0{\cdot}88T_{bsk}$. Metabolic rate was also measured using a Beckman F3 oxygen analyser in conjunction with the open draw system (Stitt & Hardy, 1971). All measurements were taken once per minute throughout the experiment, each variable being measured as a DC potential on a Hewlett-Packard digital volt-meter interfaced to an on-line IBM 1130 computer. Each minute all temperatures, M, E_{res} and EBF were calculated instantaneously by the computer and relayed back to the laboratory where they were displayed on an on-line Calcomp 4000 plotter. The data were also stored on disk by the computer. The thermodes were water perfused from a lucite chamber (Hammel, Hardy & Fusco, 1960) connected to a water source of controlled temperature. Each animal was exposed to each of the three ambient temperatures a minimum of three times. Preoptic-anterior hypothalamic thermosensitivity in the control of respiratory evaporative heat loss was measured by applying several step changes to T_{hy} and measuring the resulting change in E_{res}. Each displacement lasted 15 min and the level of E_{res} attained was taken as the average of ten determinations of E_{res} made during the final 10 min of the clamp. T_{hy} was then allowed to return to its normal level. Displacements of T_{hy} were spaced at least 30 min apart to ensure that body temperatures had returned to normal and that E_{res} had regained its control value before the next clamp was initiated.

After the experiments were completed the animals were killed and their brains were examined for histological verification of the sites of implantation.

RESULTS

The influence of hypothalamic temperature on the regulation of E_{res} was investigated at ambient temperatures of 20, 29 and 39° C. Fig. 3 illustrates a typical experiment carried out at 20° C. It will be noted that at this temperature panting does not occur at normal hypothalamic temperatures and respiratory evaporative heat loss is at a minimum value (0·2–0·3 W/kg). However, when hypothalamic temperature is raised above 40° C, panting is induced and the increase produced in E_{res} is proportional to the degree of increase in T_{hy}. Fig. 4 shows an experiment conducted at an ambient temperature of 29° C. In this case panting is present at normal T_{hy} and E_{res} has an average value of 0·6 W/kg. It can be seen that step decreases in T_{hy} suppress panting to its minimal value, while step increases in T_{hy} produce increases in E_{res} which are proportional to the degree of

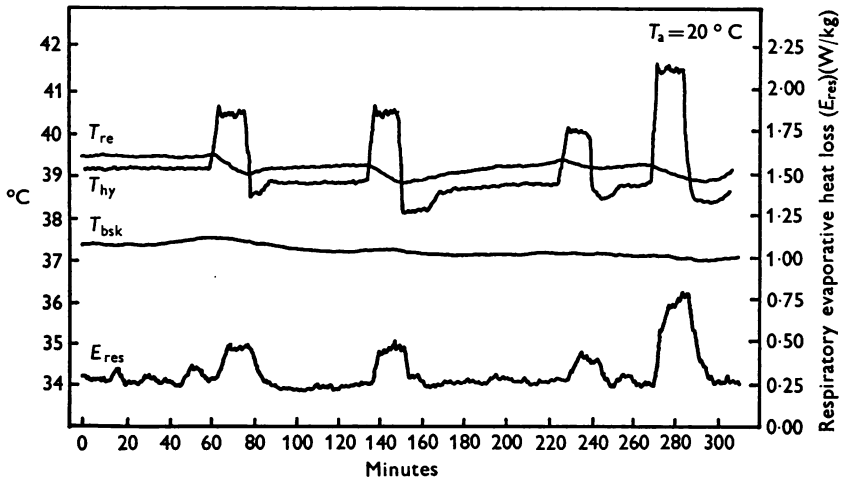

Fig. 3. A portion of an experimental protocol carried out at T_a = 20° C. At values of T_{hy} below 40° C, E_{res} is at its minimal value of 0·2–0·3 W/kg. At levels of T_{hy} above 40° C, E_{res} increases in proportion to the level of T_{hy}. Legend as in Fig. 2. For the sake of clarity, M and EBF have been omitted from the plot.

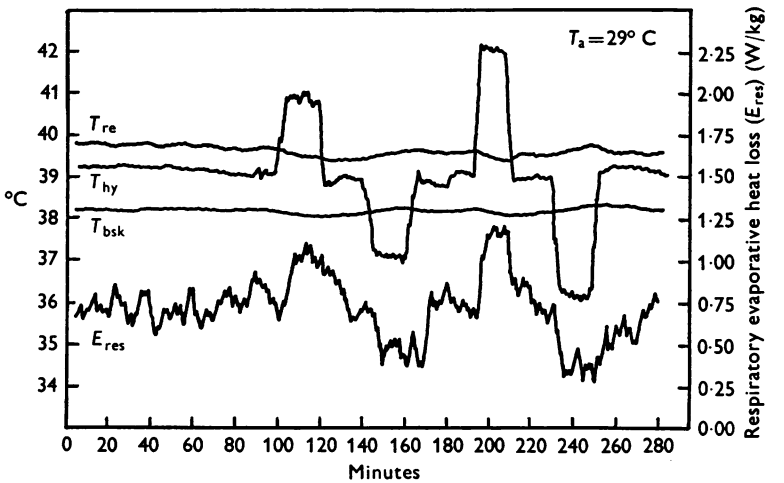

Fig. 4. A portion of an experimental protocol carried out at T_a = 29° C. At normal values of T_{hy}, E_{res} is elevated. Decreases in T_{hy} suppress E_{res}, while increases in T_{hy} augment E_{res}. Legend as in Fig. 2.

displacement of T_{hy}. Finally, Fig. 5 illustrates an experiment carried out at T_a = 39° C; it can be seen that the animal is in thermal equilibrium due to the action of the ear heat sink and the animal is panting vigorously to produce an E_{res} of 1·0 W/kg at normal hypothalamic temperature. Step displacements in T_{hy} now have a minimal effect on E_{res} so that during decreases of T_{hy} to 35° C panting is not suppressed, and E_{res} still has a value of 0·85 W/kg. By the same token, increases in T_{hy} to 42° C do not further augment panting, indicating that preoptic anterior hypothalamic thermosensitivity under these conditions is virtually non-existent.

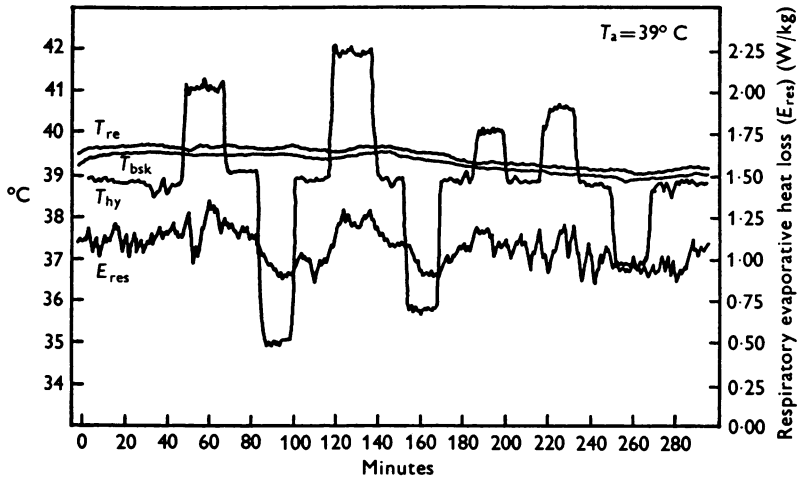

Fig. 5. A portion of an experimental protocol carried out at T_a = 39° C. E_{res} is at a maximal value of about 1·0 W/kg at normal levels of T_{hy}. Changes in T_{hy} have a minimal effect on E_{res} indicating that hypothalamic thermosensitivity is low. Legend as in Fig. 2.

Fig. 6 contains the pooled data for all four rabbits at each of the three ambient temperature conditions. E_{res} is plotted against T_{hy} and it will be noted that the data separate out into three distinct patterns according to the ambient and skin temperatures. Data collected at 20° C (T_{bsk} = 37° C) is characterized by a high T_{hy} threshold for the onset of panting and by a steep increase in E_{res} in response to increasing T_{hy} above 40° C. At T_a = 29° C (T_{bsk} = 38·3° C), the T_{hy} threshold for the onset of panting is below normal T_{hy} and the relation between E_{res} and T_{hy} is less steep indicating a reduced hypothalamic thermosensitivity compared to that at T_{bsk} = 37·0° C. The results obtained at T_a = 39·0° C (T_{bsk} = 39·5° C) are characterized by a continually high level of E_{res} at all values of T_{hy} and by a preoptic anterior hypothalamic thermosensitivity which approaches zero. In order to analyse these data and to characterize the changes of E_{res} in

response to changes in T_{hy}, regression analyses were carried out on the data from each skin temperature group. Inspection of the data obtained at T_{bsk} = 37·0° C at T_{hy} < 40·0° C reveals a constant minimal value for E_{res} which does not exceed 0·3 W/kg. Consequently, the minimum value of E_{res} was set at 0·3 W/kg and only values of E_{res} which exceeded this value were included in the regression analysis. Fig. 6 illustrates the regression lines obtained in this manner for the three groups of data, together with the slopes of thermosensitivity and their respective regression coefficients.

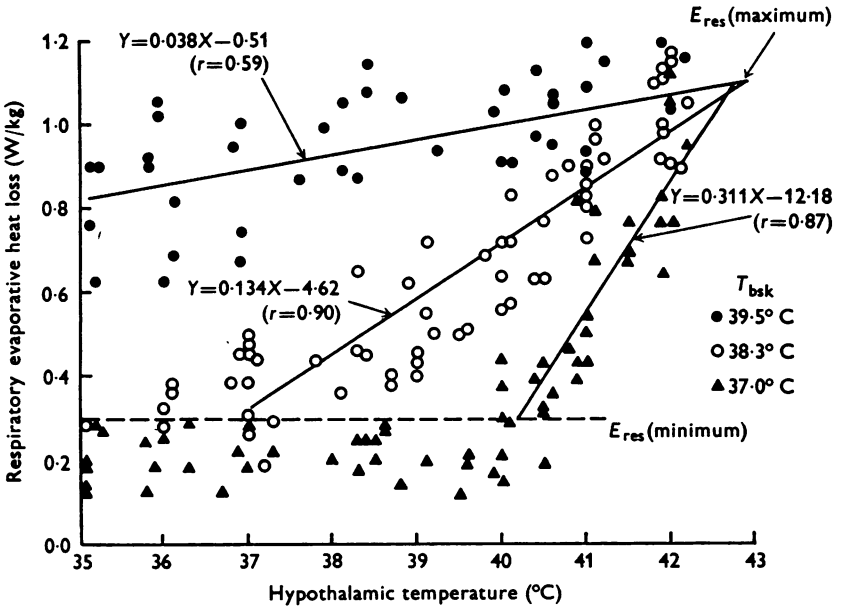

Fig. 6. Pooled data from experiments carried out on four rabbits at T_a = 20, 29 and 39° C. The regression equations calculated for each set of data are given along with their respective regression coefficients. The confluence of these three regression lines defines E_{res} maximum and T_{hy_0}. E_{res} minimum is evaluated as 0·3 W/kg.

At T_{bsk} = 37·0° C, the threshold T_{hy} for the onset of panting is 40·2° C and preoptic anterior hypothalamic thermosensitivity is 0·31 W/kg° C. When T_{bsk} is increased to 38·3° C, the T_{hy} threshold for the onset of panting is reduced to 36·8° C and the preoptic anterior hypothalamic thermosensitivity is reduced to 0·14 W/kg° C. When T_{bsk} is increased to 39·5° C, the T_{hy} threshold for the onset of panting is reduced to a virtual value of 21·3° C and hypothalamic thermosensitivity is reduced to 0·04 W/kg° C.

DISCUSSION

From the above data, it is evident that changes in skin temperature alter anterior hypothalamic thermosensitivity in the control of respiratory evaporative heat loss. At low skin temperatures hypothalamic thermosensitivity is maximal and the T_{hy} threshold for the onset of panting is higher than normal body temperature. At higher skin temperatures, however, hypothalamic thermosensitivity is markedly reduced and the T_{hy} threshold for the onset of panting is reduced to a level below normal body temperature so that panting is evoked by normal hypothalamic temperature. This implies that there is a multiplicative interaction between T_{sk} and T_{hy} in the regulation of E_{res}. Fig. 6 shows the linear regression lines describing hypothalamic thermosensitivity at each of the three levels of T_{bsk} examined. All intersect at a fixed value of E_{res} ($\sim$ 1·1 W/kg) at a single value of T_{hy} ($\sim$ 43° C). This information enables one to propose a model for the control of E_{res} in terms of T_{bsk} and T_{hy} which may be described by the equation

$$E_{res} = E_{res}\,(\text{maximum}) - \alpha\,(T_{bsk} - T_{bsk_0})\,(T_{hy} - T_{hy_0}). \qquad (2)$$

T_{hy_0} is that hypothalamic temperature at which E_{res} is maximal irrespective of the value of T_{bsk}, while T_{bsk_0} is that back skin temperature at which E_{res} is maximal irrespective of the value of T_{hy}.

This equation is qualitatively similar to eqn. (1) which was proposed for the regulation of metabolic heat production. It is different only in that E_{res} has a maximum stated value and the multiplicative portion of the expression is subtracted from E_{res} (maximum) to predict the value E_{res} for any given combination of T_{bsk} and T_{hy}. The four constants in eqn. (2), E_{res} (maximum), α, T_{bsk_0} and T_{hy_0}, can be deduced from the data in the following manner. As illustrated in Fig. 6, all three regression lines describing hypothalamic thermosensitivity at different levels of T_{bsk} intersect at a common value for T_{hy} of 42·9° C, and at maximal value for E_{res} of 1·1 W/kg. Thus one can put T_{hy_0} = 42·9° C and E_{res} (maximum) = 1·1 W/kg.

Eqn. 2 may be rewritten to express hypothalamic thermosensitivity $(\Delta E_{res})/(\Delta T_{hy})$ at any constant level of skin temperature, in the following form:

$$\Delta E_{res}/\Delta T_{hy} = \alpha(T_{bsk} - T_{bsk_0}). \qquad (3)$$

Thus, if the slopes of each of the three regression lines in Figure 6 are plotted against T_{bsk}, as is shown in Fig. 7, a value for α and T_{bsk_0} can be determined. The slope of the resulting regression line from this plot gives α a value of 0·12 and the intercept of the line at the x-axis is the value

of T_{bsk_0} (39·7° C) since $T_{bsk} = T_{bsk_0}$ when $\Delta E_{res}/\Delta T_{hy} = 0$. Substituting these four values back into the original eqn. (2), one obtains the expression:

$$E_{res} = 1{\cdot}1 - 0{\cdot}12\,(T_{bsk} - 39{\cdot}7)\,(T_{hy} - 42{\cdot}9) \geqslant 0{\cdot}3 \text{ W/kg}. \quad (4)$$

Eqn. (4) has been given a lower limit of 0·3 W/kg since this appears from Fig. 6 to be the minimal resting value for T_{res} which cannot be

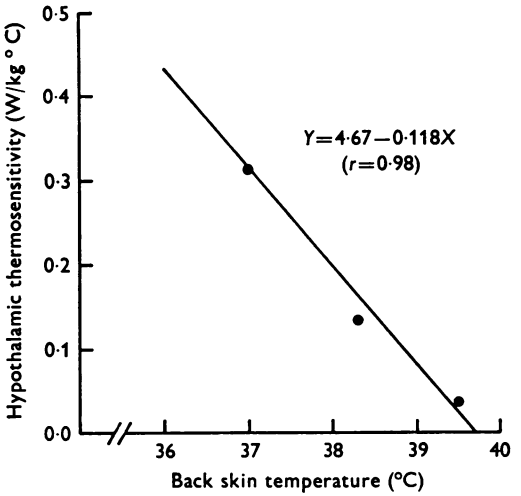

Fig. 7. The hypothalamic thermosensitivities derived from the slopes of the regression lines in Fig. 6 are plotted against their respective back skin temperatures. The resulting regression line evaluates α and T_{bsk_0}.

reduced. This equation is qualitatively similar to that (eqn. 1) which was derived for the control of metabolic heat production (Stitt *et al.* 1974). The present model for E_{res}, however, expresses the influence of skin temperature as a function of back skin temperature (T_{bsk}). This was done because of an initial uncertainty of the influence that cooling one ear might have on the usual measure of skin temperature, $T_{sk} = 0{\cdot}12T_e + 0{\cdot}88T_{bsk}$ and on E_{res} itself through input from any ear thermoreceptors. However, for two reasons, it appears that such effects are minimal. Firstly, because the heat transfer coefficient between the cooled ear and the water in the heatsink is very high, the actual decrease in T_e produced by ear cooling during exposures to $T_a = 39°$ is very small ($< 5°$ C). Calculation of mean skin temperature using a value of $T_e = 34°$ C yields a value of $\bar{T}_{sk} = 39{\cdot}2°$ at $T_a = 39°$ C which is not very different from $T_{bsk} = 39{\cdot}5°$. Secondly, sensory denervations of the perfused ear of two rabbits according to the information provided by Feldberg (1926) showed that this operation in no way altered the response of E_{res} in animals exposed to high ambient

temperatures with the heat sink attached to the denervated ear. For the above reasons it is felt that one can express the influence of peripheral temperature on hypothalamic thermosensitivity in terms of mean skin temperature ($\bar{T}_{sk}$). Fig. 8 shows a replot of the data contained in Fig. 7

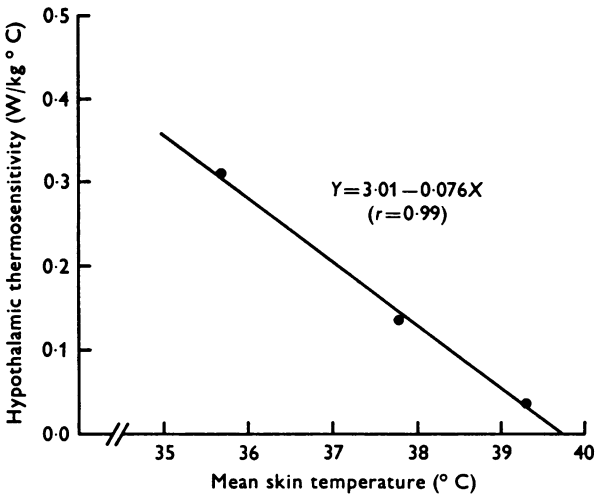

Fig. 8. The hypothalamic thermosensitivities derived from the slopes of the regression lines in Fig. 6 are plotted against their respective mean skin temperatures. The resulting regression line evaluates α and T_{sk_0}.

except that the values of preoptic anterior hypothalamic thermosensitivity are now plotted against $\bar{T}_{sk}$. Evaluation of the constants gives $\alpha =$ 0·076 W/kg °C^2 and $\bar{T}_{sk_0} = 39{\cdot}7°$ C. This means that the equation control of E_{res} expressed in terms of T_{hy} and $\bar{T}_{sk}$ is

$$E_{res} = 1{\cdot}1 - 0{\cdot}076(\bar{T}_{sk} - 39{\cdot}7)\,(T_{hy} - 42{\cdot}9) \geqslant 0{\cdot}3 \text{ W/kg}. \quad (5)$$

Furthermore, by expressing changes in preoptic anterior hypothalamic thermosensitivity in response to change in $\bar{T}_{sk}$, one can compare the control constants of the model for E_{res} with those of the previous model for heat production (M). Specifically, one can compare the effect of changes in $\bar{T}_{sk}$ in altering this thermosensitivity measured as change in E_{res}/° C change in T_{hy} with the effect of changes in $\bar{T}_{sk}$ in altering preoptic anterior hypothalamic thermosensitivity measured as change in M/° C change in T_{hy}. One can also compare the value of $\bar{T}_{sk}$ at which such thermosensitivity becomes zero. Such a comparison is made in Fig. 9. The open circles are the values of preoptic anterior hypothalamic thermosensitivity derived at values of $\bar{T}_{sk}$ = 35·7, 37·8 and 39·5° C using E_{res} as the controlled output and the closed circles are the values of thermosensitivity

derived at values of $\bar{T}_{sk}$ = 30·6, 32·3 and 34·5° C using M as the controlled output from Stitt *et al.* (1974). It will be noted that the E_{res} derived preoptic anterior hypothalamic thermosensitivity coefficients are now plotted as negative coefficients. This is done in order to make a comparison, since in the heat balance equation, E_{res} is a heat loss factor which by convention has a negative value. It can be seen that the regression line calculated by the method of least squares fits all six data points with an r value of 0·99 This line yields values of α = 0·094 W/kg ° C^2 and $\bar{T}_{sk_0}$ = 39·4° C, which are close to the values of α and $\bar{T}_{sk}$ given in eqns.

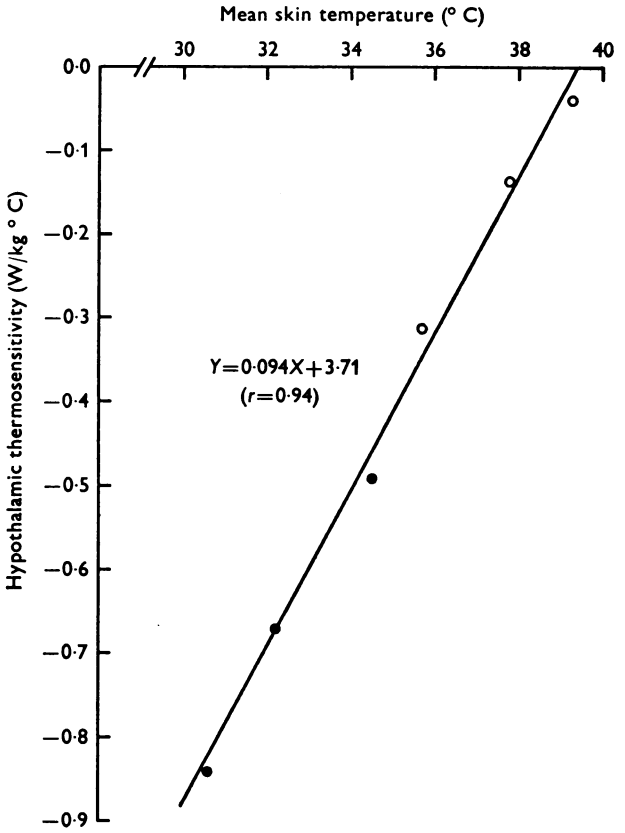

Fig. 9. Hypothalamic thermosensitivities derived from $\Delta E_{res}/\Delta T_{hy}$ in this study at warmer mean skin temperatures are compared with hypothalamic thermosensitivities derived from a previous study (Stitt *et al.* 1974) using $\Delta M/\Delta T_{hy}$ at colder mean skin temperatures. The values of thermosensitivity are plotted against the respective mean skin temperatures at which they were determined. The resulting regression line gives a common value for α and $\bar{T}_{sk_0}$.

(1) and (5). These results are interpreted as indicating that a single continuum of thermal peripheral input from the skin modifies preoptic anterior hypothalamic thermosensitivity in a consistent fashion across the range of skin temperatures from $\bar{T}_{sk}$ = 30·0° C to $\bar{T}_{sk}$ = 40·0° C such that at $\bar{T}_{sk}$ = 30·0° C the thermosensitivity is high, while at $\bar{T}_{sk}$ approaching 40·0° C the thermosensitivity is virtually zero. From an examination of the results of neurophysiological investigations of peripheral thermoreceptors in the skin of furred animals (Dodt & Zotterman, 1952; Hensel, & Kenshalo 1969; Iggo, 1969) it is suggested that tonic cold fibre activity fulfils the characteristics of this skin input into the C.N.S. All of these investigators agree that tonic cold fibre input is maximal at values of skin temperature of 26–28° C and that it approaches zero at values of skin temperature of 38–40° C. Furthermore, it is suggested that warm fibre input from the skin plays a small and insignificant role in the regulation of autonomic thermoregulatory effectors in thermal steady states, since single fibre recording results indicate that warm fibre activity does not become substantial until skin temperature exceeds values of 39–40° C. In normally regulating furred animals, values of $\bar{T}_{sk}$ of this magnitude are only achieved when the animals are approaching hyperthermia and are unable to thermoregulate by physiological means.

Finally, mention is made of the difference between the value of T_{hy_0} derived in equation (1) (T_{hy_0} = 45° C) and that derived in eqn. (5) (T_{hy_0} = 42·9° C). At present this discrepancy cannot be explained and it is suggested that it may be due to the different methods of extrapolation used to determine T_{hy_0} in each case. In the earlier study of the control of M (Stitt *et al.* 1974), T_{hy_0} was derived as the point of intersection of the three lines of preoptic anterior hypothalamic thermosensitivity derived from $\Delta M/\Delta T_{hy}$. Since one could not measure any values of M below resting metabolic rate, this was a relatively long extrapolation, thus incurring a larger probability of error. In the present case of E_{res} control, data points could be collected almost to the point of intersection of the three lines of preoptic anterior hypothalamic thermosensitivity and a more secure identification of T_{hy_0} could be achieved.

This study was supported by a grant from N.I.H. NS11487. The author acknowledges the skilful technical assistance of Mr D. Barboza, II, and Mr E. Farhi. The suggestions and criticisms of Dr J. D. Hardy were invaluable in the preparation of the manuscript.

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