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Effects of thermal influences upon the pons and medulla and upon the mid brain and diencephalon after ligation of the basilar artery.

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<https://doi.org/10.18297/etd/682>

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UNIVERSITY OF LOUISVILLE

EFFECTS OF THERMAL INFLUENCES UPON THE PONS AND MEDULLA
AND UPON THE MID BRAIN AND DIENCEPHALON
AFTER LIGATION OF THE BASILAR ARTERY

A Dissertation

Submitted to the Faculty

Of the Graduate School of the University of Louisville

In Partial Fulfillment of the

Requirements for the Degree

Of Master of Science

Department of Physiology

By, -

Franklin Jelsma, B.S., M.D.

May 1, 1930.

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EFFECTS OF THERMAL INFLUENCES UPON THE PONS AND MEDULLA
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During the past two decades, substantial advances have been made toward the understanding of various phases of heat regulation. Many threads leading to the explanation of the complete mechanism of heat regulation of the body have been unraveled. Altho the exact anatomical location, extent and relations have not yet been determined, it has become evident that the chief control of body temperature is thru the central nervous system. Especially important regions are the basal nuclei and the brain stem.

Barbour₁ has produced evidence, confirmed by Hashimoto₂, Prince and Hahn₃, Rogers₄, Bazett and Penfield₅, that temperature control occurs by means of temperature influences upon the central nervous system as well as indirectly by way of the skin. Altho the heat and cold were applied in the vicinity of the caudate nucleus, they undoubtedly influenced the thalamus and hypothalamus, as well as the corpus striatum.

Barbour₁ in 1921, and Bazett₆ in 1927, reviewed the literature very thoroughly in regard to "The Heat Regulating

Mechanisms Of The Body", and "Physiological Responses To Heat", respectively. From Pembrey₇, Lefèvre₈ and Richet₉, may be secured references of earlier work. Rogers₄ has investigated many details of heat regulation upon normal and decerebrated pigeons. Other workers have used all types of animals, many have used various degrees of decerebration and of spinal transection; some have made heat punctures, placed tubes within the brain for heating and cooling purposes; some have heated the carotid blood; all with the idea of solving some phase of heat regulation.

The purpose of the present investigation has been to distinguish between the effects of various temperature influences upon the pons and the medulla on the one hand and the mid brain and telencephalon on the other. Heat and cold were applied to these two regions both simultaneously and separately. For the purpose of greater clarity, it was assumed provisionally that, as with living cells in general, heat is essentially a stimulant and cold a depressant of brain centers. By thus stimulating or depressing the activities of these regions one can estimate the anatomical level at which certain functional responses may be secured. Heymans₁₀ found in dogs that reflexes of the isolated head continued until the subdural temperature reached from 45°C. to 46°C., when the brain died. In spinal cats maximum muscular responses are received with a temperature at 38°C.

The brain was divided into the above portions for separate study because it is anatomically and functionally

suited for division here. Its blood supply is easily separated to correspond and thereby offers a ready method for the conduction of various temperature influences to each part independent of the other as well as avoiding the effects of trauma to the immediate brain tissue of these areas.

With the basilar artery ligated at the level of the fifth nerve, the carotid blood carries the various thermal stimuli to the upper portion and the vertebral blood carries the thermal influences to the pons and medulla. Thus, the thermal variations conducted by the carotid blood can be observed independently of, or simultaneously with, the thermal influences conducted by the vertebral blood. The division is in reality only a division of the stimulating or depressing mechanisms. This leaves the brain anatomically intact and permits the observation of stimulating and depressing effects upon two portions of a normal functioning brain.

From evidence arrived at upon decerebrate cats, Bazett and Penfield₅ placed the mechanism for temperature control "between the level of the middle of the superior colliculus and 2mm. in front of the pons and the upper limit of the thalamus." Sherrington₁₁ thinks that the central localization of the cold shivering mechanism "may correspond with that for general nervous temperature control." Bazett₆ again, in 1927, cited Isenschmid and Krehl₁₂, Leschke₁₃, Isenschmid and Schintzler₁₄, de Barenne₁₅, and Rogers₄ as considering the "actual position of the center or centers

controlling the body temperature" to be in the "thalamus, hypo-thalamus or tubercinereum, tho certainly above the level of the pons and medulla." These are found within one upper division and can receive stimulation or inhibition by way of the carotid blood. The vasomotor and respiratory mechanisms are in the lower portion and can receive stimulation or inhibition by way of the vertebral blood. Muscular activity can be influenced from both regions, as will be discussed below.

METHODS AND APPARATUS

METHODS AND APPARATUS

The preparation of the animals constituted the preliminary step. Short-haired dogs, of moderate size and with a fairly broad head, were selected. Highly excitable animals were avoided, as the final thermal observations were to be made without narcosis or hypnosis.

The operation for the occlusion of the basilar artery was performed under ether anesthesia. Under amytal, given intra-peritoneally, several sudden respiratory failures with death were noticed, when the basilar artery was occluded. We do ~~not~~ know that the anesthetic was the cause of the respiratory failure, yet no such difficulty was encountered under ether anesthesia. Of course another factor contributing to the fatalities of this procedure is the manipulation of the artery itself. Tension on the basilar artery may cause anemia of the pons and medulla as well as rupture of some of the smaller branches coming from it.

The route for the exposure of the vessels was described by Pollock and Davis¹⁶ for purposes of destroying the function of centers above this point. The technique used by us, is as follows:-

With the animal under ether and a preliminary of .5mg. of atropine and no morphine, the mouth is held open with a side mouth gag. The tongue is tied over the mandible fairly taut. The soft palate is then injected with normal saline (with 6 drops of adrenalin 1-1000 per oz.) in the mid line to control oozing. The soft tissues of the naso-pharynx

are likewise injected and incisions made thru both to expose the base of the skull. With the tympanic bullae as bony land marks, a small piece of bone is chiseled out in the mid-line beginning on a line traversing the tympanic bullae thru the middle. A specially adapted rongeur is then used to remove as much bone as necessary to expose the artery for clipping. The artery can be seen pulsating thru the dura.

The dura is then opened and the spinal fluid removed by suction. A right angle hook with about 2mm. horizontal length is carefully placed under the artery and silver clips applied. (Three are usually sufficient.) Care must be exercised not to move the vessel to any extent.

The soft tissues are sutured with interrupted catgut. It is well to use a Cushing head light for illuminating purposes.

The animal is now allowed from one to three weeks for recovery. About twenty-four hours before observations are to be made, the secondary operation is performed. The metal jackets for heating and cooling are placed about the carotid and vertebral arteries.

Light ether anesthesia, or local, can be used. Fortunately the entire procedure can be accomplished thru one mid-line incision, extending well down on the sternum. It is not necessary to transect any of the neck muscles. It is also better to expose the vertebrae at their entrance into the cervical foramen at the sixth cervical vertebra,

rather than at their origin from the brachial arteries. When both carotid and vertebral arteries are exposed, the jackets are applied with the slot outward and gauze is packed carefully about them to prevent spread of temperature influences to the adjacent structures, particularly to the vagus nerves. The tubings leading to and from these jackets are especially insulated. The next day the animal is ready for study.

Figure 1.

(Pollock and Davis,¹⁶) Base of brain showing point of ligation of basilar artery. 2 - Vertebral artery; 3 - posterior inferior cerebellar artery; 4 - basilar artery; 5 - posterior superior cerebellar artery; 6 - posterior cerebral artery; 7 - middle cerebral artery; 8 - anterior cerebral artery.

Figure 2.

(Taken from Pollock and Davis¹⁶) Shows relative areas supplied by vertebral circulation and carotid circulation after the basilar artery is ligated at level of fifth nerve.

The jackets used are similar to those described by Kahn¹⁷. We found it to advantage to move the slot toward the inflow and outflow tubes, also to slant these tubes on the jackets used for the vertebral arteries. (See Figure 3.)

Figure 3.

Legend:-

- Water jackets for carotid and vertebral arteries.
 A. and G. - lumens thru which vessels pass.
 E. - slots. B. - tape. C. - Asbestos for insulation.
 D. - rubber tubing. F. - Slanted metal tubing on vertebral jacket.

The resevoirs for hot and cold water were made from five gallon bottles placed in barrels with sawdust about them. Temperature can be maintained fairly constantly in this way. Small thermometers were fitted into the inflow tube and outflow tube on the carotid and vertebral systems. Thus the temperature of the inflow and the loss or gain in temperature can be determined from outflow thermometer. The quantity of water passing thru each can be measured and amount of heat gained or lost can be estimated for each system. Ordinary rectal thermometers were used to take rectal and vaginal temperatures. Skin temperature was taken

with a thermocouple. Respiratory tracings were made thruout the observations.

When ready to study, the animal is placed on a well padded table and made comfortable but not restricted or covered. No narcotics or hypnotics are used. Water at various degrees of temperature is passed thru the carotid jackets at the same time or independently of, water at various temperatures passing thru the vertebral system.

The possibilities are: (1) The carotid system may be heated alone. (2) The carotid system may be cooled alone. (3) and (4) The vertebral system may be heated or cooled alone. (5) The carotid system may be cooled and the vertebral system heated simultaneously. (6) The carotid system may be heated and the vertebral system cooled simultaneously. Of course both may be heated or cooled at the same time.

Regardless of the combination used, the skin temperature is recorded, also the rectal or vaginal temperature, respiratory tracing made, evidence of muscle tone noted, and temperature of inflow and outflow of water kept.

RESULTS

RESULTS

Results of observations upon normal dogs and those having the basilar artery occluded are presented in tabular and graphic form.

Table 1.

3/20/30.

Time	Inflow Temperature °C.		Outflow Temperature °C.		Skin Temp. °C.	Vag. Temp. °C.	Muscular Tone	Room Temp.
	Carotid	Vert.	Carotid	Vert.				
6:16	-	-	-	-	33.98	39.6	Relaxed	24°C.
6:21		45		44	33.88		Shivered	
6:25		45		44	33.85	39.7	General Shivering	24°C.
6:26	Heat discontinued							
6:29	-	-	-	-	34.44	39.7	Relaxed	24°C.

Thermal influences upon the C.N.S.; showing changes in skin temperature, body temperature, and muscular tone. No hypnotics or narcotics. Both external carotid arteries ligated. Basilar artery occluded.

When the vertebral blood is cooled, vaso-dilatation occurs and the skin temperature rises, while the body temperature falls. These two actions are augmented by heating the carotid blood. Conversely, cooling the carotid blood causes vaso-constriction and a fall in skin temperature and a rise in body temperature. Heating the vertebral blood augments the action of cooling the carotid blood. These facts are illustrated in Figure 4.

In Table 1. it may be observed that shivering occurs when the vertebral blood is heated. There is an associated vaso-constriction and a rise of vaginal temperature.

Figure 4.

Legend:-

Effects of temperature upon the medullo-pontine region and upon the mid brain and telencephalon separately and simultaneously. Bars represent heating, and rectangular outline represents cooling; ordinates: °C.; abscissae: time; triangles: skin temperature; large dots: vaginal or rectal temperature in °C.

Table 2.

2/7/30.

Time	Inflow Temperature °C.		Outflow Temperature °C.		Skin Temp. °C.	Rect. Temp. °C.	Respiration.	Room Temp.
	Carotid	Vert.	Carotid	Vert.				
5:57	-	-	-	-	37.	38.9	48	25°C.
6:05	-	-	-	-	36.4	39.2		
6:15	55	28	48	29	Started			
6:21						39.1		
6:26	54	20.5	47	23	37		60	
6:30	-	-	-	-	37.4			
6:37	53 1500cc	17.5 *1300cc	43	19	.	39.	60	25°C.
6:42		58		58		39	Periodic	25°C.
6:50		58		58		39.4	Periodic	
6:52		58		58		39.6	Periodic	
* Total flow.								

Typical results of temperature influences by way of carotid and vertebral blood; showing skin temperature, body temperature, and respiratory changes. Basilar artery occluded.

Simultaneous heating of the carotid blood and cooling of the vertebral blood, as again shown in Figure 5, causes a vaso-dilatation with a rise of skin temperature and a fall of body temperature. Immediate heating of the vertebral blood causes a marked rise in body temperature which continues to rise after heat is discontinued below and the carotid blood cooled. 13,500 calories of heat were introduced by the hot water thru the carotid blood, and only 2,080 calories were removed by means of the cold jackets about the vertebral arteries, yet the body temperature was diminished. This illustrates the thermostatic control exerted by the upper region.

Figure 5.

Legend:-

Same as Figure 4. (See Table 2.)

Table 3.

2/6/30.

Time	Inflow Temperature °C.		Skin Temp. °C.	Vag. Temp. °C.	Respiration	Room Temperature
	Carotid	Vert.				
3:40	-	-	38	40.5	28	26°C.
3:45	-	-	38	40.5	28	
3:52	-	6	-	-	-	-
3:57	-	6	38.8	40.4	22	26°C.
4:00	-	6	-	40.4	22	-
4:11		Off	38.1	40.4	-	
5:12	-	-	38.2	40.5	44	26°C.
5:14	46	9	Started		-	-
5:19	46	8	38.8	40.4	32 Shallow	
5:24	48	7	-	40.3		
5:33	47	9	38.2	40.1		
5:43	46	9	38.0	40.1		
5:45	Off	Off		40.1		
5:51		49		40.2	60 Deep	26°C.
5:56		49 Off		40.1		
6:02	10		38	40		
6:08	8		37.2	40.1	32 Deep	26°C.

Separate and simultaneous temperature influences carried by carotid and vertebral blood. Basilar artery occluded.

In Table 3. and Figure 6. it will be observed that cooling the vertebral blood causes a vaso-dilatation and a sharp rise in skin temperature. There is a slight fall in body temperature. Cooling the vertebral blood reinforced by

heating the carotid blood gives a temporary vaso-dilatation, the skin temperature however returning to normal before the thermal influences were discontinued. Heating the vertebrae and cooling the carotid blood causes a characteristic fall in skin temperature. The body temperature changes to a less marked degree.

Figure 6.

Legend:- Same as in Figure 4. (See Table 3.)

Table 4.

2/22/30.

Time	Inflow Temperature °C.		Outflow Temperature °C.		Skin Temp. °C.	Vag. Temp. °C.	Respiration.	Room Temp.
	Carotid	Vert.	Carotid	Vert.				
9:38	-	-	-	-	33.9	39.6	28	25.3
9:57	-	-	-	-		39.6		
10:02	-	10.7		22.2				
10:16		10		20		39.6	Slower Shallow	
10:20		Off		Off				
10:33		40		23		39.6		
10:44		45		24		39.5		
10:59		47		25		39.5		
11:00		43		22		39.5		
11:07		45		29		39.4		25.3
11:11		Off		Off				
11:26		-		-	34.8			
11:28		40		28	35.	39.4		
11:29		41		30				
11:32		43		32	33.5	39.4		
11:44		43		33	33.8	39.4	Hyper- pnea.	25.3
11:55		42		33	34.3	39.6		
11:56		Off		Off			Dimin- ished.	
12:00	43		30					
12:12	43		32		34.6			
12:13	44		38			39.6		
12:17	44		42		34.9			
12:19	44		43		35	39.5		
12:24	44		43		34.7	39.6		

Temperature influences by way of carotid and vertebral blood upon normal dog. (See Figures 7 and 8.)

Figure 7.

Legend:-

Same as Figure 4. (See Tables 4. and Figure 8.)

Animals in which the basilar artery has not been clipped react somewhat differently to temperature influences as noted in Figure 7 and Table 4. Immediate and temporary vasomotor changes with corresponding skin temperature variations occur as in animal with the basilar artery ligation. The body temperature changes little. A given temperature has opposing influences when allowed to affect the two portions of the brain simultaneously.

Figure 8.

Legend:-

Temperature influences upon respiration in a normal dog.

A respiratory tracing from a normal dog is shown in Figure 8. At first the vertebral blood is cooled with a

resulting inhibition of the respiratory center. Respirations are slowed and diminished. As the temperature influences approximate body temperature, respiration returns to normal, but when they rise to 40 or above respiration becomes markedly increased in rate and depth. Periodicity results, as often occurs in such cases. Heating the carotid blood stimulates the upper inhibitory mechanism and respiration becomes slow as when the medullo-pontine region was cooled. However, as the basilar artery was not ligated the heat spreads to the respiratory center below and typical periodic breathing is recorded. In the animals with the basilar artery occluded, no such evidence of spread of thermal influences was secured.

DISCUSSION

DISCUSSION

The central application of temperature separately to the two regions of the brain appears to help in the localization of function. The vasomotor results of the thermal treatment of the parts supplied by the vertebral circulation indicate that heat can arouse vasoconstriction and inclines one strongly to believe that constrictor influences dominate in the medullo-pontine region.

To rule out peripheral reflex influences, the external carotid arteries were ligated in one case with no change in the vasomotor results.

It may be noted that with the introduction of heat by the vertebral system to the pons and medulla that respiration increases in both rate and volume. The same thing occurs when cold is introduced by way of carotid blood to the upper region. On the other hand, cold applied to the medullo-pontine region slows the respiration and decreases its amplitude. This is true with heating the upper region. It may also be observed that heat at 43°C . to 46°C . by way of the vertebral circulation, and cold at 8°C . to 12°C . introduced above by the carotids, causes periodic respiration; i.e. periods of marked hyperpnea alternating with apnoea. This hyperpnea must be due to the direct stimulation of the respiratory center by the heat, or in the other case to indirect stimulation by the release of inhibitions from above by cold. The respiration probably becomes periodic because the increased ventilation washes out the C O_2 .

Kahn₁₇ was able to produce polypnea when he heated the carotid blood. Moorehouse₁₈ used further precautions to protect the vagi and then secured both slow deep respira-

tion, and a rapid shallow respiration when the carotid blood was heated. In some instances respiration did not change. Moorehouse applied heat however while the animal was under the influence of narcotics and hypnotics. (He found the vasomotor center to be very easily influenced by heating the carotid blood.)

In contrast to others who have heated the blood supplying the brain in dogs we have never observed the shallow rapid respiration defined as heat polypnea. When heated, the respiratory center of the medulla evokes an increase in both depth and rate of the respirations, thus affording the additional ventilation needed to support the extra muscular activity. Cooling the carotid has the same effect (by removing the inhibition exerted by the basal ganglia upon the medullo-pontine region). But heating the carotids (in the ligated dog, and until the heat spreads in the unligated animal) decreases respiratory rate as well as depth.

Shivering was noted when the upper region was cooled and the lower portion was heated, separately or simultaneously.

Body temperature ~~was~~ indicated by rectal and vaginal temperature, changed with various thermal influences indicating a thermostatic temperature regulating mechanism in the upper portion of the divided brain. For, as has been shown in rabbits by directly heating the base of the brain, carotid heating lowered the rectal temperature and carotid cooling raised it.

With the idea that heat is a stimulant and cold a depressant to the areas affected, it seems that the following deductions may be arrived at from the above findings.

The vasomotor and respiratory mechanisms are aroused by vertebral heating, hence are located in the lower of the two brain portions. Inhibiting influences upon them originate from the upper system. Stimulating or heating the mechanism directly by means of the vertebral blood supply produces vaso-constriction and increased respiration, while cooling this blood causes depression of these mechanisms, giving vaso-dilatation and decreased ventilation.

Rogers₄ caused shivering in pigeons, as others have in rabbits, by applying cold to the thalamus. Our carotid cooling (8°C. to 15°C.) does the same. Heat by way of the vertebral blood likewise causes shivering with inflow temperatures ranging from 42°C. to 46°C. on different animals. This would indicate a stimulation of a medullo-pontine mechanism directly by heated blood and that cold above releases the inhibition of the same.

Above, on the inhibition system, stimulation by heat would further inhibit the actions of the lower mechanisms and give the same as cold below, while cold, depressing the inhibition mechanism, would increase the action below and give the same results as direct stimulation.

Inhibitory control by the mesencephalon and the basal ganglia affords a mechanism for body heat regulation; it presides over vasomotor tone, respiration, muscular (and doubtless other metabolic activity). While undoubtedly

influenced largely by afferent impulses from the skin, our work adds support to the view that the upper central region is directly influenced by temperature just as is the sensitive element of a thermostat.

CONCLUSION

CONCLUSION

1. Heat acts as a stimulant and cold as a depressant to the important brain centers concerned with temperature regulation.
2. Heating the medullo-pontine region alone, causes peripheral vaso-constriction, increased muscular action, and often times shivering, increased ventilation, and a rise in body temperature. Cooling the carotid blood produces similar responses.
3. Cooling the medullo-pontine region causes vaso-dilatation peripherally; lessens muscular activity, diminishes ventilation and causes a fall in body temperature. Heating the carotid blood produces similar changes.
4. When both regions are treated simultaneously with opposing temperature influences, the effects of one are augmented by the other.
5. When both regions are treated simultaneously with like temperature influences, (as occurs to some extent when the thermal influence is applied to but one of the two arterial systems in dogs with intact basilar arteries) the effects upon one tend to counteract the effects upon the other.

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