AMRL-TR-67-144

BEHAVIORAL THERMOREGULATION IN RESPONSE TO HEATING AND COOLING OF THE HYPOTHALAMIC PREOPTIC AREA OF THE DOG

JAMES J. ROBINSON

HAROLD T. HAMMEL

FOREWORD

The work reported herein was conducted by the John B. Pierce Foundation Laboratory, New Haven, Connecticut, under Contract No. AF 33(615)-2825 with the Aerospace Medical Research Laboratory, Wright-Patterson Air Force Base, Ohio 45433. Abbott T. Kissen, PhD Biothermal Branch, Environmental Medicine Division, was contract monitor for the Aerospace Medical Research Laboratory. This research was performed in support of Project 7222, "Biophysics of Flight," Task 722207, "Biophysics of Flight: Human Thermal Stress." Harold T. Hammel, PhD was the principal investigator for the contract with the John B. Pierce Foundation Laboratory. The research was begun in May 1965 and completed in April 1967.

The investigation was presented by James J. Robinson for the degree of Doctor of Medicine in Yale University.

This technical report has been reviewed and is approved.

C. H. KRATOCHVIL, Colonel, USAF, MC
Commander
Aerospace Medical Research Laboratory

ABSTRACT

Cooling the hypothalamic-preoptic tissue to a temperature of 32 C causes greatly increased motivation in the dog to press a bar for heat in a cold environment of -5 C. Heating the same region of the brain to a temperature of 42 C causes almost complete suppression of bar pressing. These strong behavioral responses to changes in hypothalamic temperature take place with only very slight changes in rectal temperature. There appears to be an active pathway, between the hypothalamic-preoptic region and the sensory cortex, capable of thermoregulatory function and sensitive to both heat and cold in the hypothalamic-preoptic region.

SECTION I

INTRODUCTION

In a variety of animals including the dog, the hypothalamic-preoptic area of the brain plays a central role in the regulation of body temperature. Heating this area with stereotaxically implanted thermodes causes vasodilatation of the skin vessels and panting in the dog. This, in turn, causes a decreasing body temperature. Cooling the same area elicits vasoconstriction and shivering, which yield a rising body temperature (Bligh, 1966; Hammel, 1968).

In addition to these involuntary physiological responses, there are also behavioral thermoregulatory responses to temperature changes induced by thermodes in this area of the brain. Satinoff (1964) has shown in rats that cooling of the hypothalamic-preoptic area, at environmental temperatures of 5 and 24 C, caused an increase in rectal temperature, vigorous shivering, and a more frequent pressing of a bar to turn on an overhead heat lamp. She did not report experiments in which this area of the brain was warmed. Murgatroyd (1966) has both heated and cooled the preoptic tissue of the rat, and has found bar-pressing to be a function of both central and peripheral inputs. Baldwin, et al. (1966) found similar results in the pig. Cooling of the hypothalamus always increased the voluntary bar pressing to turn on the heat lamp, but this response declined markedly if the environmental temperature was above 25 C. Cabinac, et al. (1965) found that the dog will voluntarily seek a warmer environment when it ingests quantities of cold water, and conversely it seeks a colder environment when ingesting hot water.

The purpose of the present work is to investigate the behavioral response to both heating and cooling of the hypothalamic-preoptic area in the dog.

SECTION II

METHOD

The dog was an adult mongrel female weighing about 17 kgs. Seven thermodes were implanted around the hypothalamic-preoptic area by the method of Hammel, et al. (1963), figure 1. A reentrant tube in the center of the array of thermodes was provided for a thermocouple with which to measure the hypothalamic-preoptic temperature. These implantations were made more than 2 years before the present study and after a brief recovery period the dog has had the run of an outside pen and appears to behave normally in all respects.

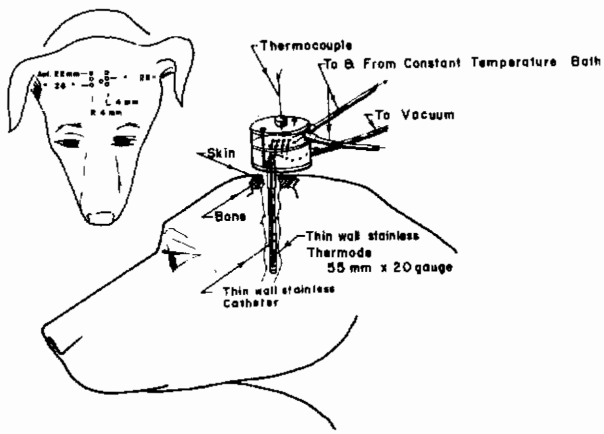

Figure 1. Details of thermode (or reentrant tube) and circulator construction. The circulator is shown in place for thermal stimulation of the hypothalamus. Only the lower acrylic plate or bottom of the circulator is left permanently attached to the thermodes and guides by epoxy resin. (Hammel, H. T., D. C. Jackson, J. A. J. Stolwijk and J. D. Hardy, 1963)

The environmental chamber was an insulated and soundproofed chamber 6 feet x 4 feet x 8 feet with a large squirrel cage fan, which circulated the air through cooling coils to provide a low and constant temperature.

The dog was partially restrained in the chamber in the prone position on an insulated floor. From a point on the top of its harness, a chain extended down each side to hooks in the floor and a third chain led back horizontally and attached to a frame member 10 inches above the floor. A board 6 inches high and placed close behind the dog kept him from backing up. This arrangement restrained the dog, but left his paws free to press the bar, and also permitted free circulation of environmental air around the animal.

A horizontal bar 2 to 3 inches above the floor was located in front of the dog within reach of his paws. A firm downward push of this bar resulted in a 10-second burst of heat from six 250-watt heat lamps suspended 18 inches above the clipped back of the dog. Pushing the bar when the lamps were already on did not prolong the period of heat, and the bar had to be released by taking the pressure off in order to open the actuating microswitch before a second push would reactivate the lamps. This made certain that the dog would not receive a continuous heat reward when holding his head or paws on the bar continuously.

Each press and release of the bar was recorded by a counter and on an event recorder. All bar presses were recorded, including those made during the time the lamps were on, which as mentioned, did not keep the lamps on longer than the original 10-second interval. The actual number of times the lamps were turned on was also recorded.

The thermodes around the hypothalamus were perfused with water pumped through them at a rate of about 100 cc/min in a closed circuit containing a heat exchanger. The latter was located outside the environmental chamber and consisted of a coil of 25 feet of 1/4 inch copper tubing connected in the circuit by flexible plastic tubing, so that the coil could be dropped into one of three constant temperature baths without interrupting perfusion or distracting the dog in any way.

A bypass in the water lines close proximity to the thermodes returned about 90% of the water to the heat exchanger without passing through the thermodes. Only about 10% went through the thermodes. This feature plus insulation of all hoses in the environmental chamber achieved a well controlled water temperature in the thermodes and a fast temperature response when the heat exchanger was moved to a bath of a different temperature. The whole system was designed so that the dog in the soundproofed chamber would not be affected by any noise or other stimuli associated with induction of temperature changes in the hypothalamic-preoptic area of his brain.

The temperatures of the hypothalamic-preoptic area, the rectum, the water just before it entered the thermodes, the skin of the mid-back, and of the environmental chamber were continuously recorded on a Leeds & Northrup recording potentiometer. The bar pressing was separately recorded. The skin thermocouple also reflected the heating of the dog's back by the lamps, causing a small peak in the record each time the dog presses for heat.

Training of the Animal

Certain problems in training a dog to bar-press for heat were considered: (1) He had to be motivated. This was achieved by a cold environmental temperature of -5 C. (2) He had to be trained to lie quietly without trying to escape from the sealed chamber. This training required many hours and was started at room temperature. (3) When placed under a severe cold stress sufficient to motivate him to seek warmth, the natural responses were (a) to seek to escape to warmer environment; (b) to try to move against the restraint and exercise to keep warm; or (c) to curl up in a ball. None of these reactions is conducive to learning to press a bar for heat from the lamps to relieve his discomfort.

The dog was trained to bar-press under less stressful conditions. An automatic feeding machine was designed that delivered a slice of meat when he pressed the bar. The same rules applied as for a heat reward. That is, he must release the bar so as to be able to reactivate the circuit for further reward. This proved to be one of the most difficult things to learn. The dog would tend to hold the bar constantly down, seeking further reward.

After the animal mastered the art of bar pressing for food rewards requiring about twenty sessions over a period of 2 months, he was then placed in the chamber at moderately cold temperatures. Unless the temperature was below 10 C, he did not seem to mind the cold enough to bar-press for heat. At a temperature of -5 C, the dog showed active interest in bar-pressing for heat.

It required about fifty sessions over a period of 6 months to train the dog thoroughly to bar-press consistently for heat every time he was placed in the chamber at about -5 C. The dog's mastery of the system was demonstrated by his waiting until the lamps switched off after 10 seconds before he pressed the bar again for heat, and by his release of the bar to reactivate the system.

Great care was taken to prevent overheating of the dog. A fail proof timing circuit was used to prevent heating overtime. The number and placement of the lamps were such that painful skin temperatures would not be obtained in the -5 C environment even if the lamps were on continuously. Temperatures at many points of the body during continuous use of the lamps were measured with a radiometer to make sure that painful skin temperatures were never reached. The maximum temperature so measured was 42 C. Even one occurrence of overheating the dog might have impaired the authenticity of his future behavioral response.

After training was completed, the thermodes were circulated with water at a temperature of 38.5 C, which was close to his undisturbed hypothalamic temperature. Perfusion at this temperature was continued as a control for 60 minutes. Then the hypothalamic-preoptic tissue was alternately heated and cooled at 15-minute intervals to temperatures of 42 C and 32 C, by placing the heat exchanger alternately in hot and cold constant temperature baths located outside the environmental chamber, without opening the door of the chamber or causing any other noise to distract the dog.

SECTION III

RESULTS

When the thermodes surrounding the hypothalamic-preoptic tissue were circulated with water at body temperature during the control period, the dog bar-pressed at a rate of about 1 press/minute. This was close to the rate observed during the training sessions.

During the 15-minute intervals of heating, bar-pressing was reduced almost to zero. On the other hand, during the 15-minute intervals of cooling the rate of bar-pressing was greater than during any period of training or control.

Figures 2 through 5 show the results of two runs, A and B, on consecutive days. During the control period when the hypothalamic-preoptic tissue was circulated with water at body temperature; an average bar-pressing rate of 0.65 bar presses / minute for run A, and 1.12 bar presses / minute for run B, was noted. This response rate dropped to an over-all average for all the 15 minutes of heating, to 0.20 bar presses / minute for "A", and 0.15 bar presses / minute for "B". During the 15-minute intervals of cooling of the hypothalamic tissue, the over-all average rate increased to 6.0 bar presses / minute for run A, and 4.4 bar presses / minute for run B. Thus, the bar-pressing rate was about 30 times greater when cooling the hypothalamus than when heating it.

Table 1 shows the average bar presses / minute for each 15-minute interval during which the hypothalamic-preoptic area was heated to 42 C, cooled to 32 C or maintained at body temperature (38.5 C) by the implanted thermodes.

The rectal temperature increased slightly when the hypothalamus was cooled and decreased slightly when it was heated.

The skin temperature increased markedly during the cooling intervals when the dog was vigorously bar-pressing for heat. As mentioned above, the spikes in the record are due to direct heating of the recording skin thermocouple by the heat lamps. During the intervals of hypothalamic heating, the skin temperature decreased.

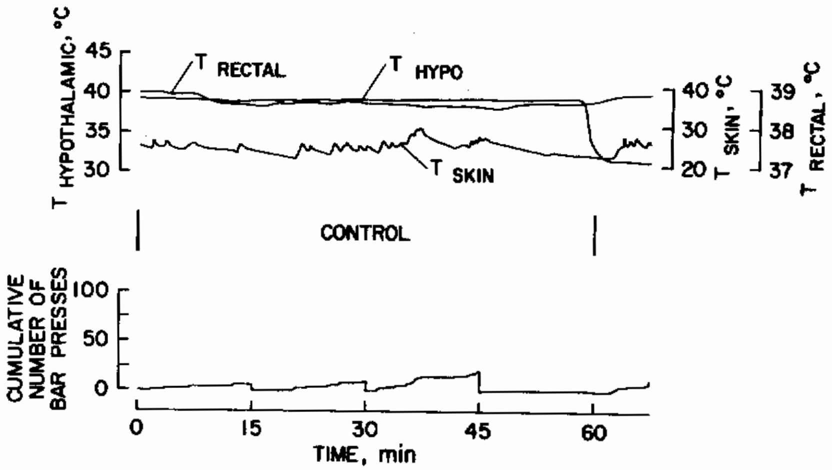

Figure 2. Run A—Control level of bar pressing for heat in a -5 C environment and with hypothalamic temperature at 38.5 C.

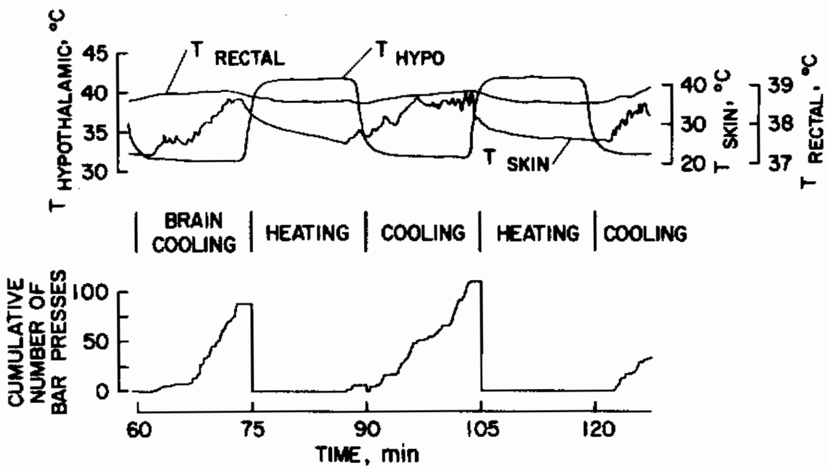

Figure 3. Run A—Bar pressing for heat in a -5 C environment with hypothalamic temperature alternately displaced to 32 C and 42 C for 15-minute intervals.

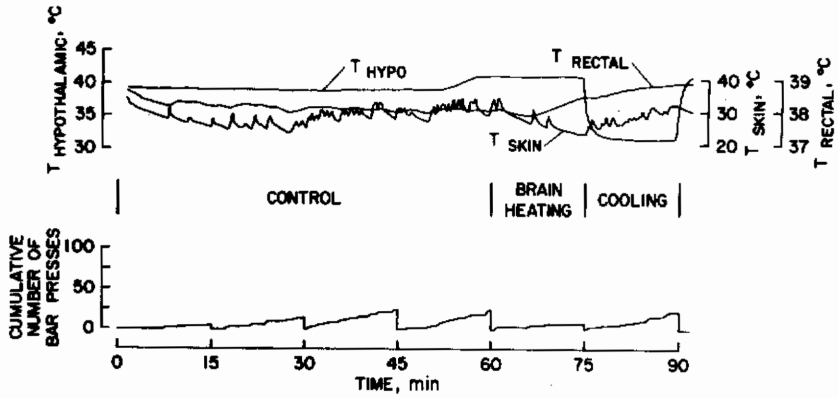

Figure 4. Run B—Control level of bar pressing for heat in a -5 C environment and with hypothalamic temperature at 38.5 C.

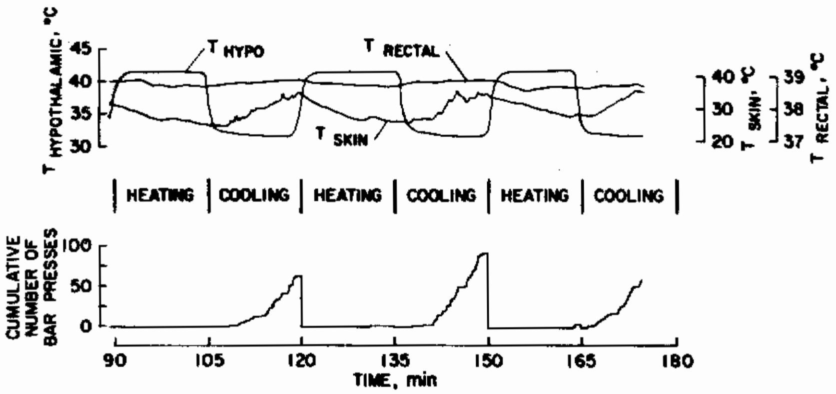

Figure 5. Run B—Bar pressing for heat in a -5 C environment with hypothalamic temperature alternately displaced to 32 C and 42 C for 15-minute intervals.

TABLE I

Bar Presses for Heat per Minute vs. Hypothalamic Temperature

	Run A (Fig. 2 & 3)		Run B (Fig. 3 & 4)	
Time (min)	Presses / min	T_{hypo} °C	Presses / min	T_{hypo} °C
0				
	0.4	38.5	0.3	38.5
15				
	0.7	38.5	1.0	38.5
30				
	1.4	38.5	1.7	38.5
45				
	0.1	38.5	1.7	38.5
60				
	6.0	32	0.5	42
75				
	0.4	42	1.6	32
90				
	7.5	32	0.0	42
	0.0	42	4.3	32
120				
	4.5	32	0.1	42
135				
			6.3	32
150				
			0.0	42
165				
			5.3	32
180				

SECTION IV

DISCUSSION

Changing the thermal environment of a dog activates behavioral and physiological thermoregulatory responses which conserve or dissipate heat as required in order to maintain a constant central body temperature. Also, heating or cooling the hypothalamic-preoptic tissue activates physiological responses that dissipate or conserve heat respectively. The purpose of this work was to show that behavioral thermoregulatory responses are similarly activated by the displacement of the temperature of the hypothalamic-preoptic tissue.

The normal dog can make thermoregulatory responses to a given thermal stress that fall into two classes:

1. Physiological (i.e., vasoconstriction, shivering)
2. Behavioral.

Behavioral responses to a cold stress, as with physiological ones, may be several types:

A. Changing the body configuration to alter the amount of exposed surface, such as curling up in a ball to keep warm.

B. Exercising to keep warm.

C. Moving to a new location to seek a more suitable external environment.

D. Special, trained responses like bar-pressing for heat in a fixed location.

A completely restrained dog must depend entirely on physiological responses for thermoregulation. A dog that is free of restraint may make any combination of the behavioral and physiological responses listed. In responding to a thermal stress, it may:

1. Make only physiological thermoregulatory responses,
2. use a mixture of behavioral and physiological responses, or
3. make only behavioral responses.

The most likely response of the unrestrained dog is to move to a more suitable external environment. The animal used in this work was partially restrained with his paws free to press a bar for a heat reward. Type A behavioral response was difficult with the restraint. Type B could be made only by moving against the restraint. Type C was unrewarding if attempted. The dog had only physiological responses as a satisfactory alternative to bar pressing for heat to maintain his central body temperature. For example, in a cold environment he could vasoconstrict and shiver instead of bar-pressing for heat.

In this work, bar-pressing was chosen as a behavioral thermoregulatory response that could be easily and quantitatively recorded when the dog was restrained in a constant location under fixed environmental conditions. The only change in the environment being the 10-second burst of heat upon pressing the bar. Other behavioral thermoregulatory responses which would complicate the interpretation of the data were kept at a minimum by the partial restraint. The use of measuring thermocouples and thermode circulation equipment in a chamber undisturbed by the experimenter for several hours, also required partial restraint of the animal.

Training of the dog required several steps. First, the dog had to learn to lie quietly while partially restrained in the chamber at room temperature with all equipment operating. Second, it had to learn to bar-press for heat in substitution for the normal behavioral thermoregulatory responses Types A, B and C. It had not only to learn a new response (bar-pressing), it also had to learn that the natural behavioral thermoregulatory responses, A, B and C, are inappropriate in the experimental situation. This was a key step in the training of the dog. Three other dogs were trained to accept restraint and bar-press for a food reward, but would either attempt to escape restraint or would shiver to maintain body temperature instead of bar-pressing when they were placed in the chamber at colder temperatures. Very thorough training was required to get the dog to accept a new form of response, bar-pressing, in place of old patterns of behavioral thermoregulatory responses. A particular dog's performance was also dependent on his level of anxiety and any distractions during his stay in the chamber. Both of these would affect the dog's bar-pressing if he were poorly trained.

In this study, the dog's external environment was kept at -5 C. He could decrease the cold stress by pressing a bar for heat. During the period of hypothalamic cooling, the dog bar-pressed for heat at a rate many times the rate observed when heating the hypothalamus. This result was obtained in spite of the fact that the dorsal skin temperature increased to over 35 C during hypothalamic cooling and decreased to below 25 C during hypothalamic heating. Thus a behavioral response, which may be classed thermoregulatory, was found to depend, in part, upon the temperature of the hypothalamus. Thermoregulatory behavioral responses are, in this regard, like thermoregulatory physiological responses.

If thermoregulatory behavioral responses are controlled by a regulating system, then there must exist a reference temperature with which the actual temperature is compared; and the response is made in accordance with the sign and magnitude of the temperature difference between the actual and the reference temperatures. It would seem that the rate of bar-pressing is compatible with this thesis. The reference temperature was apparently greater than 38.5 C when the dog was bar-pressing at about 1 press / minute in an air temperature of -5 C and with a hypothalamic temperature of 38.5 C. When the brain was heated to 42 C, bar-pressing stopped; so, presumably, the hypothalamic temperature was now above the reference temperature. On the other hand, dropping the hypothalamic temperature to 32 C increased the bar-pressing to 5 presses / minute; presumably, because the difference between the hypothalamic and reference temperatures was increased.

Variations in the normal hypothalamic temperature in the dog are small and do not depend upon the temperature of the external environment; that is, the mean, the standard deviation and the range of hypothalamic temperatures in the hot environment when the dog is stretched out and panting vigorously are the same when the same dog is curled up and shivering vigorously in a cold environment (Hellstrøm and Hammel, 1967). If the hypothalamic temperature is the regulated temperature, it would appear that the effect of a cold environment is to increase the reference temperature for both behavioral and physiological thermoregulatory responses. Conversely, the effect of a hot environment is to decrease the reference temperature for all thermoregulatory response. Presumably, the link between the environment and the regulating system includes thermal receptors somewhere in the skin surface.

The dog used in this work seemed to be well trained and his learned behavioral thermoregulatory response (bar-pressing) was affected by heating and cooling the hypothalamic-preoptic tissue. However, his rectal temperature declined little even with prolonged hypothalamic heating at 42 C for 1 hour in a -5 C environment. Therefore, the dog appeared to be maintaining his central body temperature by shivering, which was not suppressed by heating the hypothalamus even when bar-pressing for heat was suppressed. Prolonged cooling of the hypothalamus beyond the usual 15-minute interval resulted in the continuation of vigorous bar-pressing and finally in attempts to escape the restraint. Normally, this dog did not attempt to move against the restraint.

Based on the experience gained in this study, several improvements in the design of the experiment may be suggested. Only dogs which respond well to hypothalamic heating and cooling by panting and shivering in a neutral environment should be used.

Training should begin at an early age. A thinly furred, highly intelligent and uniform breed of dog - such as the foxhound - should be used. Measurement of physiological regulatory responses should be made concurrent with the behavioral response. A search for a more natural behavioral response should be undertaken for the dog. The response should be a graded response, as easily measured and as quantitative as is bar-pressing. One possibility would be to give the dog a choice between two extreme thermal environments and the freedom to move back and forth between them. The quantitative measurement would be the length of time spent in each environment. Heating the hypothalamus ought to extend the time spent in the cold environment and shorten the time spent in the hot environment for one cycle.

REFERENCES

1. Baldwin, B. A. and D. L. Ingram. "Effects of Cooling the Hypothalamus in the Pig." The Physiological Society, Demonstrations. 15 July 1966, Cambridge.

2. Bligh, J. "The Thermosensitivity of the Hypothalamus and Thermoregulation in Mammals." Biological Reviews 41: 317-367, 1966.

3. Cabanac, M. and J. Chatonnet. "Influence de la Temperature Interne sur le Catactere Affectif d'une Sensation Thermique Cutanee." J. Physiol. 56: 540-541, 1964, Paris.

4. Hammel, H. T., D. C. Jackson, J. A. J. Stolwijk and J. D. Hardy. "Hypothalamis Temperatures in Dog and Monkey and Thermoregulatory Responses to Environmental Factors." Technical Documentary Report No. AMRL-TDR-63-5, Wright-Patterson Air Force Base, Ohio, January 1963.

5. Hammel, H. T. Regulator of Internal Body Temperature. Ann. Rev. Physiol. 30: 301, 1968.

6. Hellstrøm, B. and H. T. Hammel. "Some Characteristics of Temperature Regulation in the Unanesthetized Dog." American J. of Physiol. 213: 547-556, 1967.

7. Murgatroyd, D. "Central and Peripheral Factors in Behavioral Thermoregulation in the Rat. The Physiologist 9: 251, 1966.

8. Satinoff, E. Behavioral Thermoregulation in Response to Local Cooling of the Rat Brain. Am. J. Physiol. 206: 1389-94, 1964.

Security Classification

DOCUMENT CONTROL DATA - R & D

(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classified)

1. ORIGINATING ACTIVITY *(Corporate author)* John B. Pierce Foundation Laboratory 290 Congress Avenue New Haven, Connecticut 06519	2a. REPORT SECURITY CLASSIFICATION 2b. GROUP

3. REPORT TITLE

BEHAVIORAL THERMOREGULATION IN RESPONSE TO HEATING AND COOLING OF THE HYPOTHALAMIC PREOPTIC AREA OF THE DOG

4. DESCRIPTIVE NOTES *(Type of report and inclusive dates)*

Final Report, May 1965-April 1967

5. AUTHOR(S) *(First name, middle initial, last name)*

James J. Robinson
Harold T. Hammel

6. REPORT DATE	7a. TOTAL NO. OF PAGES	7b. NO. OF REFS
February 1968	13	8

8a. CONTRACT OR GRANT NO. AF 33(615)-2825 b. PROJECT NO. 7222 c. Task No. 722207 d. Work Unit No. 722207003	9a. ORIGINATOR'S REPORT NUMBER(S) 9b. OTHER REPORT NO(S) *(Any other numbers that may be assigned this report)* AMRL-TR-67-144

10. DISTRIBUTION STATEMENT

This document has been approved for public release and sale; its distribution is unlimited.

11. SUPPLEMENTARY NOTES	12. SPONSORING MILITARY ACTIVITY Aerospace Medical Research Laboratory Aerospace Medical Div., Air Force Systems Command, Wright-Patterson AFB, OH 45433

13. ABSTRACT

Cooling the hypothalamic-preoptic tissue to a temperature of 32 C causes greatly increased motivation in the dog to press a bar for heat in a cold environment of -5 C. Heating the same region of the brain to a temperature of 42 C causes almost complete suppression of bar pressing. These strong behavioral responses to changes in hypothalamic temperature take place with only very slight changes in rectal temperature. There appears to be an active pathway, between the hypothalamic-preoptic region and the sensory cortex, capable of thermoregulatory function and sensitive to both heat and cold in the hypothalamic-preoptic region.

DD FORM 1 NOV 65 1473

Security Classification

Security Classification

14. KEY WORDS	LINK A		LINK B		LINK C	
	ROLE	WT	ROLE	WT	ROLE	WT
Behavioral thermoregulation responses Physiological thermoregulatory responses Hypothalamic heating Hypothalamic cooling Thermoregulation in dogs						

Security Classification