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Factors Influencing Hypothalamic Temperatures

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FACTORS INFLUENCING HYPOTHALAMIC TEMPERATURES

by

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BIOGRAPHY

Robert Devon Mc Cook was born in Columbus, Georgia, January 23, 1929.

He graduated from Byrd High School of Shreveport, Louisiana in June, 1945. In September, 1945, he entered Centenary College in the same city. Three years later he transferred to Louisiana State University in Baton Rouge, Louisiana. In February of 1950 the College of Chemistry and Physics of that institution conferred upon him the degree of Bachelor of Science. In August of 1952 he received the degree of Master of Science from the same college.

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List of Publications:

1. McCOOK, R.D. and PEISS, C.N. An integrating cardiotachometer for optical or pen recording. J. Applied Physiol. 14: 473, 1959.

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CHAPTER I

INTRODUCTION AND LITERATURE REVIEW

The warm blooded animal or homoiotherm maintains a remarkably stable body temperature under changing ambient conditions. This temperature is regulated by different means in different species. Most animals are capable of raising their internal temperature by shivering, and heat may be conserved by vasoconstriction. Vasoconstriction would be of more use to the animals having less hair such as man as compared to the hairy animals such as the dog and cat. However, vasoconstriction of effective radiating areas such as the ears of these animals would have a useful effect.

The reaction of these animals to excess heat is vasodilatation in most species but with the same reservations that apply to vasoconstriction. Many animals such as the dog and cat pant and there is evidence for human panting under extreme conditions. Humans rely largely upon sweating for effective heat loss, and are one of the few animals that do. The foot pads of dogs and cats show sweating, but these areas are too small to have significant thermoregulatory function.

Much research has been done on the control of these temperature regulating mechanisms. Warming of the blood flowing in the carotid artery of experimental animals results in foot pad sweating, peripheral vasodilation and hyperventilation (1, 2). The inference is made that these are the effects of the heat reaching regulating centers within the brain. If the preoptic and supraoptic regions of the hypothalamus in the cat are heated, the animal exhibits strong heat loss reactions including panting and sweating of the foot pads (3). This heating is best accomplished by using high frequency alternating current (1 megacycle) of low voltage. This current is passed between two electrodes of insulated wire with an active uninsulated portion at the tips. These wires may be inserted in exact areas of the brain using stereotaxic techniques, and the heat produced between them may be carefully controlled by varying the voltage. A voltage of 11 to 15 volts will produce a temperature rise of 6 to 12°C.

The importance of the hypothalamus as a temperature regulating center was further elucidated by Clark et al (4, 5). In a large series of cats, lesions were placed by stereotaxic means in the hypothalamus. These lesions varied in size and location but were as bilaterally symmetrical as possible. These cats were allowed to recover in an incubator and were tested afterwards in a cold box at about 44°F and in a hot box at about 104°F. Damage to the

preoptic and supraoptic areas, if not large enough to cause death, led to loss of ability to regulate in the hot box. The animal did not pant or sweat on the foot pads and rectal temperature rose until the experiment was terminated. Lesions in the caudal part of the lateral hypothalamus were most effective in eliminating cold response mechanisms. When the animal was placed in the cold box he was unable to maintain a normal temperature and shivering was usually abolished. These same animals also showed impaired tolerance to heat, with loss of panting and sweating. In contrast, cooling of the hypothalamus in the intact animal led to shivering (6).

It is thus seen that the hypothalamus is important in the control of temperature in the cat, and its importance in the human is thought to be as great. Benzinger (7, 8, 9, 10) believes that it is the only regulator of sweating in man. Man regulates against heat mainly by vasodilation and sweating. Vasodilation is effective only in climates which are cooler than mean skin temperature. Sweating must account for most of the heat loss in man and for almost all of the heat loss at ambient temperatures above 35°C. The extreme importance of sweating in man is thus seen. Benzinger in a careful set of measurements using a gradient calorimeter (11, 12) has attempted to show a direct relationship between hypothalamic temperature and sweat rate in man. The hypothalamic temperature was assumed to be the same as that of the

tympanic membrane because the internal carotid artery supplies most of the blood to these two areas.

The subject was placed in the warm calorimeter and the mean skin temperature, the tympanic temperature and the total sweat loss were measured. Benzinger found, under these conditions, that total sweat loss closely followed tympanic membrane temperature, and he then equated this with hypothalamic temperature. Further elucidation of the relationship between hypothalamic and tympanic temperatures will be given in the experimental portion of this dissertation. Benzinger worked with steady state conditions and his results differed from others working with dynamic conditions (13).

Once the importance of hypothalamic temperature has been established it is necessary to show what factors affect this temperature. Most workers have assumed that hypothalamic temperature is the same as the temperature of the arterial blood that perfuses it (7, 8, 14). This blood comes from the internal carotid and vertebral arteries in man, and from the external carotid and vertebral arteries in the cat. A very small amount of blood is also supplied by the anterior spinal artery in both species and by the very small internal carotid in the cat.

The hypothalamus lies deep within the brain and has a very high rate of metabolism (15). The heat thus formed must be carried away by the

blood passing through the area, as it cannot be effectively lost to the surrounding area by conduction because of the small temperature gradient and the low thermal conductivity of the tissue. The hypothalamus, especially the anterior portion, is extremely vascular and therefore well suited for transferring this heat to the blood (16, 17). Under these conditions the blood should be cooler than the hypothalamus and a reduction of blood flow should cause an elevation in hypothalamic temperature. This elevation was shown by Donhoffer (18) in a short communication but no explanation or significance was given. Lowenbach (14) also noted this change, but he believed that the blood was warmer than the hypothalamus. He interpreted the hypothalamic temperature elevation as a reflex increase in metabolism caused by lowered oxygen tension.

Lowenbach worked with cats under pentobarbital anesthesia which were maintained in a steady thermal state by means of a heating pad. His animals were also under artificial respiration. He concluded that: 1) "The hypothalamus, probably very active metabolically, exceptionally well supplied with blood that has had little chance to lose heat on its short and well insulated path, maintains a temperature below that of the blood. 2) The same region when deprived of sufficient oxygen either by occlusion of the carotid artery or by asphyxiation, responds selectively with prompt increase of this temperature."

It thus appears that further elucidation of the effect of blood flow upon the hypothalamic temperature, and the effect of barbiturates upon the blood flow and temperature of the hypothalamus is desirable.

CHAPTER II

MATERIALS AND METHODS

The cat was chosen as the experimental animal in this study due to its uniform head shape. Forty mongrel cats of both sexes were used, weighing between 1.5 to 3 kilograms. The cats were anesthetized with 3 mg/Kg of Sernylan (phencyclidine HCl) injected into the saphenous vein. Sernylan was chosen as the anesthetic because it appears to cause less disturbance of the temperature regulating mechanisms than any other anesthetic tested. Animals treated with Sernylan maintain an even unlabored respiration and normal heart rate and blood pressure. These animals were capable of maintaining steady internal temperatures provided they were not subjected to great thermal stress. Animals anesthetized with the more common induction agents such as pentobarbital or chloralose exhibited a steady decline in body temperature and could only be maintained by applying external heat. Sernylan is claimed to act primarily on the cerebral cortex. Cats treated with 3 mg/Kg of Sernylan intravenously rapidly reach a surgical anesthesia level but do not exhibit muscular relaxation.

Once the cat was anesthetized, an incision was made in the throat, both carotid arteries exposed and a loose ligature placed around each. The animal was then placed in a Johnson or Kopf stereotaxic instrument and carefully aligned. The scalp was retracted from the top of the head and small (about 2 mm) holes were drilled through the skull directly above the areas of the brain to be studied. Bone bleeding was controlled with bone wax when necessary. The dura was carefully punctured with a needle and 22 gauge hypodermic needle thermistors were lowered into these holes until the tip containing the thermistor was at the point to be investigated. In every animal, the stereotaxic coordinates were: anterior hypothalamus - A 14, RL 1.5, H-4; posterior hypothalamus - A 8, RL 1.5, H-4 (17).

Arterial temperatures were measured with a thermistor placed in the end of a small polyethylene tube. This tube was inserted into the femoral artery and fed in until the tip was in the aorta. Axillary temperatures were measured through the brachial artery. Several measurements were taken of carotid artery temperature by directly penetrating the artery with a 24 gauge needle containing a thermistor. This procedure was very difficult due to bleeding and clotting and usually could only be used as a terminal procedure.

Tympanic membrane temperature was measured by inserting a teflon tubing with an exposed bead thermistor at its end through one of the hollow

insulated ear bars that hold the cat in the stereotaxic instrument. This same type of probe was also used to measure temperature of the cerebral cortex by placing the bead 2 - 4 mm under the surface of the brain. The three probes described above are shown in Figure 1. The 22 gauge needle probe (YSI No. 514) is on the left, the teflon probe (YSI No. 520) is in the middle, and the polyethylene probe (YSI No. 511) is on the right.

These probes are each connected in a Wheatstone Bridge circuit, the other three arms of which are wirewound resistors. The wirewound resistors were chosen because they have a low temperature coefficient of resistance, thus reducing errors caused by resistance changes in the inactive arms of the bridge. The bridges can be balanced for thermistors of varying resistances over a wide temperature range. The balance values were recorded from a ten-turn potentiometer. The minimum voltage that will cause self heating of the thermistor in free air was determined by balancing the bridge at one voltage with the thermistor placed in still air, and checking for balance at one half of the voltage. Minimum voltage causing self heating was found to be about 640 millivolts. The voltage across the bridge was then reduced to 160 millivolts which reduced the power in the thermistor to one sixteenth of the value that caused self heating. The total power in the thermistor was approximately 5 microwatts.

The voltage developed across the bridge was recorded with a Grass Polygraph using a Model 5P1 preamplifier. Sensitivities were in the range of 5 cm deflection/$^{\circ}$C. Early records were taken using a photokymograph and sensitive Kipp galvanometers. The sensitivity with the galvanometer was about 4 cm/$^{\circ}$C.

The probes were calibrated by placing them in a thermos of water that was gently stirred. Once the water was at the desired temperature, a small amount of heat was continuously added to maintain an extremely stable temperature. The thermistors being calibrated served as indicators of the stability of the calibrating water temperature. The temperature was measured with a Certified thermometer calibrated to 0.1°C and estimated to 0.01°C. All thermistors to be used in a single experiment were calibrated at the same time so that errors in the water bath would cancel out. Temperature measurements, therefore, have an absolute accuracy of about 0.05°C and a relative accuracy of 0.01°C. The probes were rechecked at a later date and were found to have drifted less than 0.05°C over a three year period. Whenever possible the positions of the probes were changed for different experiments so that the anterior hypothalamic probe in one experiment was used for the posterior hypothalamic probe in another experiment. This also served to cancel out errors in relative temperatures. The time constant for the hypodermic needle probes was 0.6 sec in air.

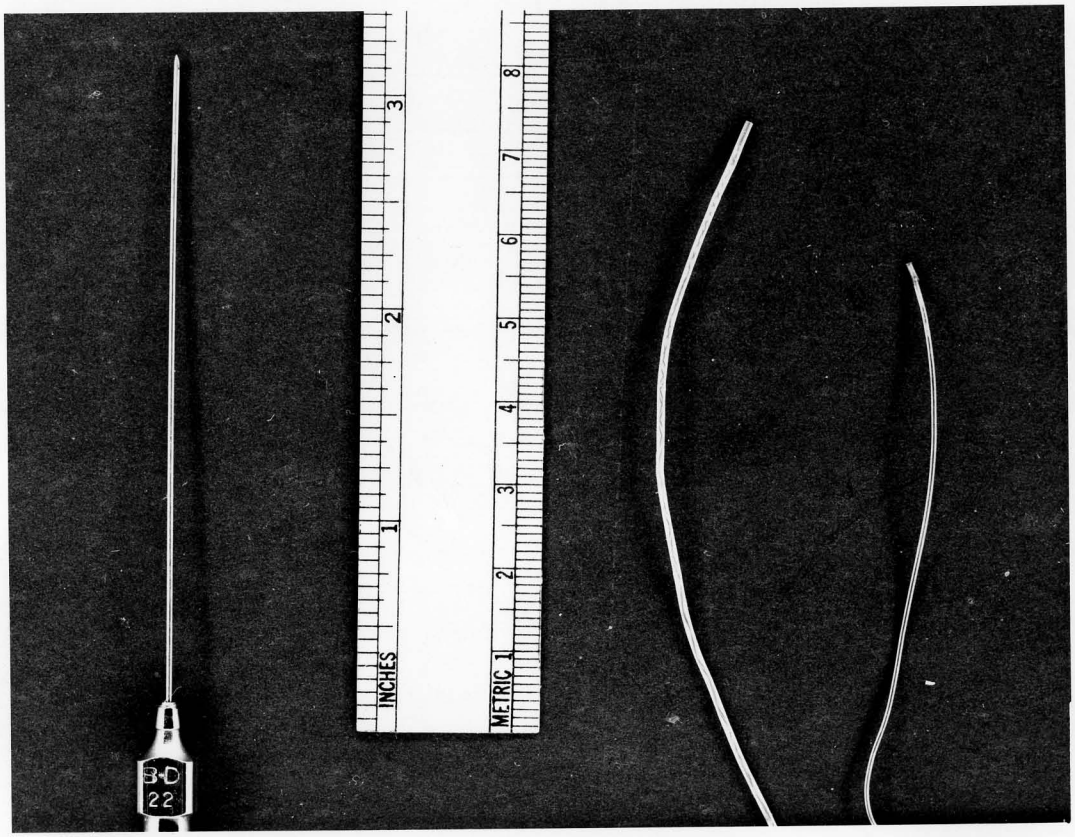

FIGURE 1

THREE TYPES OF THERMISTOR PROBES

See Text for Description

Carotid occlusion was done by rapidly pulling upon the loose ligatures previously placed around the carotid arteries and clamping the thus exposed arteries with miniature artery clamps. The occlusion was released by removing both clamps. Pentobarbital, when given, was administered through the saphenous or femoral vein. Cold saline was given through the same route. At the end of the experiment the animal was sacrificed with an overdose of thiopental.

CHAPTER III

RESULTS AND DISCUSSION

Ten separate measurements performed in ten cats showing the relationship of blood temperature to hypothalamic temperature are given in Table I. It may be seen that blood temperature was below hypothalamic in all cases except cat 106. This contrasts sharply with the findings of Lowenbach (16) who found aortic and subclavian blood temperatures to be above hypothalamic. A critical examination of his published data however shows at least some exceptions. Blood leaving the heart is probably of a uniform temperature but immediately begins to exchange heat through the arterial wall to the surrounding tissues. The more peripherally the blood is measured the more chance there has been for exchange. Ideally for these experiments the blood in the arteries leading to the hypothalamus should have been measured. The carotids should be the most appropriate of the available arteries for these measurements. It will be noted that the difference between carotid blood and hypothalamic temperatures (underlined in Table I) are consistently higher than other arterial to hypothalamic temperature differences. On the basis of the gradients measured in these experiments, it must be concluded that the hypothalamus is cooled by the arterial blood perfusing it.

TABLE I

COMPARISON OF ARTERIAL AND HYPOTHALAMIC TEMPERATURES IN CONTROL CONDITIONS

Cat No.	Artery	Arterial Temp. °C	Hypothalamic Temp. °C	ΔT °C
102	carotid	38.95	39.70*	.75
103	aorta	36.38	36.40	.02
104	axillary	33.68	33.91	.23
105	axillary	38.15	38.20*	.05
106	aorta	39.83	39.78*	-.05
111	aorta	39.34	39.71	.37
112	aorta	39.41	39.47*	.06
113	carotid	37.95	38.30	.35
114	carotid	36.39	36.98	.59
139	carotid	38.18	38.74	.56
MEAN				.29

* Posterior hypothalamus; all others anterior hypothalamus.

Different areas of the hypothalamus show different temperatures. The anterior hypothalamus was always found to be cooler than the posterior, as shown in Table II and in Figure 2. This could, of course, be due either to lower metabolism or higher blood flow in this area. The data of Finley (16) and Craigie (17) suggest the later cause. This high vascularity of the anterior hypothalamus may aid in its role as a blood temperature sensor.

When both common carotid arteries are occluded the temperature of the anterior and posterior hypothalamus was elevated. These results were obtained without fail in all animals. The amount of elevation varied considerably. This elevation should be related to the amount of blood flow reduction and to the metabolism of the tissues in the area of the probe. If arterial blood actually warms the hypothalamus, total occlusion of the blood supply to the brain should result in a fall in these hypothalamic temperatures (20). Within 15 - 20 seconds following bilateral carotid occlusion (vertebrals intact), both anterior and posterior hypothalamic temperatures rose continuously for two minutes (the length of the occlusion), reaching a maximum approximately 0.5 $^{\circ}$C higher than the pre-occlusion control level (Figure 2). The extent and slope of the temperature rise would, of course, be greater if the vertebral arteries had also been occluded. The slope of both curves was steeper following release than during occlusion. It is quite clear, therefore, that arterial

TABLE II

COMPARISON OF ANTERIOR AND POSTERIOR HYPOTHALAMIC TEMPERATURES IN CONTROL CONDITIONS

Cat No.	Anterior Hypothalamus °C	Posterior Hypothalamus °C	ΔT °C
103	36.40	36.54	.14
104	33.91	34.02	.11
105	38.17	38.35	.18
106	39.61	39.78	.17
111	39.71	39.85	.14
112	39.34	39.47	.13
113	38.30	38.42	.12
114	36.98	37.13	.15
120	37.67	37.83	.16
121	38.17	38.23	.06
122	39.55	39.76	.21
123	40.85	40.93	.08
130	38.24	38.80	.56
131	37.32	37.80	.48
132	37.03	37.35	.32
133	37.80	38.15	.35
134	38.20	38.43	.23
135	38.83	39.02	.19
136	37.55	37.78	.23
140	37.45	37.69	.24
141	38.20	38.50	.30
147	39.57	39.69	.12
148	38.80	39.07	.27
MEAN			.21

blood temperature must be lower than that of the hypothalamus (as shown by previous measurements) and that the flow of blood through the highly vascular hypothlamus normally cools the thermosensitive elements.

Figure 3 shows an actual record with tangents drawn giving the maximum rate of rise and of fall in both areas. The temperature in both areas begins to rise shortly after occlusion as was shown in Figure 2 and quickly reaches a maximum slope. After about one minute the slope of the anterior hypothalamic temperature shows a definite decline, and the posterior temperature also shows a smaller rate of rise soon after this. Upon release of occlusion, there is an almost immediate fall in anterior temperature and a delayed fall in the posterior. The maximum rise and fall of each area is indicated by the tangents drawn to the curves and the value of this maximum is given in the Figure. The anterior hypothalamic temperature curve shows a slight but real overshoot when the occlusion was released. This overshoot was a common feature of the anterio hypothalamus and occasionally appeared in the posterior hypothalamus. The initial rise in temperature should be proportional to the local metabolic rate. The reduction in rate of rise should be due to lowered oxygen tension and to increased loss of heat through the blood that is entering by means of the vertebral supply. More heat would be lost to this blood because of the increased hypothalamic blood temperature gradient and possibly because of the increased blood flow from the vertebral arteries. The flow increase

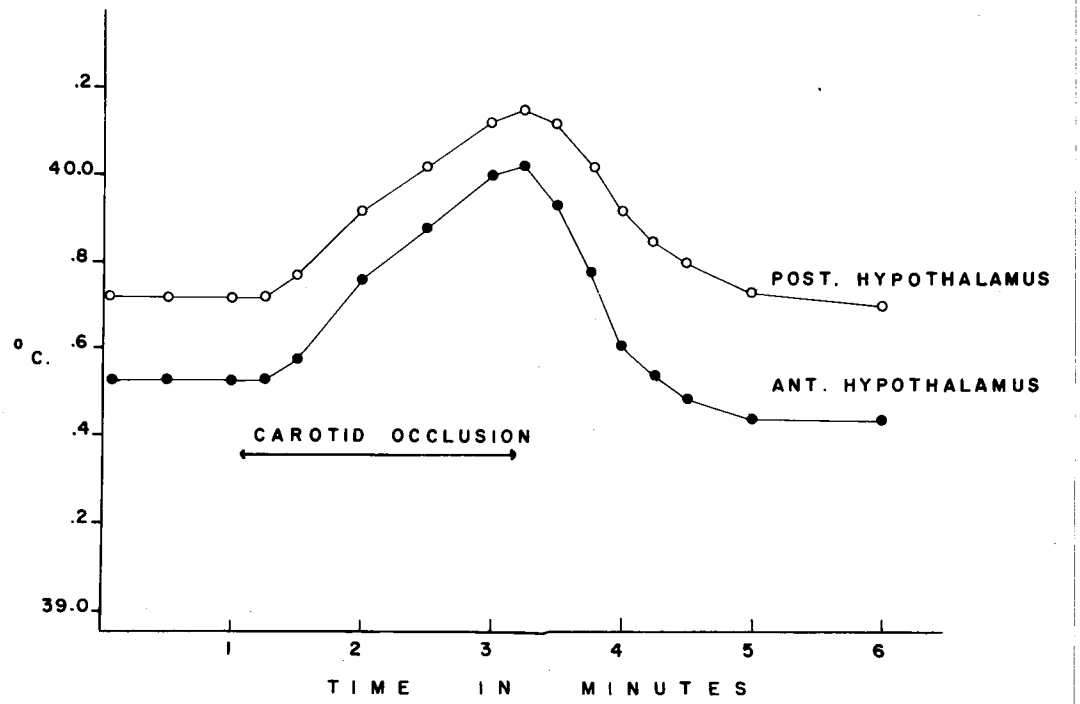

FIGURE 2

CAROTID OCCLUSION

Effect of bilateral carotid artery occlusion on temperatures in the anterior and posterior hypothalamus. Stereotaxic coordinates were: **Anterior Hypothalamus A 14,** RL 1.5, H-4. **Posterior Hypothalamus A 8,** RL 1.5, H-4.

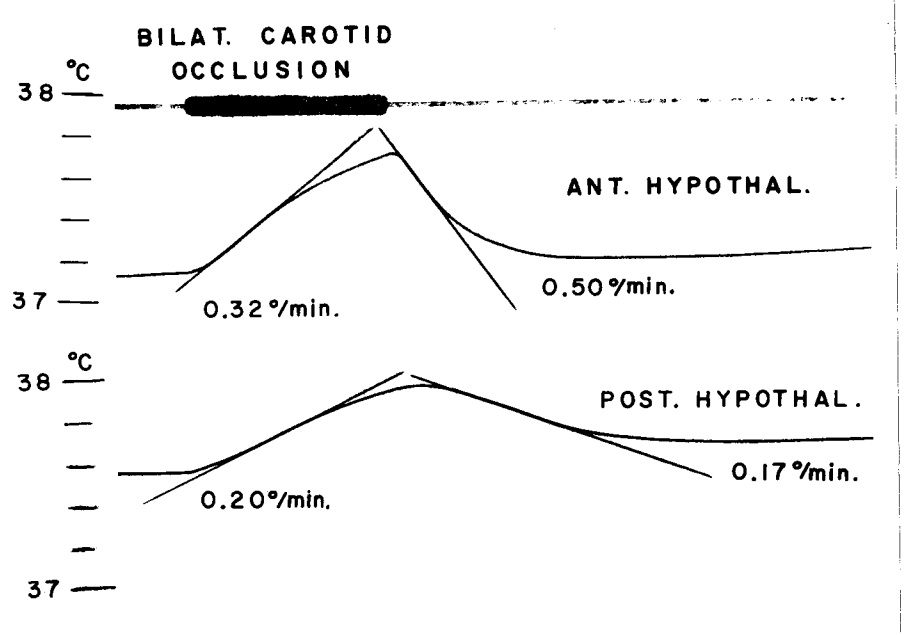

FIGURE 8

SLOPE OF TEMPERATURE CHANGE OF ANTERIOR AND POSTERIOR HYPOTHALAMUS UPON BILATERAL CAROTID OCCLUSION

Top to Bottom:

1) Signal Marker, showing occlusion duration.

2) Anterior Hypothalamic Temperature A 14, RL 1.5, H-4.

3) Posterior Hypothalamic Temperature A 8, RL 1.5, H-4.

might result from local vasodilatation and a reflex increase in arterial pressure. That local vasodilation (reactive hyperemia) has occurred is strongly suggested by the rapid return of the temperature to control upon release of the occlusion and by the presence in many cases of an overshoot where the temperature goes below control for a short period.

The difference in slopes of rise in the anterior and posterior hypothalamic temperature (Table III) is most likely due to a difference in metabolic rate of the two brain areas. It is possible that this difference might be due to differential rates of blood flow to the two hypothalamic areas during the period of carotid occlusion. However, there is no convincing support of this hypothesis at the present time. The anterior rate of rise is seen to be higher than the posterior in all except cat no. 147 where the posterior slope is slightly greater. It may therefore be concluded that the metabolic rate of the anterior hypothalamus is greater than the posterior. Since the temperature of the anterior is lower, the flow through this area must be much greater in order to conduct away the higher heat production and leave it cooler than the posterior hypothalamus.

When the occlusion is released, the initial slope of the temperature drop (Table IV) should be proportional to the temperature difference between hypothalamus and blood and to the increased rate of blood flow through the area.

TABLE III

SLOPE OF RISE IN ANTERIOR AND POSTERIOR HYPOTHALAMIC TEMPERATURE UPON CAROTID OCCLUSION

Cat No.	Anterior ^{o}C/min	Posterior ^{o}C/min
103	.10	.08
104	.16	.15
111	.10	.09
112	.26	.23
120	.12	.07
121	.25	.20
122	.32	.18
130	.27	.13
131	.15	.14
132	.28	.20
133	.12	.10
134	.38	.28
135	.09	.08
136	.28	.18
140	.38	.27
141	.27	.13
147	.23	.25
148	.34	.32
MEAN	.23	.17

The much higher slope of the temperature fall in the anterior hypothalamus is best explained by its large vascularity. As previously noted, the rapid decline of temperature upon the release of occlusion, and the appearance of overshoot in one or both curves, strongly suggests that reactive hyperemia has occurred. Reactive hyperemia is a common occurrence in other tissues such as muscle but has not previously been demonstrated for brain. Due to this hyperemia the rate of fall of temperature upon carotid release cannot be used to calculate the flow of blood through the area under resting conditions. Relative flow through these areas might, however, be estimated by use of the relative metabolic rate obtained from the rising slope and the relative temperature of the areas.

If all of the blood flow were removed from the area the initial rise in temperature should be equal to the resting rate of metabolism. Therefore, the metabolic rate (assuming no blood flow) for the anterior hypothalamus as seen in Figure 3 would be 0.32 calories per gram of tissue per minute. Similarly the metabolic rate of the posterior hypothalamus would be 0.20 cal/g/min. These calculations assume a specific heat of brain tissue of 1.0 and therefore the temperature rise in ^{o}C/min would be equal to the heat produced in cal/g/min. Assuming a R.Q. of 1.0, the heat produced should be approximately 5 Kcal/L O_2 or 5 cal/cc O_2. The oxygen consumed in the anterior

TABLE IV

SLOPE OF FALL IN ANTERIOR AND POSTERIOR HYPOTHALAMIC TEMPERATURE UPON RELEASE OF CAROTID OCCLUSION

Cat No.	Anterior ^{o}C/min	Posterior ^{o}C/min
103	.23	.13
104	.35	.18
111	.09	.05
112	.40	.25
120	.20	.11
121	.36	.20
122	.74	.29
130	.33	.13
131	.32	.14
132	.65	.26
133	.20	.17
134	.41	.24
135	.05	.05
136	.48	.24
140	.33	.22
141	.23	.09
147	.38	.25
148	.40	.20
MEAN	.34	.18

hypothalamus would be:

$$\frac{0.32 \text{ cal/g/min} \times 100}{5 \text{ cal/cc } O_2} = 6.4 \text{ cc/100g/min}$$

Similarly, the oxygen consumption of the posterior hypothalamus would be 4.0 cc/100g/min. These values compare favorably with the value found by Kety (21) for the whole brain of man. This value calculated from A-V differences and flows obtained from the H_2O method was 3.3 cc/100g/min with a reported R.Q. of 0.99. Values of metabolism obtained by carotid occlusion are minimum values since they neglect the continuing flow of blood through the vertebral arteries. The actual values should be somewhat higher but due to the small size of the vertebrals are probably no more than 50% greater than this value. That the metabolic rate of the hypothalamus is greater than that of the whole brain has been shown by in vitro studies (12).

SODIUM PENTOBARBITAL EFFECTS

When intravenous sodium pentobarbital in a sub-anesthetic dose (5 mg/Kg) was given to the animal, an immediate and pronounced fall in hypothalamic temperatures occurred. These effects are shown in Figure 4, and tabulated in Table V. This fall in hypothalamic temperatures occurred without fail and reached an average value of 0.46° within six minutes after which the

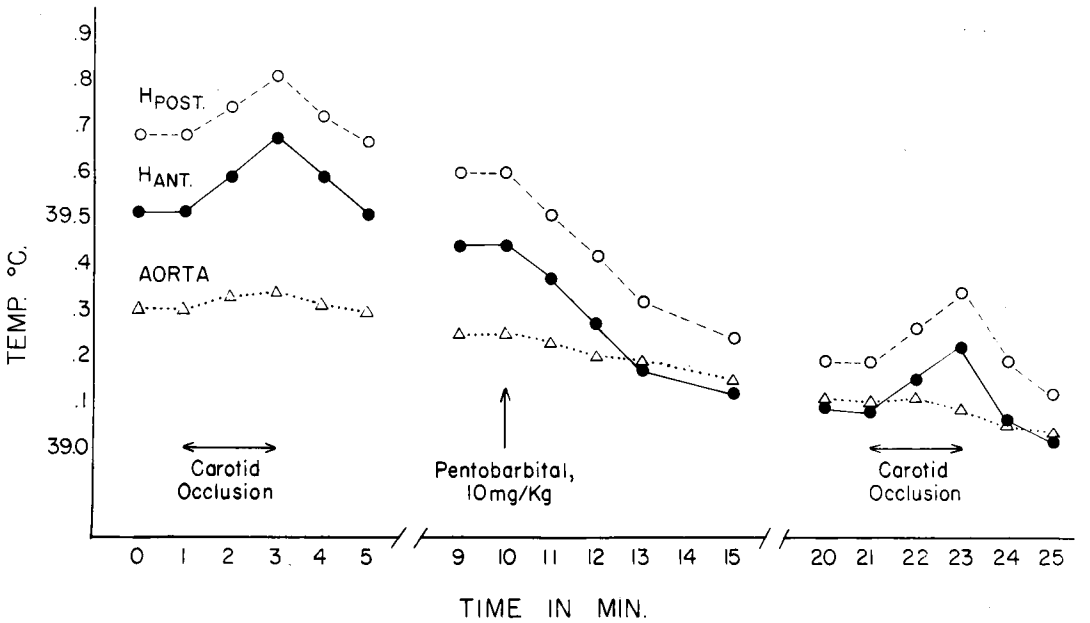

FIGURE 4

PENTOBARBITAL EFFECTS ON CAROTID OCCLUSION RESPONSE

Top to Bottom:

1) **Posterior Hypothalamus A 8, RL 1.5, H-4.**

2) **Anterior Hypothalamus A 14, RL 1.5, H-4.**

3) **Central Aorta.**

Note break in time scale.

TABLE V

HYPOTHALAMIC TEMPERATURE DECLINE WITHIN SIX MINUTES AFTER INTRAVENOUS INJECTION OF PENTOBARBITAL

Cat No.	Temperature Decline °C
103	.34
111	.29
112	.73
120	.38
121	.60
122	.60
130	.56
131	.50
134	.43
135	.78
136	.33
140	.18
141	.43
147	.50
148	.18
MEAN	.46

rate of decline was much slower. Occlusion of the carotid arteries after the pentobarbital, however, produced the same magnitude of temperature increase as observed before pentobarbital. Figure 4 shows such an experiment with occlusion before and after 10 mg/Kg pentobarbital. Even with this larger dose no difference can be detected in the rise in hypothalamic temperature upon carotid occlusion before and after pentobarbital. The slope of rise in the anterior hypothalamus before and after pentobarbital is tabulated in Table VI and the slopes in the posterior are shown in Table VII. It may be seen that there is no decrease in these slopes after pentobarbital, and in fact, there is a slight increase from 0.24°/min to 0.31°/min in the anterior hypothalamus and from 0.18 to 0.21 in the posterior. Since the rise in temperature upon occlusion is proportional to the metabolic rate, pentobarbital in these doses does not lower the metabolic rate. It follows, therefore, that the fall in hypothalamic temperature that results when small doses of barbiturate are given cannot be due to a decreased heat production by hypothalamic cells. The blood flow through the hypothalamus must, therfore, have gone up after pentobarbital if we are to explain this temperature drop. These profound effects of pentobarbital on the blood flow and temperatures in the hypothalamus point out the complete fallacy of using animals anesthetized with this agent in experiments where either brain temperatures are measured or where temperature regulation is studied. Doses

TABLE VI

SLOPE OF RISE IN ANTERIOR HYPOTHALAMIC TEMPERATURE UPON OCCLUSION BEFORE AND AFTER 5 mg/Kg SODIUM PENTOBARBITAL

Cat No.	Before Pentobarbital ^{o}C/min	After Pentobarbital ^{o}C/min
103	.10	.12
111	.10	.12
121	.25	.37
122	.32	.31
131	.15	.42
134	.38	.34
135	.09	.19
136	.28	.33
140	.38	.38
141	.27	.35
147	.23	.26
148	.34	.52
MEAN	.24	.31

as small as 5 mg/Kg or less cause these changes, and doses as large as 35 mg/Kg must be given for effective anesthesia.

TYMPANIC MEMBRANE TEMPERATURES

The measurement of hypothalamic temperatures in the cat is fairly simple once the techniques described in this dissertation have been mastered. Hypothalamic temperature measurement in man, however, presents apparently unsurmountable obstacles. In an effort to overcome these difficulties, Benzinger (7, 8) has measured many areas within the human cranium. These included most of the sinous cavities and the tympanic membrane. Benzinger believes the tympanic membrane to be the more accurate of these and equates membrane temperature to hypothalamic temperature. The hypothalamus and the tympanic membrane are separated by a considerable thickness of bone which should serve as an excellent insulator, and should have similar temperatures only because they are perfused by a blood supply of common origins. In the human the principal supply to each is by means of the internal carotid artery, and similarly in the cat both are supplied by the external carotid. However, as we have shown the temperature of the hypothalamus depends not only on arterial blood temperature, but upon its metabolic rate. Simultaneous measurements of the temperature of these two areas should show whether their temperatures are related.

TABLE VII

SLOPE OF RISE IN POSTERIOR HYPOTHALAMIC TEMPERATURE UPON OCCLUSION BEFORE AND AFTER 5 mg/Kg SODIUM PENTOBARBITAL

Cat No.	Before Pentobarbital °C/min	After Pentobarbital °C/min
103	.08	.10
111	.09	.10
121	.20	.29
122	.18	.18
131	.14	.18
134	.28	.19
135	.08	.12
136	.18	.22
140	.27	.25
141	.13	.17
147	.25	.32
148	.32	.43
MEAN	.18	.21

Simultaneous measurement of the hypothalamic and tympanic membrane temperatures in four cats showed a consistent difference between these two areas (Figure 5). It may be seen that at rest tympanic temperature was about 1° cooler than hypothalamic temperature and showed a consistent fall upon carotid occlusion, concurrent with a rise in both anterior and posterior hypothalamic temperatures.

These results are to be expected from an area such as the tympanic membrane, with its relatively low metabolism and high blood flow. These results cast doubt upon the use of tympanic membrane temperature as a measure of hypothalamic temperature as proposed by Benzinger. At best, tympanic temperature represents an approximation of carotid blood temperature. The two areas will maintain a fixed difference in temperature only as long as there is no change in the metabolic rate or the blood flow of either. Tympanic membrane temperature may therefore be used for estimating changes in hypothalamic temperature only under static conditions.

COLD SALINE EFFECTS

Lowenbach believes that heat exchange between the hypothalamus and the blood that supplies it is slight. This idea is hard to reconcile with the well-documented vascularity of the region. Where blood flows through an area,

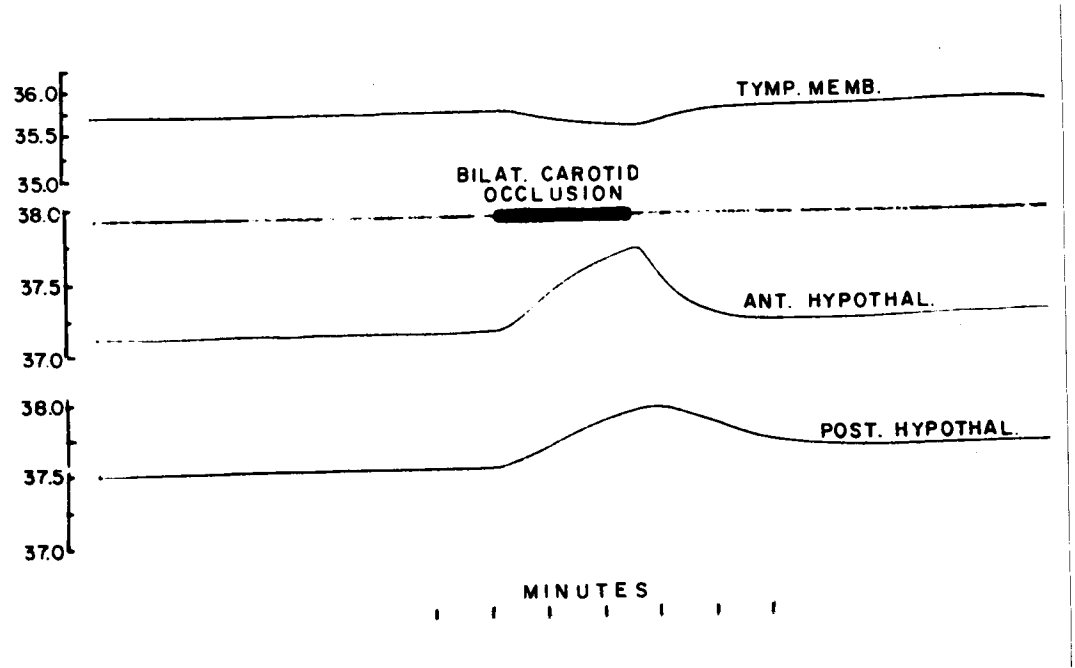

FIGURE 5

EFFECTS OF CAROTID OCCLUSION ON TEMPERATURES OF THE TYMPANIC MEMBRANE AND HYPOTHALAMUS

Top to Bottom:

1) Tympanic membrane.

2) Signal marker.

3) Anterior Hypothalamus A 14, RL 1.5, H-4.

4) Posterior Hypothalamus A 8, RL 1.5, H-4.

especially through capillaries which are freely permeable to water, heat exchange must also freely take place. To test the transfer of heat from the hypothalamus to the blood, small amounts of cold saline were injected into the femoral artery of the cat.

When 10 ml of 29°C saline were injected intravenously there was a drop in hypothalamic temperature within 20 seconds that reached a maximum within 60 seconds. Figure 6 shows this experiment. Note the drop in hypothalamic temperature which is about 0.15° in this experiment, also note that the anterior hypothalamus, consistent with its higher vascularity, shows a more rapid drop than the posterior hypothalamus. This rapid exchange of heat is in direct contrast to the work of Lowenbach (18) who found a much delayed response. These data again repudiate his "well insulated path" of blood through the hypothalamus.

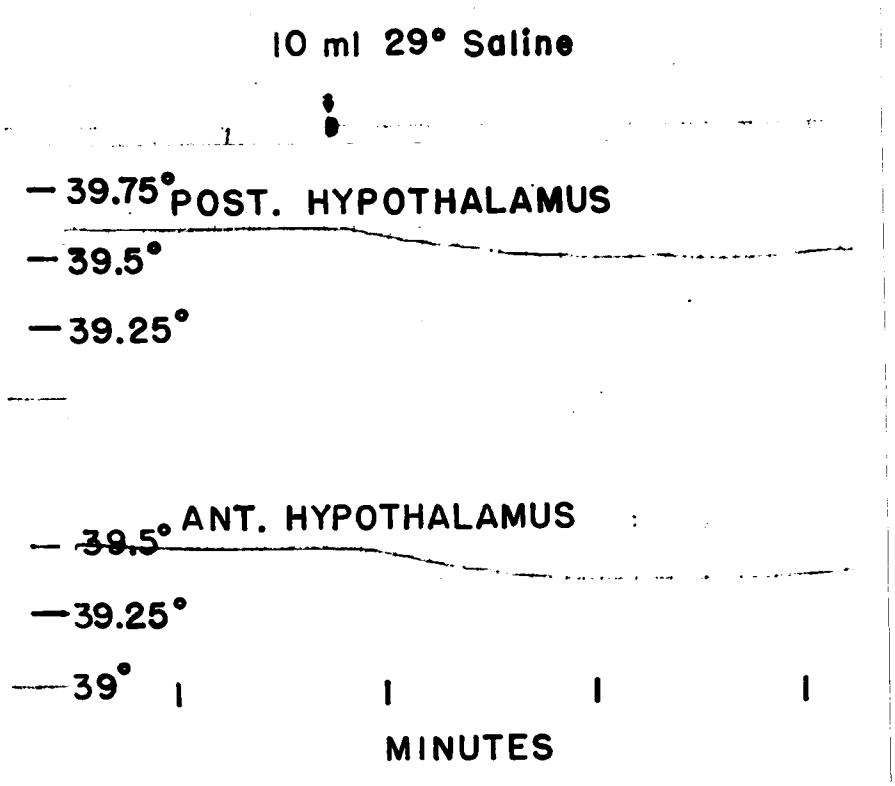

FIGURE 6

COLD SALINE EFFECTS

ON

HYPOTHALAMIC TEMPERATURES

Top: Posterior Hypothalamus A 8, RL 1.5, H-4.

Bottom: Anterior Hypothalamus A 14, RL 1.5, H-4.

CHAPTER V

SUMMARY

1. In cats under Sernylan anesthesia it has been demonstrated that hypothalamic temperature is warmer than that of blood in the carotid arteries. Because of this temperature gradient, the hypothalamus is cooled by the blood which perfuses it. Conversely, if the blood flow to the hypothalamus is reduced by procedures such as carotid artery occlusion, the temperature in the hypothalamus rises.

2. The initial slope of the rise in hypothalamic temperature following bilateral occlusion of the carotid arteries is proportional to the metabolic heat production of the tissue. The data in this dissertation support the conclusion that the metabolic heat production of the anterior hypothalamus is higher than that of the posterior hypothalamus.

3. The slope of the fall in hypothalamic temperatures after release of carotid occlusion indicates a greater blood flow through the anterior hypothalamus, which also tends to show an overshoot in the temperature fall characteristic of reactive hyperemia.

4. It has also been established that the posterior hypothalamus is warmer than the anterior hypothalamus. Since it has been postulated that metabolic heat production in the anterior portion is greater than that in the posterior, these data support the conclusion that blood flow is greater through the anterior hypothalamus even under control conditions at rest. These findings are consistent with anatomical evidence in the literature which demonstrates greater vascularity in the anterior hypothalamus.

5. Small, sub-anesthetic doses of sodium pentobarbital cause a prompt fall in hypothalamic temperatures. Measurement of slopes of temperature rises produced by carotid occlusion after administration of this drug indicate no significant alteration in hypothalamic heat production. Therefore, the decline in temperature produced by this barbiturate must be due to an increase in hypothalamic blood flow.

6. Tympanic membrane temperature in our experiments was lower than hypothalamic temperature. It has been claimed by other investigators that the temperature of the tympanic membrane is a reliable indicator of hypothalamic temperature. The experiments reported herein indicate that this relationship is valid only under the special condition when the organism remains in thermal equilibrium. In any experimental or physiological situation involving dynamic changes in temperature relationships of the organism to his internal

and external environment, the tympanic membrane temperature becomes a completely unreliable indicator of either absolute hypothalamic temperature or of direction of change in hypothalamic temperature.

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APPROVAL SHEET

The dissertation submitted by Robert Devon McCook has been read and approved by five members of the faculty of the Graduate School.

The final copies have been examined by the director of the dissertation and the signature which appears below verifies the fact that any necessary changes have been incorporated, and that the dissertation is now given final approval with reference to content, form and mechanical accuracy.

The dissertation is therefore accepted in partial fulfillment of the requirements for the Degree of Doctor of Philosophy.

May 25, 1964
Date

Clarence N. Lewis
Signature of Advisor