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THE EFFECT OF HEATING AND COOLING THE HYPOTHALAMUS ON BEHAVIOURAL THERMOREGULATION IN THE PIG

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SUMMARY

1. Pigs were trained to push a switch with their snouts in order to obtain a short burst of infra-red heat on the skin.

2. When the preoptic region of the hypothalamus was cooled by means of an implanted thermode, the rate at which the heaters were turned on increased at environmental temperatures ranging from 0 to 25° C. At 30 and 35° C cooling sometimes had no effect.

3. The preoptic region was warmed either by means of a thermode or using radio-frequency heating from implanted electrodes. Warming the preoptic region decreased the rate at which the infra-red heaters were turned on, but the effect was not as obvious as the increases observed during cooling.

4. Pigs placed in a cold or neutral environment did not learn to push a switch in order to obtain radio frequency heating of the preoptic region.

INTRODUCTION

In a previous study it was shown that when pigs are exposed in a cage to low ambient temperatures they readily learn to press a switch with their snouts in order to turn on a short burst of infra-red heat. The frequency with which they turn the heat on declines at high ambient temperatures (Baldwin & Ingram, 1967).

A series of similar experiments on the shaved rat by Weiss & Laties (1961) led them to conclude that a fall of subcutaneous temperature of some 8° C is necessary to initiate a high rate of responding. By contrast, trained pigs begin to turn the heat on as soon as they are exposed to low ambient temperatures.

The above experiments were concerned with the effects of peripheral cold stimulation on behavioural thermoregulation. The central mechanisms involved have been studied by Satinoff (1964) who implanted thermodes into the hypothalamus of shaved rats which had been trained to turn on infra-red heating in a cold environment. When the hypothalamus was cooled, while the animals were exposed to an ambient temperature in the region of their thermoneutral zone, the rats increased the rate at which they turned the heat on. Recently, Carlisle (1966) investigated the effect of heating the hypothalamus of the rat on the rate at which a trained animal turned on an infra-red heater. It was demonstrated that, during the periods when the hypothalamus was heated, there was a decrease in the rate at which the rats turned on the heat. Similar results have been reported by Murgatroyd (1966) who also heated and cooled the preoptic region of the rat.

The above evidence from behavioural studies accords with the demonstration by electrophysiological methods that cold as well as warm receptors exist in the hypothalamus (Hardy, Hellon & Sutherland, 1964).

In the present study, the technique of operant conditioning, by which an animal learns to turn on a burst of heat, has been used to assess the importance of central thermal stimuli in the control of behavioural thermoregulation in the pig and particular attention has been paid to the following points: (1) Will cooling the hypothalamus increase the frequency with which a pig turns on the heaters? (2) Will warming the hypothalamus decrease the frequency with which a pig turns on the heaters? (3) Will pigs learn to press a switch in order to obtain a short burst of radio-frequency heating delivered to the hypothalamic region? A preliminary account of this work has been published (Baldwin & Ingram, 1966).

METHODS

Animals. Seventeen Large White pigs aged between 8 and 12 weeks were used. The group included both females and castrated males.

Training. After the animals had been removed from the pig herd, they were housed individually in pens. During this period the pigs became tame and were fitted with a leather harness which did not impede their movement.

The animals were exposed in a cage 90 × 60 cm to a temperature of 5° C. A metal box 15 × 20 × 5 cm with a panel in the centre 8 cm square (Fig. 1), was attached to one wall of the cage. When the pig exerted a slight pressure on the centre panel with its snout a micro-switch turned on 12 × 250 W infra-red heaters (Phillips) suspended 20 cm above the pig's back. After 4 sec, the heaters were automatically switched off. Operating the switch while the heaters were on did not prolong the period of heating and the pressure on the switch had to be released before the heaters could be operated again. It was thus impossible to keep the heaters on continuously. All the animals learned to operate the switch within a few hours (Baldwin & Ingram, 1967).

Once a pig had learned to operate the heater switch, in the cage described above, it was restrained in a stand by means of the harness in such a way that it could operate a panel-switch and lie down but was prevented from turning round (Fig. 2). This restraint often resulted in the animals ignoring the switch for the first hour or two but after a further training period they stood quietly in the stand and again operated the switch which turned on the heaters. In this situation, it was possible to attach tubes to a thermode implanted into the brain (Fig. 2).

In some experiments using radio-frequency heating where the only attachments which had to be made to the animal were flexible wires the experiments were performed while the animal was free to move about in a cage like that used for initial training.

Surgical. All surgical procedures were performed with sterile precautions under general anaesthesia. The pigs were given 0·2 ml. phencyclidine hydrochloride intramuscularly 15 min before surgery. Anaesthesia was induced with halothane administered through a face mask

(a) (b)

Fig. 1. Illustrates the switch panel which the pigs pushed in order to turn on the heaters. (*a*) Front view. (*b*) Vertical section through the switch.

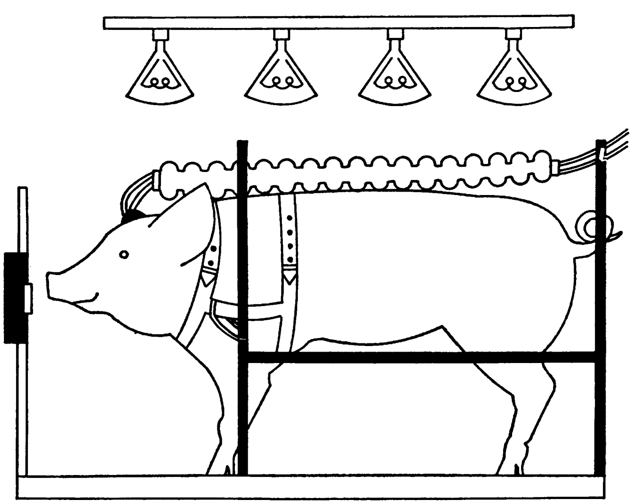

Fig. 2. Illustrates a pig, with a thermode implanted, and restrained in a stand. The tubes conducting the fluid to the thermode were encased in the corrugated tubing to prevent contact with the animal's skin. Pressing the switch panel mounted on the stand turned on the infra-red heaters.

and then following induction and intubation maintained by halothane and oxygen administered through a McGill endotracheal tube from a Boyles apparatus. The animal's head was fixed in a stereotaxic frame developed in this laboratory. A mid line incision was made in the scalp and the periosteum scraped away from the parietal bone. Using a portable X-ray apparatus a radiograph was taken to establish the position of the hypothalamus, since there is no stereotaxic atlas of the pig's brain. The thermode was placed in the preoptic region by reference to the optic foramina which can be seen clearly on a radiograph (Fig. 3). The thermode was securely attached to the skull by means of self-tapping stainless-steel screws and Acrylic dental cement. Animals were ready to be tested about 12 days after surgery. When the experiments were completed the pigs were killed and the position of the thermode determined by dissection. The thermodes were located within 1 mm of the mid line.

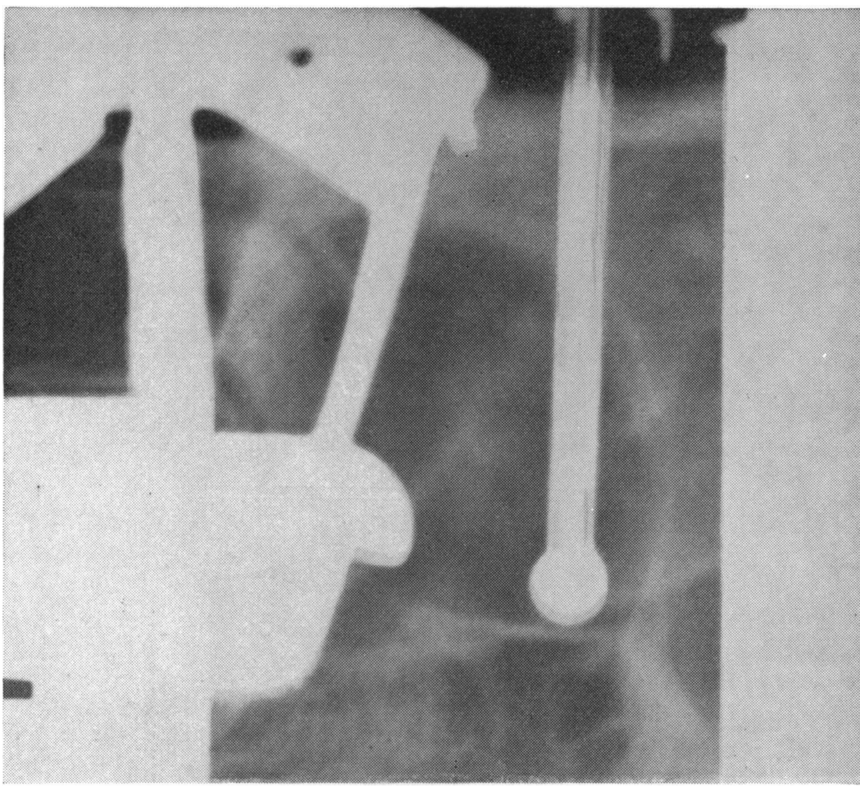

Fig. 3. A radiograph taken in the antero-posterior plane with the animal's head in the stereotaxic instrument. The chamber at the end of the thermode has been placed in the preoptic region. The optic foramina can be seen below the thermode.

Thermode. The thermode (Fig. 4) consisted of a small disk-shaped copper chamber (diameter 5 mm) mounted at the end of stainless-steel tubes. The whole apparatus was coated with a thin layer of 'Araldite' to reduce toxicity to the brain tissue. A bead thermister (Stantel) was embedded in the Araldite to one side of the copper cooling chamber and thus permitted measurement of the temperature near the wall of the chamber.

Radio frequency heaters. A 2 Mc/s, 10 W maximum output radio-frequency generator was used. The electrodes consisted of oval-shaped silver disks (5 × 3 mm) attached to rigid stainless-steel tubes. All metallic surfaces except the inner face of the silver disks were coated with Araldite. The disks were 10 mm apart and a thermister mounted at the end of a stainless-steel tube was placed 3 mm from one electrode, this arrangement was used because it was found that in experiments using egg albumin the mean temperature between the electrodes during heating was represented by measurements taken at a point 3 mm from one electrode.

Temperature controlled room. The temperature in the room used in these experiments was controlled to within $\pm 0{\cdot}5°$ C. The insulation in the walls and the noise of the circulation fan considerably reduced outside sounds which might otherwise have disturbed the animal.

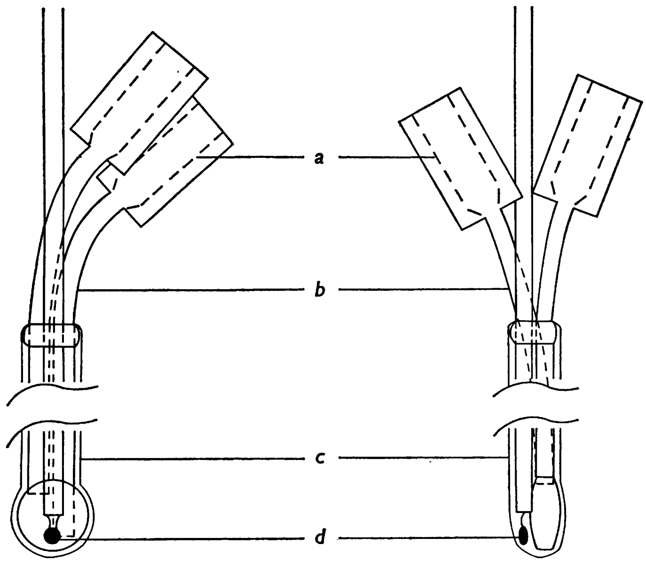

Fig. 4. Illustrates the construction of the thermode. The copper chamber at the end was mounted on stainless-steel tubes. The bead thermister recorded the temperature close to the wall of the chamber. The parts of the thermode implanted into the animal were coated with Araldite. (*a*) Connectors for cooling tubes. (*b*) Stainless-steel tube. (*c*) Araldite coating. (*d*) Thermister.

Recording of data. The frequency with which the pigs turned on the heaters was recorded on a standard cumulative recorder. Each time the pig pressed the switch (response) the penwriter moved a set distance across the chart and each time the heaters came on (reinforcement) the pen gave a brief downward deflexion. It should be noted that several responses in quick succession gave only one reinforcement since the heaters had to go off before a further reinforcement could be obtained.

Use of the thermode. Recordings were begun 15 min after the pig had been placed in the stand and the tubes and wires connected.

In the studies of the effect of cooling the hypothalamus recordings were taken for ½ hr at normal brain temperature. Alcohol from a reservoir at $-50°$ C was then drawn through the thermode by means of suction and the rate of flow adjusted to give a temperature reading on the thermode of 10° C. The very low temperature of the cooling solution was made necessary by the low rates of flow possible through the thermode and the warming effects along the length of the tube from the reservoir outside the room to the animal. This warming was particularly marked at a room temperature of 35° C. Because the temperature of the tubes carrying the alcohol was low, care was taken to insulate them from contact with the animal's skin (Fig. 2).

As a control in some experiments warm water was perfused through the thermode at such a rate as to cause no more than 0·5° C change in thermode temperature.

In some animals the thermode was used to warm the hypothalamus by perfusing water from a bath at 52° C so raising the temperature on the thermode to 43° C.

The temperature gradients produced in the brain by these procedures were determined in acute experiments in which a thermode was implanted into the preoptic region along with a number of thermojunctions at set distances from the thermode. The temperature of the thermode surface was then changed and the temperature changes at each site recorded (Table 6).

Experimental. Pigs were exposed to a series of ambient temperatures between 0° C and 35° C, the sequence being chosen at random. When the animals were exposed twice on one day, different temperatures were used on each occasion.

RESULTS

Effect of cooling the hypothalamus

At the start of the study, two animals were exposed to a series of temperatures and the rate at which the heaters were turned on during a 30 min period when no fluid was passed through the thermode was compared with a similar period when the thermode was cooled (Table 1).

Cooling the hypothalamus increased the number of times the heaters were turned on, especially at temperatures in the region of the thermoneutral zone.

TABLE 1. Thermode cooling. No. of times the heaters were turned on during cooling of the preoptic region and during similar periods preceding and following the cooling)

Animal no.	Ambient temp. (°C)	30 min periods: Before cooling	During cooling	After cooling
1238	0	64	122	68
		111	151	111
	15	35	101	11
		148	262	140
	20	52	84	2
		68	176	67
	25	2	158	4
		17	52	0
	30	0	48	0
		0	29	—
	35	0	0	0
		9	0	0
	Mean of all temperatures	42	99	35
1366	20	58	75	0
		0	107	17
	25	43	79	38
		7	140	4
	30	0	73	34
	35	0	10	0
		0	14	0
	Mean of all temperatures	15	71	12

During the training of these animals and at the end of an exposure, it was noted that, if the experimenter entered the room while the animal was lying down, it tended to get up and begin to respond. The possibility thus arose that any stimulus might arouse the pig and thus increase its response rate. This suggested that the passage of fluid through the thermode might

TABLE 2. Thermode cooling and neutral stimulus. No. of times the heaters were turned on during cooling of the preoptic region compared with a similar period in which a neutral stimulus was applied when the thermode temperature was not changed by more than 0·5° C

Animal no.	Ambient temp. (°C)	Consecutive 30 min periods				
		Neutral	Cool	Neutral	Cool	Neutral
1428	0	285	450	288	—	—
	15	155	347	154	361	30
	20	0	301	35	255	0
		122	326	22	—	—
	25	29	241	0	—	—
		15	320	40	207	0
	30	0	0	0	—	—
	35	0	101	0	—	—
Mean of all temperatures		76	260	67	274	10
1412	0	—	150	69	237	—
	15	16	140	5	88	0
	20	115	118	50	226	69
	25	13	76	5	103	10
	30	—	0	0	0	—
	35	—	0	0	0	—
Mean of all temperatures		48	81	21	109	26
1487	0	149	171	189	236	150
	15	0	104	9	139	6
	20	0	83	0	133	0
	25	15	137	35	58	9
	30	0	71	0	25	0
	35	0	1	0	0	0
Mean of all temperatures		27	96	37	99	28
1424	0	176	365	184	281	126
	15	159	111	156	284	164
		0	15	5	88	0
	25	3	146	6	182	14
	25	0	116	22	0	—
	30	0	128	9	—	—
	35	0	0	0	—	—
Mean of all temperatures		27	125	55	167	76

of itself provide such an arousal stimulus which was independent of the cooling effect. In order to investigate this possibility, the next four pigs were treated as follows. During the first 30 min the thermode was perfused with water at body temperatures (neutral): it was then perfused with cold alcohol (cool) for a further 30 min period (Table 2).

With one exception (animal 1424 at 15° C, Table 2), in animals at ambient temperatures below 30° C cooling the hypothalamus was accompanied by an increase in the number of times the heaters were turned on (Fig. 5 and Table 2). In some instances at ambient temperatures 20 and 25° C the animal was lying down apparently asleep when the cooling period started, but such animals always got up and started to respond.

At environmental temperatures of 30 and 35° C with three exceptions

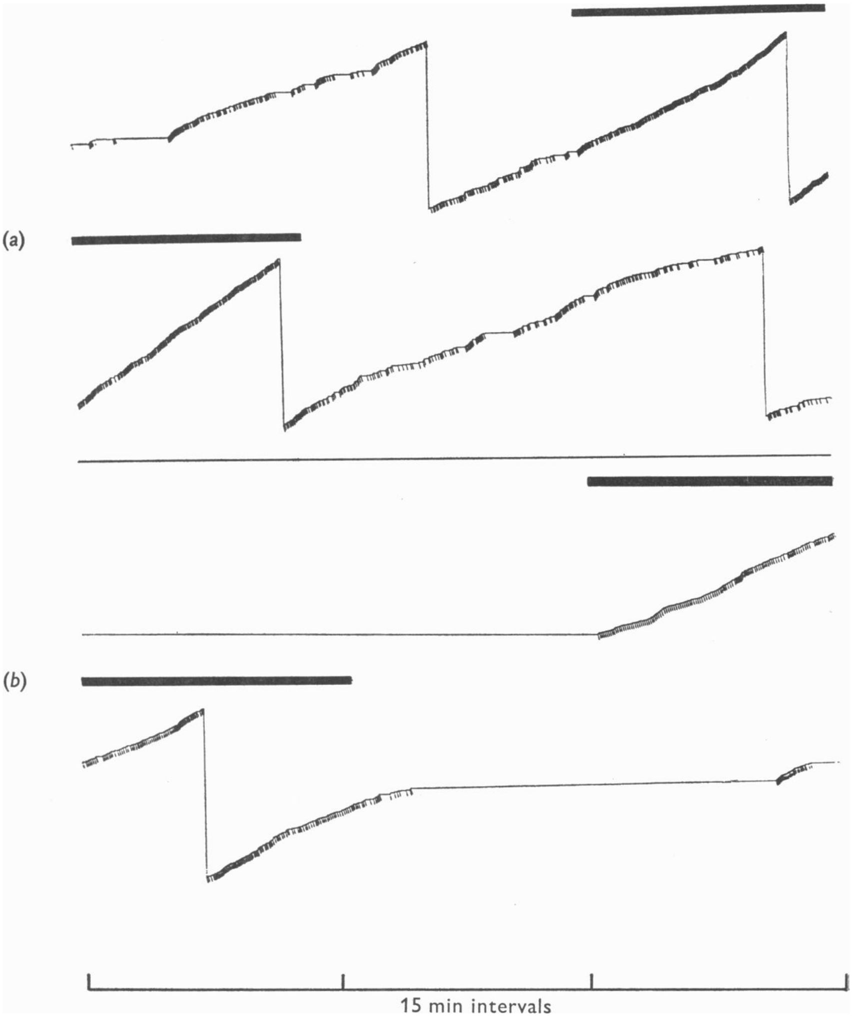

Fig. 5. Records from the cumulative recorder illustrating the effect of cooling the preoptic region by means of a thermode. The slope of the line represents the rate of responding and each downward dash signifies the turning on of the infra-red heaters. Vertical lines are caused by resetting of the recorders and horizontal lines indicate absence of responding. The heavy black lines above the record designate the 30 min period of continuous cooling. (*a*) Recorded at 0° C ambient temperature. (*b*) Recorded at 20° C ambient temperature.

the animals turned the heaters on only during the cooling period and, in about half the experiments, the animals did not respond during either control or cooling periods (Tables 1 and 2).

At environmental temperatures of 30 and 35° C observations of the animals during the period when the hypothalamus was cooled did not reveal any change in posture and the pigs did not shiver.

Thermode controls. It was possible that the increased rate at which the pig responded during periods in which the hypothalamus was cooled was related to non-specific cooling of bone, dura or brain tissue which was

TABLE 3. Thermode cooling-controls. No. of times the heaters were turned on during cooling of region outside the hypothalamus compared with a similar period of neutral stimulus when the thermode temperature was not changed by more than 0·5 °C

	Ambient temp.	Consecutive 30 min period				
Animal no.	(°C)	Neutral	Cool	Neutral	Cool	Neutral
1363	20	50	14	2	5	69
Thermode slightly		41	37	161	86	171
posterior to the		43	87	77	—	—
optic chiasma and	25	85	71	52	31	45
displaced laterally		61	23	38	—	—
almost against the		25	0	0	0	0
bone						
	Total	305	232	330	122	285
	Mean	51	39	55	31	71
1639	15	41	178	139	94	145
Thermode between		25	30	98	20	49
the cerebral hemi-	20	0	0	0	10	43
spheres in the region	25	0	35	26	24	0
of the frontal pole						
	Total	66	243	263	148	237
	Mean	17	61	66	37	59

adjacent to the shaft of the thermode. To test this possibility, two pigs were prepared in which the thermodes were placed outside the preoptic region of the anterior hypothalamus. In one animal (pig 1363, Table 3), the cooling chamber of the thermode was located 1 mm behind the optic chiasma and displaced 7 mm to the right so that it almost touched the bone. In the other control animal (pig 1639, Table 3), the thermode was placed between the cerebral hemispheres in the frontal region of the brain. Table 3 illustrates the results obtained during cooling. It can be seen that an increase in the rate of responding did not take place during periods of cooling.

Effect of heating the hypothalamus

Thermode heating. In the first series of experiments, the brain was warmed by means of a thermode. The number of reinforcements obtained during warming was compared with the mean number of reinforcements imme-

TABLE 4. Thermode heating. (*a*) No. of times the heaters were turned on during 30 min in which the preoptic region was warmed with a thermode compared with similar control periods preceding and following the warming. The percentages refer to the changes in rate made during the period of warming compared with the mean of the rates preceding and following the warming. +ve sign indicates increased rate, −ve sign indicates decreased rate. (*b*) Similar table in which warming lasted 15 min

Animal no.	Ambient temp. (°C)	Control	Warming	Control	Warming	Control	Warming	Control	Warming	Control
					(*a*) 30 min period					
1694	5	145	47 (−47 %)	31	—	—	—	—	—	—
	10	273	149 (−31 %)	156	141 (−77 %)	182	—	—	—	—
1761	0	111	120 (−2 %)	134	—	—	—	—	—	—
	5	100	126 (−4 %)	162	—	—	—	—	—	—
	15	78	59 (−26 %)	83	—	—	—	—	—	—
1734	0	177	159 (−13 %)	190	130 (−32 %)	190	—	—	—	—
	5	116	54 (−42 %)	70	—	—	—	—	—	—
	10	169	83 (−26 %)	90	—	—	—	—	—	—
	15	142	113 (−29 %)	176	124 (−14 %)	114	—	—	—	—
	20	122	81 (−30 %)	121	77 (−40 %)	136	—	—	—	—
					(*b*) 15 min period					
	10	96	17 (−79 %)	67	30 (−64 %)	101	91 (−5 %)	92	78 (−7 %)	68
		101	96 (+28 %)	40	54 (−31 %)	116	8 (−92 %)	82	67 (−26 %)	100

diately before and after warming. The results from three pigs in which the hypothalamus was warmed for 30 min are shown in Table 4*a*. In all instances there is evidence that warming the hypothalamus had an inhibitory effect on the rate at which the heaters were turned on, but the results are not as decisive as those obtained during cooling of the hypothalamus. At no environmental temperature did the animal cease to turn the heaters on during the warming period. Similar results were obtained using 15 min periods of warming (Table 4*b*).

TABLE 5. Thermode heating-controls. No. of times the heaters were turned on during 30 min periods in which the heating or neutral stimulus was applied compared with similar periods preceding and following. The percentages refer to the changes in rate during the period of warming or neutral stimulus compared with the mean of the rates in the 30 min periods preceding and following. +ve sign indicates increase, −ve indicates decrease

	Ambient temp. (°C)		Warming		Warming	
(*a*) Thermode between the cerebral hemispheres. Thermode temperature raised to 43° C	0	166	147 (+15%)	90	106 (+15%)	95
	5	244	204 (−5%)	185	179 (+5%)	155
	10	211	189 (+1%)	165	138 (+13%)	79
	15	154	150 (−1%)	150	163 (+17%)	129
	20	141	102 (−32%)	14	123 (+78%)	125
			Neutral		Neutral	
(*b*) Thermode in preoptic region. Thermode perfused with water at body temperature	0	183	151 (−17%)	178	174 (+12%)	123
	5	169	173 (+11%)	145	137 (−13%)	170
	10	123	131 (−2%)	144	159 (+11%)	139
	15	124	63 (−41%)	88	89 (−11%)	139

Thermode controls. Two types of control were used. In the first, the possibility that the inhibitory effect observed during warming could be elicited by warming any area of the brain, was investigated. A thermode was placed between the cerebral hemispheres and perfused with warm water. The results, presented in Table 5*a*, suggest that warming this region tended to increase rather than reduce the rate at which the heaters were turned on.

The second control was to investigate the possibility that the reductions in the rate of turning the heaters on (Table 4) were associated with the sensations arising from the passage of fluid through the thermode placed in the preoptic region. A thermode was placed in the preoptic region and perfused with water at body temperature. Table 5*b* illustrates that there was no tendency for this procedure to result in a consistent change in the rate at which the heaters were turned on.

Temperature gradients during warming and cooling of the preoptic region with the thermode. Temperature readings were taken from five thermo-junctions at distances between 4 and 15 mm from the surface of the thermode during warming and cooling in five anaesthetized animals. The results are given in Table 6. It can be seen that the temperature changes induced in the brain around the thermode were in the range which might occur naturally. The asymmetrical distribution of the temperature gradients around the thermode is most likely to have been related to differences in the vascularity of the tissue.

TABLE 6. Mean thermal gradients produced in the brain during heating and cooling. Results from five anaesthetized animals

		Position of thermocouple in relation to thermode				
				Lateral		
Heating	Thermode surface	Anterior 9 mm	Posterior 4 mm	5 mm	9 mm	Diagonal 15 mm
		Changes in brain temperatures (°C)				
	43	+0·1	+2·3	+1·1	+0·7	+0·1
				Lateral		
Cooling	Thermode surface	Anterior 7 mm	Posterior 11 mm	5 mm	9 mm	Diagonal 15 mm
		Changes in brain temperature (°C)				
	10	−0·9	−1·1	−2·8	−0·6	0

Radio-frequency heating. The second method used for warming the pre-optic region was by means of radio-frequency heating. This technique had the advantage that the animal could be connected to the radio-frequency generator by means of light wires and was therefore relatively free to move about in a cage during heating.

The rate at which the heaters were turned on while the hypothalamus was warmed to 41·5–42° C was compared with the mean rate observed before and after warming. The rate at which the heaters were turned on during the 15 min of warming declined in most, but not in all instances, and on one occasion (animal 1702 at 30° C) the rate markedly increased (Table 7).

As in the results obtained using the thermode, the effect of warming is not as immediately obvious as the increases obtained during cooling. The first three records displayed in Fig. 6 all illustrate a decrease in the number of reinforcements obtained during the warming period but only in the first record is the effect obvious from casual inspection of the chart. In the fourth record at 30° C the pig had started to turn the heaters on just before

TABLE 7. Radio-frequency heating. No. of times the heaters were turned on during 15 min periods of warming the preoptic region by means of radio-frequency currents compared with 15 min periods immediately preceding and following the warming. The percentages refer to the change in rate during warming compared with the mean of the rates preceding and following the stimulus. + ve indicates increase, − ve indicates decrease

Animal no.	Ambient temp. (°C)	15 min periods Control	Warming	Control	Warming	Control
1693	5*	80	28 (−56%)	46	—	—
	—	87	61 (−28%)	83	73 (−5%)	73
	—	98	46 (−55%)	99	70 (−20%)	76
	—	27	36 (0%)	46	20 (−13%)	1
	—	52	14 (−46%)	1	—	—
	—	25	38 (−27%)	80	—	—
	10	60	76 (+17%)	71	60 (−13%)	68
	15	35	1 (−62%)	18	—	—
		9	6 (0%)	3	7 (+77%)	3
	20	124	86 (+39%)	0	0 (—)	104
1702	10	68	67 (+3%)	62	44 (−19%)	47
	15	86	81 (+14%)	56	—	—
	—	82	88 (−22%)	144	—	—
	—	14	0 (—)	37	—	—
	—	110	23 (−68%)	0	—	—
	20	154	55 (−50%)	66	—	—
		94	80 (−15%)	95	60 (−30%)	80
	30	11	89 (+56%)	21	—	—
1610	5	30	6 (−84%)	44	35 (−40%)	73
	15	58	30 (−54%)	71	51 (+13%)	20
1652	0	53	32 (+12%)	0	—	—
	—	40	41 (+46%)	17	—	—

* Only 1693 at 5° C provides enough data for a *t* test. The effect of warming is statistically significant ($P < 0{\cdot}001$).

the preoptic region was warmed; however, the animal continued to respond throughout most of the period of warming.

General behaviour. Observations of the animal during heating of the preoptic region did not suggest that the process was painful. The panel

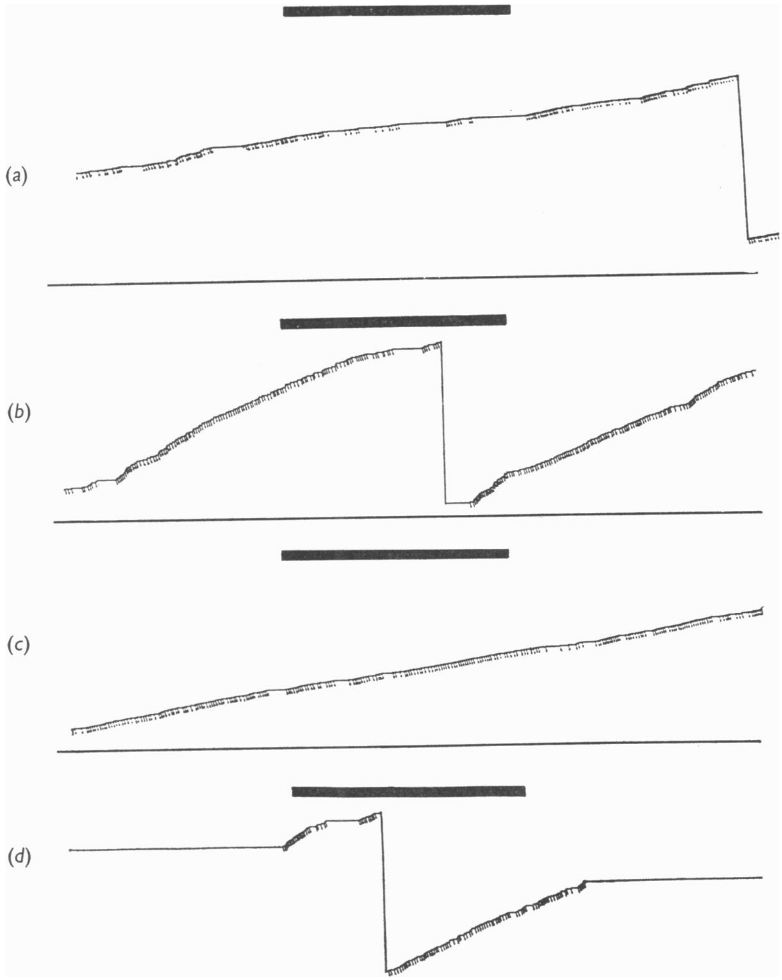

Fig. 6. Records from the cumulative recorder illustrating the effect of warming the preoptic region by means of radio frequency heating. The slope of the line represents the rate of responding and each downward dash signifies the turning on of the infra-red heaters. Vertical lines are caused by resetting of the recorder and horizontal lines indicate absence of responding. The heavy black line designates the 15 min periods of heating. (*a*) Recorded at 15° C ambient temperature. (*b*) Recorded at 20° C ambient temperature. (*c*) Recorded at 5° C ambient temperature. (*d*) Recorded at 30° C ambient temperature.

switch was removed and attempts were made by one observer who was in the room with the pig to determine when the heating was applied by the other investigator who was outside the room. Close observation at an environmental temperature of 20° C failed to reveal any sign that the heating had been applied.

Heating the hypothalamus as a potential reinforcement. Attempts were made to train animals to respond by pushing a panel when the potential reinforcement was a 3 sec burst of radio-frequency heating in the hypothalamus in place of infra-red heat on the skin. The heating was so arranged that hypothalamic temperature increased to over 40° C within less than 0·5 sec of the response and then increased to 41·5–42° C. The animals were either held in the stand or were free to move in a cage. In order to increase the chances of learning, the experimenter gave the potential reinforcement whenever the pig approached the switch, or touched the wall on which the switch was mounted with its snout. Five animals were used, but none displayed any signs of learning to push the panel at either cold or neutral temperatures. Those animals which had been subjected to this procedure for several days were afterwards difficult to train when the reinforcement was infra-red heating, and no attempt was made to use such animals in other experiments. One animal which had received radio-frequency heating to the hypothalamus on approaching the switch over a period of only 2 hr however, rapidly began responding when external infra-red heat to the skin was given in place of radio-frequency heat to the hypothalamus.

DISCUSSION

It is known that local cooling of the preoptic region can produce physiological responses similar to those which occur on exposure to low environmental temperatures, e.g. shivering, increased metabolism, vasoconstriction and release of thyroxine (Hammel, Hardy & Fusco, 1960; Andersson, Grant & Larsson 1956; Andersson, Ekman, Gale & Sundsten 1962). Recently, Satinoff (1964) demonstrated that local cooling of this region can also influence the animal's behaviour. In her experiments, the hair coat was removed and it was shown that when the preoptic region was cooled, the animal increased the amount of heat which it delivered to itself at both 5 and 25° C. The results of the present study confirm and extend these observations in an animal with a naturally sparse coat. The pig will readily learn to press a switch panel in order to obtain infra-red heat (Baldwin & Ingram, 1967) without the necessity for shaving off the coat in order to increase the sensitivity of the animal to cold. This point is important in view of the fact that, when the coat is removed, the physiological responses of an animal may be considerably modified. Thus Bligh (1963) found that the onset of panting in the sheep could be blocked for more than 30 min by removal of the coat, an effect which he attributes to the exposure of cold receptors.

The present results also demonstrate that the stimulus provided by cooling the preoptic region may not always be effective in influencing behaviour at high environmental temperatures. Similarly, the heat sensitivity of the hypothalamus with respect to a purely physiological mechanism can also be modified by environmental temperature (Ingram & Whittow, 1962). The fact that the pigs in the present experiments sometimes ignored the cooling stimulus at temperatures of 30° and 35° C, but never at 25° C, suggests that, when the ambient temperature exceeds the animal's critical temperature, the central stimulus becomes less effective.

Warming the preoptic region slowed the rate at which the heaters were turned on. There is, however, an inherent difficulty associated with experiments in which a potentially painful stimulus slows the rate at which an animal is making a given response. It is always open to question whether the observed inhibition is related to the specific property of the stimulus under investigation (heat) or is simply associated with some aversive sensation. In the present experiments, there was no indication from the pigs' demeanour that the heating was painful, nor did the animals show any signs of reluctance to enter the room, even after several experiments. Moreover, two distinct methods of applying heat to the preoptic region were used with essentially similar results.

Carlisle (1966), using rats, demonstrated that when the hypothalamus was warmed by means of a small electrical heating coil, a reduction occurred in the rate at which the animals turned on an infra-red heater. He observed that even the animal in which the reduction was most marked did not stop responding and, on repeated trials, the effect became smaller. Carlisle concluded from observations on his animals that the heating did not cause pain in spite of the fact that the heaters were found to have produced brain damage.

The failure of pigs to learn to press the switch in order to obtain a short burst of radio-frequency heating to the preoptic region is probably related to the fact that such high hypothalamic temperatures would only occur naturally during severe hyperthermia. This finding is not incompatible with the capacity of such heating to modify the rate at which animals performed a previously learned response to obtain infra-red heating. Moreover, as discussed above, radio-frequency heating did not completely abolish the demand for external infra-red heat which suggests that it does not produce such a powerful sensation of warmth as does peripheral heating.

There is electrophysiological evidence demonstrating the presence of temperature sensitive neurones in the preoptic region of both cats and dogs (Nakayama, Hammel, Hardy & Eisenman, 1963; Hardy *et al.* 1964). Some cells were shown to increase their rate of firing when the local temperature was increased while others responded with an increased firing rate to a decrease in temperature. The heat-sensitive cells were more numerous than the cold-sensitive cells in the dog while in the cat, cold-sensitive cells were not found.

As discussed by Hardy *et al.* (1964) these cells may not be the actual thermal receptors but could be interneurones which were modulated by such receptors. In a recent review, Ogata, Sasaki & Murakami (1966) suggested an alternative explanation for the decrease in activity of the cold-sensitive cells when the hypothalamus was warmed. In their view, when the hypothalamus is heated the warm-sensitive cells suppress the cold-sensitive cells through inhibiting pathways. These authors did not consider the possibility that the decreased activity of the warm-sensitive cells observed during cooling of the hypothalamus would be due to a similar inhibition from the cold-sensitive cells. In any event, it is probable that the response of these temperature-sensitive elements plays a part in the behavioural responses elicited by warming or cooling the preoptic region. Hitherto, it has usually been considered necessary to postulate only central warm receptors in addition to peripheral warm and cold receptors (Benzinger, 1964; Thauer 1961). Probably the neglect of the role of central cold receptors stems from the fact that it is not easy to think of situations in which the deep body temperature falls, without the peripheral cold receptors being previously stimulated. The additional evidence for the existence of cold-sensitive elements in the preoptic region, obtained from behavioural studies, makes it essential that such receptors are included in formulating a hypothesis about control systems to account for the regulation of body temperature.

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