THE AMERICAN JOURNAL OF PHYSIOLOGY

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THE AMERICAN PHYSIOLOGICAL SOCIETY

VOLUME 169 May 1, 1952 NUMBER 2

Relationship Between Hypothalamic Temperature and Thermo-regulatory Effectors in Unanesthetized Cat

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The existence of temperature sensitive regions in the hypothalamus of the cat has been established (1-3). Though capable of controlling thermo-regulatory effectors (central control), their relative importance in the unanesthetized animal as compared to the effect of afferent impulses (hereafter called 'reflex control'), is not so clear. The present experiments were designed to determine a) whether hypothalamic temperature, directly measured in the unanesthetized cat, varied in a manner consistent with its being an important factor in temperature control under normal circumstances, and b) the limits within which central and reflex mechanisms may act.

For these purposes a small thermistor was implanted in the preoptic region of the hypothalamus of eight cats, with leads coming out through the scalp. After the cats had recovered from this operation, they were placed in a thermoregulated chamber to study the relation between hypothalamic, rectal, ear and ambient temperatures, panting, and respiratory rate. The respective roles of central and reflex control of body temperature in the cat will be discussed.

METHODS AND PROCEDURE

Cats were used because their temperature regulating centers in the hypothalamus had already been accurately located (1, 4), and because uniform skull size permitted placing the thermistor precisely in the hypothalamus with the aid of a standard Horsley-Clark stereotaxic instrument. Female cats were used because they were more docile. They were kept in quarantine until free from all obvious disease for at least 2 weeks.

The thermistor needles were constructed as shown in figure 1 and consisted of a
1-mm. diameter thermistor⁴ mounted on the end of a 2.1-cm. length of double lumened glass capillary tubing, 0.07 to 0.15 cm. in diameter. The needle was set in a stainless steel base with dental cement. The flexible leads from the needle sidearm were made of 28 strands of 0.008-cm. copper wire threaded through vinylite tubing,⁵ and were lashed onto the sidearm with silk ties. All joints or irritant surfaces were covered with red enamel⁶ and black baking varnish.⁷ The vinylite tubing was covered with a nonreactive vinylite solution.⁸ Prior to use in a cat, each needle was calibrated over the expected temperature range and totally immersed in saline for at least 24 hours to test the integrity of the electrical insulation. Two needles were tested again after removal from the cat and the calibration had not changed.

The flexible leads and the thermistor made up one arm of a Wheatstone bridge whose sensitivity was adjusted to give 5 microvolts/0.05° C. The resistance of the thermistor leads was less than 2 ohms, compared to 1000 to 2000 ohms for the thermistor. The only unusual feature of the bridge was a triple throw switch which could increase the bridge current and heat the thermistor without changing over-

all sensitivity. All brain temperatures were registered by a recording potentiometer⁹ to 500 microvolts full scale. Ear and air temperatures were measured by no. 36 B.S. copper constantan thermocouples and recorded on an eight-channel printing potentiometer. All temperatures were ultimately referred to the same precision thermometer which was guaranteed to ±0.1° C. as compared to the Bureau of Standards reference. Owing to various thermoelectric potentials that could not be eliminated entirely, the ear temperatures were accurate to only ±0.3° C. and the room temperature to ±0.2° C. Rectal temperatures were taken 6 to 8 cm. within the anal orifice with a clinical rectal thermometer which was accurate to ±0.05° C., in reference to the standard. Brain temperatures were considered accurate to 0.05° C. compared to the same standard. Respiratory rates were counted with a stopwatch while observing the animal. Humidity and air movement were not measured.

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⁴ Western Electric Co.
⁵ Outside diameter, 0.025-0.029 inches, Surprenant Co., Boston, Mass.
⁶ Glyptal No. 1201 Red Enamel, General Electric Co.
⁸ Fifteen per cent VCMH, two per cent DOP and eighty-three per cent Hexone which was kindly suggested and supplied by G. W. Seagren, Administrative Fellow, Mellon Institute of Industrial Research, Pittsburgh, Pa.
⁹ Brown Instrument Co.
Once the cat was out of isolation and accustomed to handling, control preoperative studies were done in a thermoregulated chamber which could be set at any desired temperature between 0° and 45° C. To avoid disturbing the cat it was observed through peepholes or one-way vision glass. A minimum of four preprandial rectal temperatures under quiet conditions and at room temperatures of 22° to 28° C. were taken on different days over a period of at least a week. On two to five occasions each animal was heated in the chamber until panting occurred, while rectal temperatures and respiratory rates were observed. In four animals, steady state car temperatures were measured over a range of ambient temperatures from 18° to 32° C. The rectal temperatures following exposure to an ambient temperature of 10° C. or below for 1½ hours or more were measured in four animals.

When these control studies were completed, the cat was anesthetized (intraperitoneal sodium pentobarbital anesthesia and atropine), mounted in the stereotaxic instrument, and under sterile precautions, a hole was drilled in the skull at coordinates right 2 mm., anterior 14.5 mm. with a no. 4 drill. The bushing (fig. 1) was screwed perpendicularly into this hole, the dura punctured with a sharp scalpel, and the needle lowered into place by means of the needle holder (fig. 1) which was in turn clamped in the stereotaxic instrument. The flexible leads were brought out through a stab wound in the scalp 3 to 4 cm. behind the needle base. The scalp was closed with silk sutures, dusted with sulfadiazine and covered with a permanent collodion dressing to prevent scratching. A leather collar around the neck was used to anchor all lead wires and relieve any strains on them.

Immediately after operation, the location of the thermistor was checked on a lateral x-ray film of the skull (fig. 2A). The animals usually began eating well the next day and gained weight during the period of study. A mild, superficial, chronic inflammatory reaction occurred around the exit wound in all animals. Eight animals were operated upon and maintained a sufficient time for study. The cats remained in good physical condition until they were killed because the lead wires broke (duration 6–67 days, mean 28). The head was perfused with formaldehyde and the brain sectioned grossly to verify the position of the needle and microscopically to estimate tissue damage.

**Observations**

**Characteristics of Thermistor Needle.** To determine whether conduction of heat along the length of the needle produced a significant error in observed hypothalamic temperature, a heating element was attached to the base of a needle which was inserted part way into the brain of an anesthetized cat. On activation, the heating element increased the temperature of the needle base, thus changing the tip to base temperature gradient. Although the needle base was heated 15° C. hotter than its control value for as long as 5 hours, the temperature registered by the thermistor did not alter significantly (<0.05° C.) as compared to contralateral brain temperatures or rectal temperature. It was concluded that any effect of heat conduction along the needle upon the indicated hypothalamic temperature was negligible since measurements had shown that in situ the needle base temperature varied less than 4°C. under all conditions employed. Because these experiments were too time-consuming to perform on each instrument, similar tests of accuracy were made routinely with a glycerine bath on each needle.

For normal use the electromotive force imposed on the bridge was 0.05 volts which by test heated the thermistor less than 0.05° C. when in a cat brain. The
response time of the entire system was estimated by suddenly introducing the needle into a warm constant temperature water bath. The potentiometer responded immediately and full response (>99%) required about 12 seconds. As this was the response time of the recording potentiometer alone, it can only be said that the thermal lag in the needle was considerably less than 12 seconds.

The materials employed gave no severe tissue reaction. The bushing remained firm in the skull, and while a subcutaneous fibrous tract formed about the leads, the exit wound was almost dry. Examination of the gross brain sections showed no abnormality except for physical displacement of tissue and discoloration along the track. The locations of the needle tips are shown in figures 2B and 2C. Microscopically, evidence of damage was slight and limited to room around the track of entry.

**Recovery of Animal From Operation.** The grand mean (eight animals) of the
individual means of all control rectal temperatures was $38.71^{±0.37}$° C. S.D. $^{11}$ ($±0.35$° C. S.D.)$^{12}$ before operation and increased by an average of $1.07$° C. for a few days after operation. The rectal temperature had to be increased to a grand mean of $39.94^{±0.33}$° C. S.D.$^{11}$ ($±0.72$° C. S.D.$^{12}$) to produce panting before operation and to a mean $0.61$° C. higher than this to produce panting after operation. However, all these temperatures gradually returned to preoperative levels and temperature regulation was considered to have recovered from the effects of the operation when: a) control and threshold rectal temperatures had returned to within $±2$ S.D. of their mean preoperative values; and) b the mean control hypothalamic temperatures,$^{13}$ which were highest immediately postoperatively, had fallen to a plateau or at least a region of little slope. Statistical treatment of observed values was necessary because of the extreme variability of the data. As judged by these criteria the animals had recovered from operative trauma by 2 to 9 (mean 4.6) days postoperatively. After recovery, steady state ear temperature as a function of ambient temperature in four cats was similar to that observed before operation. Likewise the ability of four cats to protect themselves against ambient temperatures of $0°$ to $10°$ C. was unaltered following operation.

Normal Hypothalamic Temperature: Relation to Rectal Temperature and Effects of Anesthesia. Figure 3A shows, for an unanesthetized animal, continuous hypothalamic and chamber temperatures as well as several readings of rectal temperature observed over a period of 4 hours. Hypothalamic temperature showed many small fluctuations within the region from $38.45°$ to $39.10°$ C., but even when the ambient temperature was changed from $2.5°$ to $34.0°$ C., mean hypothalamic temperature appeared uninfluenced by environmental temperature. These records are typical of the findings in all eight cats studied. In general, handling, activity or excitement tended to produce a slow increase in hypothalamic temperature (see fig. 7B where cat was petted) and less constantly, an increase in the magnitude of its small fluctuations. Sleep or rest produced the converse. Cyclic variations in brain temperature, synchronous with the pulse, and analogous to those found by Bazett ($5$) in the arterial blood in man were sought in one cat by means of a fast recorder, but in spite of a hundredfold increase in sensitivity, were not demonstrable. This might have been the result of the time lag of the thermistor.

In figure 3A rectal temperatures were from $0.20°$ to $0.50°$ C. above hypothalamic temperature. Investigation of 53 pairs of simultaneous rectal and hypothalamic temperatures (heated as well as control conditions) on eight healthy, unanesthetized cats disclosed a correlation coefficient of 0.86 which was highly significant. These same data yielded a regression equation: hypothalamic temperature ($°$C.) $= 9.50 + 0.752$ rectal temperature ($°$C.).

The regression coefficient was significantly greater than 0, and significantly less than 1. It is interesting that rectal and hypothalamic temperatures were equal at $38.3°$ C. The regression coefficients on a limited number of similar observations during anesthesia and during fever were not significantly different from the value given above.

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$^{10}$ This grand mean includes many observations that were not accompanied by measurements of rectal temperature at the onset of panting. It is not analogous to the grand means in table 1.

$^{11}$ This includes only the variation of a cat about its mean.

$^{12}$ This includes only the variation of the individual means about the grand mean.

$^{13}$ Estimated with a planimeter.
Figure 3B shows the effects of anesthesia (intraperitoneal sodium pentobarbital) on the relation between hypothalamic, rectal and ambient temperatures in the same cat as in figure 3A. In contrast with the previous record, when the ambient temperature varied over a range of only 20.5° to 35.0° C, the hypothalamic temperature ranged from 34.8° to 38.4° C, with the rectal temperature from 0.5° C below to 0.1° C above it. Both body temperatures were apparently following ambient temperature passively. Moreover, the small irregularities of hypothalamic temperature disappeared almost completely with narcosis.

Deep anesthesia with intraperitoneal sodium pentobarbital regularly produced the poikilothermic state demonstrated in figure 3B. In two animals graded doses of this barbiturate from 1 mg/kg. up to that necessary to produce deep anesthesia did not affect hypothalamic or rectal temperatures until the animals were deeply anesthetized. These results were, however, complicated by the excitement produced by the anesthetic.

The converse of these observations was seen during the recovery of the cats from anesthesia. The narcosis had to be light enough to permit a strong corneal reflex, withdrawal reflexes of the limbs and licking movements of the tongue before the animals were able to maintain their internal temperatures in ambient temperatures of 22° to 25° C.

**Hypothalamic Temperature and Respiration.** Heating affects respiration by
producing heat polypnea and panting. The term 'heat polypnea' will be used to designate a sustained increase in respiratory rate up to 200/minute occurring when a cat was heated, while the term 'panting' will be reserved for shallow respiration of a rate greater than 200/minute with the mouth open and tongue protruded, often occurring in bursts and often of sudden onset and cessation. Continuous close observation was required to interpret respiratory changes because excitement or interest in the environment produced periods of rapid shallow respiration which could be confused with heat polypnea. Even panting was not uniformly significant because a) it could be facilitated by meowing or yawning, and b) it could be temporarily suppressed by external stimuli or by volition.

Heat polypnea and panting were produced by two methods, convective heating and radiant heating. In the former the chamber temperature was kept between 21° and 25°C. for an hour's control period and then raised to 36° to 40°C. until panting ensued. In the latter, the chamber temperature was kept between 21° and 25°C. throughout and the cat was warmed by means of radiant heaters after a control period of 1 hour.

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14 This corresponds roughly to the 'interpanting' of Hemingway (6) and the 'polypnee thermique central organique' of Richet (7).
Figure 4A records the typical changes in hypothalamic temperature and respiratory rate observed in five of seven animals when they were heated convectively. While the ambient temperature was maintained at 25°C (control period), the hypothalamic temperature ranged between the extremes of 38.05°C and 38.90°C. When ambient temperature was increased, hypothalamic temperature gradually rose but heat polypnea and panting did not appear until hypothalamic temperature had reached 39.30°C and 39.50°C, respectively, values which were considerably outside the control range. Twenty-one similar experiments were recorded on these five cats (cats 7, 8, 10, 11 and 14). These results are in accord with the hypothesis postulating control of panting by hypothalamic temperature. Animals giving this type of result therefore can appropriately be called 'central' panters (8). The conditions of these experiments, particularly the disturbance of taking rectal temperatures, precluded correlating cessation of panting and decline of hypothalamic temperature.

### Table I: Summary of Observations on Panting and Heat Polypnea

<table>
<thead>
<tr>
<th></th>
<th>Preoperative Rectal Temp., °C</th>
<th>Postoperative Rectal Temp., °C</th>
<th>Hypothalamic Temp., °C</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Control Increment with Panting</td>
<td>Control Increment with Panting</td>
<td>Control Increment with Heat Polypnea Increment with Panting</td>
</tr>
<tr>
<td>Central panters (cats 7, 8, 10, 11, 14)</td>
<td>38.84 ± 0.12 S 1.43 S</td>
<td>38.76 ± 0.17 S 1.49 S</td>
<td>38.44 ± 0.31 0.64 S 0.04 S</td>
</tr>
<tr>
<td>Reflex panters (cats 5, 17)</td>
<td>38.83 ± 0.24 NS 0.66 NS</td>
<td>38.90 ± 0.74 NS 0.74 NS</td>
<td>38.38 ± 0.14 0.02 NS 0.38 NS</td>
</tr>
</tbody>
</table>

These figures given are the means (and standard errors) of the mean values for each cat in the group. NS denotes no significance, S denotes significance, both at the 0.05 per cent level or below. S (NS) within a box indicates that the mean does (does not) vary from zero. S (NS) between boxes indicates that the means in the contiguous boxes do (do not) vary significantly from each other.

The two remaining cats yielded results of the type seen in figure 4B. Panting occurred during convective heating without any significant change in the hypothalamic temperature readings. Similar results were obtained in 10 experiments on these cats (cats 5 and 17). As an added precaution rectal temperatures were not taken in the particular experiment illustrated in figure 4B in order to avoid disturbing the animal. Such results cannot be explained by changes in hypothalamic temperature and support the existence of a reflex (or sensory) control of panting. These animals will from now on be designated 'reflex' panters to use again the terminology of Richet (8). It is important to note that each cat was consistent in the type of response it showed.

Radiant heating then was used to reveal the effects of cutaneous temperature sensation on the control of heat polypnea and panting. The heat was sufficient to raise superficial skin temperature to 40°C. Except that the animals became more restless, the results in four cats (five experiments on three central panters and one reflex panter) were not significantly different from those obtained during convective heating, i.e. the central panters showed the type of relationship seen in figure 4A, and the reflex panters that seen in figure 4B.

Table 1 compares the means of the pertinent rectal and hypothalamic temperature measurements for the reflex and central groups during panting experiments,
radiant and convective data combined. The control data were similar in the two groups and were not altered by the operation. The increments in rectal and hypothalamic temperatures with heating were significant in the central panters but not in the reflex panters. With panting rectal temperature rose significantly more than the hypothalamic temperature in the case of the central panters ($P < 0.05$), but not in the case of the reflex panters ($P > 0.05$).

Finally, to separate more clearly the effects of changing central temperature from those of changing surface temperature, experiments similar to those of Pickering (9) in man were done on two cats (cat 7, a central panter; cat 17, a reflex panter). A stiffened vinylite tube was slipped into the stomach during 30 seconds of nitrous oxide anesthesia. The animals tolerated this very well, but had to be restrained in a light mesh bag. They were then brought to the panting state by convective heating, which was continued while 50 to 100 ml. of ice water were introduced by nasal tube into their stomachs.

![Fig. 5. Effect of ingestion of intragastric ice water during panting on respiratory rate and hypothalamic temperature.](image)

The effects of intragastric ice water on hypothalamic temperature and respiratory rate in the central panter (one of two experiments with similar results) are shown in figure 5. Immediately after cold water was introduced into the stomach hypothalamic temperature fell; at the same time panting ceased and respiratory rate returned to within normal limits, despite unchanged ambient temperature. As the brain temperature rose again, first heat polypnea, and then panting, returned, although at hypothalamic temperatures slightly lower than before.

The reflex panter (three experiments) showed a similar drop in hypothalamic temperature upon introduction of cold water, and a similar cessation of panting, but respiratory rate remained definitely above normal. Control experiments in both animals, a) using water at body temperature, and b) circulating water at $45^\circ$ C. and $5^\circ$ C. through a closed double lumened tube in the esophagus, did not affect either hypothalamic temperature or breathing.

Figure 6A summarizes the pertinent data on heat polypnea, panting and hypothalamic temperature for all seven cats. In the five central panters panting never occurred until the hypothalamic temperature had exceeded the upper extreme of the control range for each cat, with the exception of only one experiment. Heat polypnea followed the same pattern although less regularly. When radiant heating was used (indicated with an ‘R’) the results were similar to those obtained with convective heating.
In the two reflex panters, on the other hand, hypothalamic temperature at the onset of panting was always below the upper extreme of the control range in a given animal, although it was above the mean control temperature for the individual run in nine of eleven instances. On these two animals the relationship between the onset of heat polypnea and hypothalamic temperature was quite irregular. Heat polypnea thresholds are not indicated in the last two experiments on cat 17 (fig. 6A) because the respiratory rate did not return to normal between runs.

Collectively the data in table 1 and figure 6A indicate that in reflex panters (two cats) changes of hypothalamic temperature (at the site measured) cannot alone explain the onset of panting, whereas in central panters (five cats) the correspondence between hypothalamic temperature and panting is quite convincing. Two other possible factors were considered, viz. a) rate of change of hypothalamic temperature, and b) duration of heating. Neglecting the smaller irregular fluctuations of hypothalamic temperature, the rate of change of hypothalamic temperature at the onset of, or during panting was greater than control rate in only 2 out of 35 experiments (including both central and reflex panters). Similarly for heat polypnea, the rate of change was significantly greater in only 3 out of 36 experiments. Duration of heating in individual cats often varied twofold without consistent change in the level of the hypothalamic temperature which was associated with panting. However, the mean of the mean durations of heating until panting appeared was 38 ± 16 minutes S.D. in the reflex cats and 70 ± 11 minutes S.D. in the central cats. These means were significantly different (P < 0.05). Thus it can be concluded that rate
of change of hypothalamic temperature is not important. Duration of heating is probably unimportant though reflex cats on the average did pant sooner than did central panters as well as at relatively lower rectal and brain temperatures.

**Hypothalamic Temperature and Cutaneous Vasomotor Changes.** The finer control of body temperature is generally held to depend upon vasomotor responses affecting cutaneous blood flow. To study a representative area, viz. the ear, the relation between hypothalamic, ear and ambient temperature (18° to 28°C.) was investigated. In order to record ear temperature, animals were placed in a loose mesh bag with no. 37 B. and S. copper constantan thermocouples affixed to their ears with adhesive tape. As shown in figure 7 A, when ambient temperature was changed from 24° to 27° and 29° C., vasoconstriction in the ear gave way to intermittent vasodilatation, while average hypothalamic temperature fell. Conversely, change of ambient temperature from 29° to 23° C. produced vasoconstriction while average hypothalamic temperature did not change, or rose slightly. In 16 of 62 observations on five cats, hypothalamic temperature rose just prior to cutaneous vasodilatation. In 12 of these 62 observations, the change of vasomotor state could be explained by the rate of change of hypothalamic temperature. Chance alone could produce these rather small numbers of positive relationships.

It must be emphasized that observations on the vasomotor state were limited to the ambient temperature range of 18° to 28° C. for several reasons. First, the steady state ear to air temperature gradient decreased as the ambient temperature...
rose above 28° C. and could no longer be used as an index of vasomotor tone. Secondly, since exposure to ambient temperatures as low as 6° C. for a reasonable length of time did not lower hypothalamic temperature and since the cats were all vasoconstricted at 18°C, experiments at ambient temperatures below 18°C contributed little.

Figure 6B summarizes the hypothalamic temperatures at which vasodilatation and vasoconstriction were observed in the ears of five cats. Hypothalamic temperature and vasomotor state were not consistently related at ambient temperatures between 18° and 28° C. Moreover, with respect to the more rapid smaller fluctuations of hypothalamic temperature, vasodilatation was often associated with a brief drop in brain temperature, and vasoconstriction with a brief rise. The first of these effects might well have resulted from cooling of the blood produced by a sudden large increase in the circulation through cool superficial tissues. Conversely, a sudden decrease in the peripheral loss of heat owing to vasoconstriction would explain the second.

Figure 7B shows ear and hypothalamic temperatures when ice water was suddenly introduced into the stomach by nasal tube, as described above, at ambient temperatures associated with vasodilatation. In this example the hypothalamic temperature dropped as much as 0.5° to 1.0° C. in 5 minutes, accompanied by vasoconstriction of a magnitude and duration depending on the dosage of cold water. These results were typical of eight out of nine experiments in two cats (cats 7 and 17). Injecting water at 37° to 39° C. into the stomach and circulating water at this temperature through a closed double lumenated gastric tube had no demonstrable effect on ear temperature. Ice water circulated through this same tube did produce a slight vasoconstriction without demonstrable change in hypothalamic temperature but this was minor in comparison to the vasomotor changes seen upon the direct introduction of ice water into the stomach.

Vasodilatation was difficult to produce by the injection of hot water intra-gastrically, probably because of the smaller safe heat load (8 cal/gm.) of the hot water as compared to that of the ice water (34 cal/gm.) Dilatation was produced in four out of seven trials in cat 7, but as much as 230 cc. of hot water was needed. In all respects, the vasomotor responses of reflex and central panters were similar. Experiments using radiant heating with the ear shielded were unsuccessful because of the difficulties of restraint.

**DISCUSSION**

Careful preoperative and postoperative control studies were necessary to demonstrate that the cats had recovered from the effects of anesthesia, operation and insertion of the thermistor. Although operation increased temporarily both resting rectal temperature and rectal temperature at the onset of panting, these figures had returned to normal before hypothalamic temperatures were accepted with any confidence. Microscopic sections showed only a moderate tissue reaction to the thermistor limited to 100 µ from the track. Therefore the animals were considered essentially normal. As expected of normal animals, fever following operation or during infection elevated hypothalamic temperatures as well as the thresholds at which panting occurred. Intrapertoneal sodium pentobarbital interfered with thermoregulation pari passu with the development of anesthesia. Rectal and hypothalamic temperatures offered no evidence of specific effect of this barbiturate upon thermoregulation, agreeing with some reports (10) and disagreeing with others (11). Sweating
and piloerection were not studied because of the difficulties of obtaining sufficiently quantitative observations without disturbing the animal.

No convincing explanation can be offered for the small irregular variations in hypothalamic temperature seen in unanesthetized cats. They might conceivably be due to changes in local heat production or heat exchange, or to movements of the thermistor in relation to the thermal gradients within the brain. This mechanical explanation can be definitely eliminated because vigorous shaking of the cat's head had no immediate effect on registered hypothalamic temperature.

Aside from these irregular variations in hypothalamic temperature, the mean rectal and hypothalamic temperatures described here are in general agreement with other data on the cat (3, 12, 13) but differ from Bazett's data on man (5) for he found the jugular bulb temperature from 0.6° to 1.4° C. greater than the rectal. In any case it appears that rectal temperature cannot be used as a safe measure of hypothalamic temperature. The correlation between hypothalamic and rectal temperature did not change significantly in fever or under the poikilothermic conditions of anesthesia which suggests that the differences are a result of the geometric configuration of the body heat mass, rather than the result of physiologic regulation.

Part of the results are compatible with the hypothesis of central control of the thermoregulatory effectors through the temperature of the hypothalamus. First, in five out of seven cats heat polypnea and panting did not occur until the hypothalamic temperature had risen above the control range (fig. 6A). Second, the introduction of ice water into the stomach lowered hypothalamic temperature and produced vasoconstriction and a cessation of panting in spite of an unchanged ambient temperature (figs. 5 and 7B). Thirdly, radiant heating, which should have exaggerated cutaneous temperature sensation, changed neither the hypothalamic temperature nor the time at which panting appeared from those values seen with convective heating. However, the first two types of experiment could not prove the activity of a central control because regions in addition to the hypothalamus were stimulated by the procedures, while the third type was exceedingly indirect. An attempt was made to heat the hypothalamus locally with the thermistor itself but failed because of the thermistor's small size. In view of the known existence of central panting in the anesthetized cat (1) it is probable that the panting experiments are examples of central control. On the other hand, the role of hypothalamic temperature in producing vasoconstriction following the introduction of ice water into the stomach is questionable, because the hypothalamic temperature associated with this vasoconstriction was often significantly greater than the temperature associated with vasodilatation at some other time during the experiment (fig. 7B). Analogous results were seen when vasodilatation was produced by the introduction of large amounts of water at 47° C. into the stomach. While the evidence from the intragastric ice water and radiant heating experiments supports the case for central control of respiratory thermoregulation, it is weakened by the fact that the reflex panter (cat 17) gave similar results. The coarse nature of central control in these cats is demonstrated by the large hypothalamic temperature 'threshold', i.e. 0.7° and 1.0° C. for heat polypnea and panting, respectively.

Some of the data emphasize the possible importance of sensory or reflex control. First, reflex heat polypnea and panting were demonstrated in two out of seven animals in a range of hypothalamic temperatures from 0.8° C. below to 0.6° C. above the mean normal (fig. 6A). Second, the vasomotor state was clearly unrelated to hypothalamic temperature in five cats, central as well as reflex panters (fig. 6B).
These observations were restricted to a region within 0.6° C. of the mean normal hypothalamic temperature because of procedural limitations. Third, in all of four experiments on two cats, when shivering was produced by lowering the ambient temperature, it was not related to hypothalamic temperature. It is assumed that any temperature gradients between the anterior hypothalamus and the posterior heat gain center (1) are minimal. The vasomotor changes produced by the introduction of hot and cold water into the stomach may be examples of central control as discussed in the preceding paragraph, and if so, would be exceptions to the results of the second group of experiments. In spite of the lack of a relationship between vasomotor state and hypothalamic temperature under ordinary conditions, there was a critical ambient temperature between 24° and 27° C. for all cats under steady state conditions, below which they were constricted and above which, dilated.

The occurrence of reflex panting was unexpected since this is reported to be unusual (14) or nonexistent (15) in cats. It might be suggested that the registered hypothalamic temperatures in the reflex panters were in error and that the cats were actually central panters. First, the thermistor might have been misplaced. However, gross and single microscopic sections showed that the thermistors were in the region outlined by Ranson (4), except in cat 5, a reflex panter (fig. 2C) where the thermistor was in the anterior part of the third ventricle but in firm contact with the hypothalamus bilaterally and anteriorly. While the thermistors were located in only one of the four known hypothalamic thermoregulatory centers (4), the gradients between them are probably negligible (12). Second, the thermistor might have registered the hypothalamic temperature incorrectly or altered the actual hypothalamic temperature. The physical tests discussed above are considered to eliminate the possibility of an error in instrumentation and the physiological control tests to eliminate the possibility of significant damage to the temperature regulatory centers from the experimental procedures. Moreover, without regard to the accuracy of the hypothalamic temperature measurements, it may be assumed that there was a real difference between the reflex and central panters because 1) the reflex panters were distinctly more restless and apprehensive than the central panters before operation; and 2) rectal temperature increase with panting was greater in the central panters, although this difference was below the level of significance in the preoperative data (table I). No adequate explanation can be offered for the occurrence of reflex panting in some cats and not in others.

The use of the ear-air temperature gradient as an index of peripheral vascular tone might be criticized on the grounds that the ear is not representative of the peripheral vascular system. However, ear and paw temperatures were found to react similarly under changing ambient conditions (2 cats). Since sympathectomy of the ear (in the dog) abolishes its thermoregulatory vasomotor changes in the temperature ranges studied here (16), it was assumed that variations in ear-air temperature gradient of the cat result from changes in general vasomotor tone rather than from local temperature effects upon the vessels.

Under the given conditions, the thermosensitive hypothalamic temperature regulatory center of the cat is apparently a coarse thermostat, demanding changes of more than 0.6° C. for activation. This is in accord with its reported sensitivity of 0.5° C. for vasomotor changes (17) and of several degrees centigrade for panting (1). The present data and those of Ström (17) give a much larger hypothalamic temperature threshold for vasodilatation in the cat (0.5° C.) than that found by Pickering in man (9) by more indirect methods (0.01°-0.10° C.). Since thermoregulatory ac-
tivity was demonstrated in the absence of hypothalamic temperature changes of these magnitudes, reflex control must have been of considerable importance. The extent of this reflex control varied with the individual. Although reflex and central control have been discussed separately for purposes of exposition, the activation of effectors more probably depends on the summation of their several influences.

**SUMMARY AND CONCLUSIONS**

Thermistors were implanted in the hypothalamic region of eight female cats. These animals showed no ill effects and were maintained until the electrical connections broke. Hypothalamic temperature in unanesthetized cats, exposed to ambient temperatures of 0° to about 30° C., showed small irregular variations amounting to as much as 0.5° C. about a relatively constant mean which was independent of environmental temperature and was an average of 0.1° C. below the average rectal temperature. During anesthesia the small variations disappeared almost entirely and hypothalamic temperature fell or rose slowly with environmental temperature. In five out of seven cats heat polypnea and panting produced by heating were correlated with rises in hypothalamic temperature. In the remaining two cats, this correlation was lacking.

In the great majority of all experiments on all of five cats, there was no correlation between vasomotor tone, as indicated by ear temperature, and hypothalamic temperature.

It is thought that these data are compatible with the hypothesis of combined central and reflex control of thermoregulation, and that heat polypnea and panting in most unanesthetized cats are primarily under coarse central control, while vasomotor thermoregulation is primarily under fine reflex control.

The authors are greatly indebted to Dr. E. M. Landis for his advice and criticisms and to the members of the Department of Physiology and its technical staff for their suggestions. Dr. W. R. Christensen set up the x-ray methods used. Dr. David M. Hume was kind enough to test the tissue reactions of some materials used. The microscopic sections were prepared through the cooperation of Dr. William Jaques and Dr. W. E. Ehrich.

**REFERENCES**