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# Spinal Cord and Hypothalamus as Core Sensors of Temperature in the Conscious Dog

## II. Addition of Signals

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*Summary.* In two conscious dogs at standardized external conditions, the temperatures of the spinal cord and hypothalamus were altered simultaneously and were correlated with heat production (shivering) and respiratory evaporative heat loss (panting).

Combined cooling of spinal cord and hypothalamus at 18, 24, and 30°C air temperature increased heat production by up to 10.2 Kcal/(kg · h). Combined heating of the spinal cord and hypothalamus at the same environmental conditions increased respiratory evaporative heat loss by up to 4.5 Kcal/(kg · h).

Compared with the effects of cooling either the spinal cord or the hypothalamus, cooling both together increased the slope of the regression and elevated the threshold temperatures for shivering. With regard to respiratory evaporative heat loss, heating the spinal cord and hypothalamus together mainly lowered the threshold temperatures as compared with warming each area independently.

The results suggest that temperature signals, simultaneously generated in spinal cord and hypothalamus, are added to give a combined drive to the effector systems.

*Key-Words:* Temperature Regulation — Hypothalamic Temperature — Spinal Cord Temperature — Core Sensors of Temperature.

*Schlüsselwörter:* Temperaturregulation — Hypothalamustemperatur — Rückenmarkstemperatur — Kerntemperaturfühler.

As shown previously[1], the spinal cord and hypothalamus can be regarded in the dog as basically equivalent sensors of the temperature of the body core. From earlier work (Fusco; Hellstrøm and Hammel; Jessen, Meurer, and Simon) it appears likely that under normal conditions both these sensors are at nearly the same core temperature. Consequently, considerations concerning the relationship between deep body temperature sensors and the activity of the effector systems have to take into account parallel temperature deviations of spinal cord and hypothalamus. In order to simulate these conditions, the experiments now described were undertaken to ascertain the effects of simultaneous thermal stimulation of the spinal cord and hypothalamus on shivering

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and panting. The results of such combined stimulation are compared with those obtained by individual cooling or warming of one thermosensitive area. Thus, it is possible to discern some of the factors governing the central coordination of temperature signals originating in the hypothalamus and the spinal cord.

## Methods

Simultaneous thermal stimulation of the spinal cord and hypothalamus were performed. The experimental approach with respect to animals, recordings, and calculations was identical with that described in the previous paper[2]. The same two dogs were used; dog F and dog N.

In dog F, two series of 28 and of 52 periods of combined stimulation, each lasting for five min, were undertaken at constant ambient air temperatures of 18°C and 30°C. In dog N, 29 stimulation periods were performed at 24°C air temperature.

## Results

### *I*

The experiments were designed in an attempt to reveal the relationships between the intensity of simultaneous thermal stimulation of spinal cord and hypothalamus and the amount of heat production or respiratory evaporative heat loss by combining the results of complete experimental series in common stimulus-response-curves. However, the generality of the responses to simultaneous stimulation is most readily seen from the results of a typical experiment as shown in Fig. 1.

In Fig. 1, several sections of an experiment on dog F at an ambient air temperature of 30°C are shown. The first period gives the response to selective heating of the spinal cord. Immediately after the start of heating, as indicated by the rising temperature within the peridural space, the respiratory evaporative heat loss increased from 0.17 to 1.6 Kcal/(kg · h) on average. On the other hand, spinal cord cooling (2) in the warm environment gave a weak response. There was an increase in heat production of up to 3.8 Kcal/(kg · h), but this was transient. The third period of selective hypothalamic cooling induced double the heat production of that during the control period. Heating of the hypothalamus (4) alone initiated marked panting with respiratory evaporative heat loss rising to 2.8 Kcal/(kg · h) on the average.

The two last sections of Fig. 1 demonstrate the responses to combined heating or cooling of the spinal cord and hypothalamus. The intensity of thermal stimulation in either thermosensitive site corresponded to that during selective stimulation. Simultaneous heating of both spinal cord and hypothalamus (5) acted as a very strong stimulus to respiratory evaporative heat loss. Initially during this period, the

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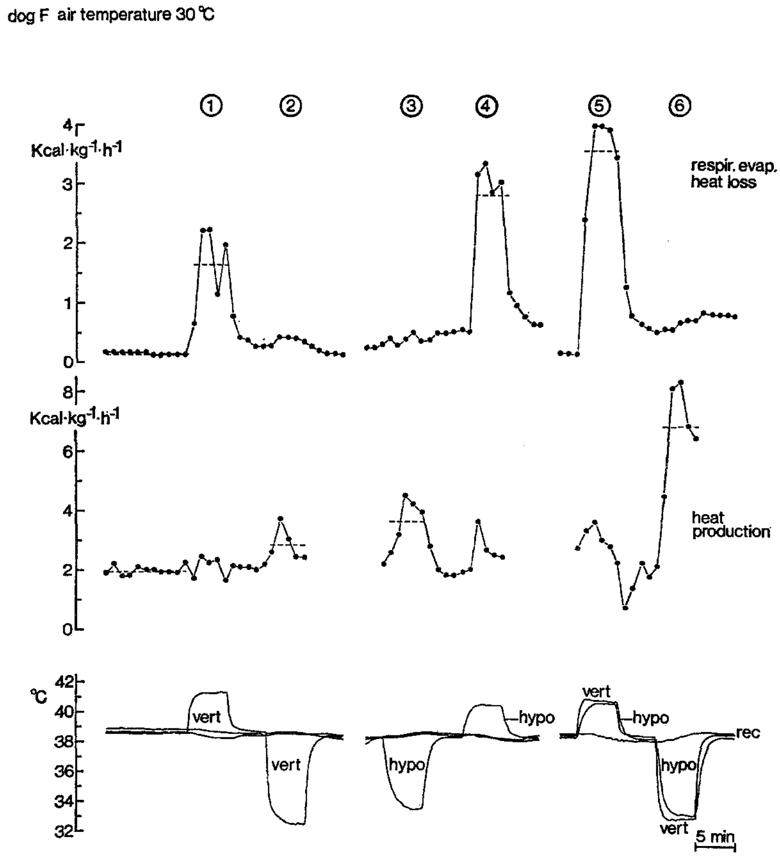


Fig. 1. Individual and simultaneous temperature changes of spinal cord and hypothalamus in a conscious dog. Air temperature 30 °C. Upper dotted lines: Respiratory evaporative heat loss and heat production. Below: Direct recordings of one temperature within the peridural space (*vert*), of hypothalamic temperature (*hypo*), and rectal temperature (*rec*). (*1*) Spinal cord heating; (*2*) Spinal cord cooling; (*3*) Hypothalamic cooling; (*4*) Hypothalamic heating; (*5*) Combined heating of spinal cord and hypothalamus; (*6*) Combined cooling of spinal cord and hypothalamus

animal showed typical second phase breathing, i.e. a slower and deeper type of panting (Findlay). The mean value of 3.6 Kcal/(kg · h) markedly exceeded the responses to heating of either spinal cord or hypothalamus alone. Similarly, simultaneous cooling of both spinal cord and hypothalamus (6) elicited pronounced shivering despite the high ambient air temperature of 30 °C. The mean heat production of 6.9 Kcal/(kg · h) exceeded the sum of responses to selective cooling and resulted in an increase of rectal temperature of 0.6 °C during five minutes.

Thus, the effect of combined thermal stimuli as compared with single ones appears to be synergistic. With regard to respiratory evaporative heat loss, simultaneous warming exceeded even the marked responses obtained by individual warming. With regard to shivering in an ambient temperature of 30° C, combined cooling was able to elicit a clear-cut reaction which was greater than the summed single responses.

## *II*

Fig. 2 shows all periods of simultaneous thermal stimulation of spinal cord and hypothalamus performed in dog F at an ambient air temperature of 18° C. During these periods, heat production or respiratory evaporative heat loss were influenced by two variables: Of the spinal cord and hypothalamic temperature which were altered simultaneously. Consequently, a three-dimensional diagram is necessary to show the results.

In Fig. 2 the basal plane is given by the temperatures of the spinal cord and hypothalamus. The amount of heat production (left side) or respiratory evaporative heat loss (right side) at each period is given by vertical lines upon the temperatures of spinal cord and hypothalamus. Each circle represents one stimulation period. Altogether, 28 periods of cooling or warming were performed.—Within this three-dimensional diagram, vertical planes were constructed in the following way. Lines A were calculated by linear regressions between mean spinal cord temperatures and hypothalamic temperatures during all periods of simultaneous cooling or warming. They delineate the relationship between the intensities of simultaneous thermal stimulation of both areas under the given experimental conditions. Above the base lines, mean values and standard deviations of heat production and respiratory evaporative heat loss during all control periods of all experiments are given by three lines (B). These lines give the normal values from where the increase of heat production or respiratory evaporative heat loss during stimulation periods is calculated. The increase is presented by lines C, which show intersections between the vertical planes and multiple linear regressions. These multiple linear regressions were calculated for all filled circles for the three variables: Mean spinal cord temperature, hypothalamic temperature, and heat production and respiratory evaporative heat loss respectively. The threshold temperatures for both effector responses are given by the intersections of lines B and C. The thresholds are virtual combinations of hypothalamic and spinal cord temperatures. These threshold values are meaningful only in relation to the threshold temperatures of selective stimulation of either spinal

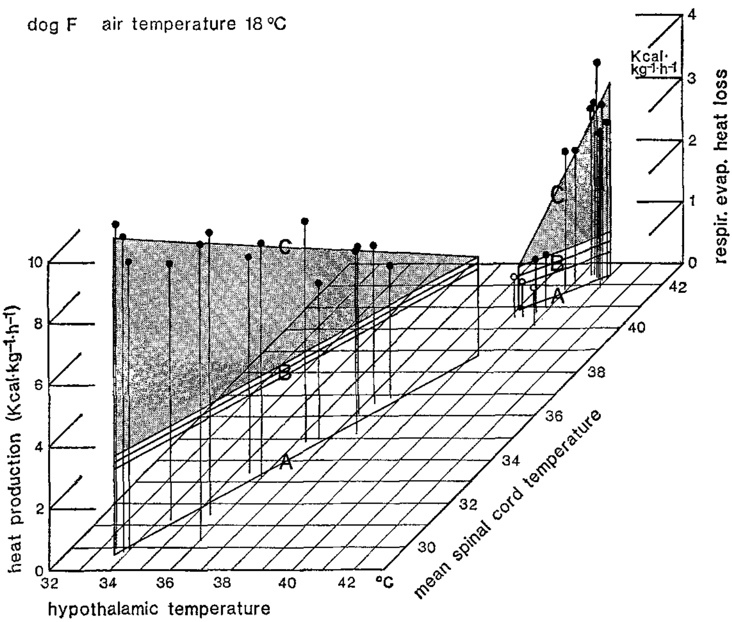


Fig. 2. Heat production and respiratory evaporative heat loss related to simultaneous temperature changes of spinal cord and hypothalamus. 28 stimulation periods in dog F at an ambient air temperature of 18° C

cord or hypothalamus, and will therefore be discussed in connection with Fig. 3.

The left part of Fig. 2 shows the increase of heat production due to simultaneous cooling of spinal cord and hypothalamus. In all periods, marked shivering was obtained. Even at very low intensities of thermal stimulation, for example at a hypothalamic temperature of 37.3° C and a mean spinal cord temperature of 36.6° C, the heat production was elevated by more than 70 % above the resting value. The highest heat production of 10.2 Kcal/(kg · h) was obtained at a hypothalamic temperature of 33.9° C and a mean spinal cord temperature of 29.9° C. This is equivalent to about 230 % above the resting heat production and emphasizes the strong combined drive to increase heat production originating in spinal cord and hypothalamus. As shown by the multiple correlation coefficient $R_{y \cdot x_1 x_2} = 0.97$, the response on the whole is well described by the calculated linear regression.—The upper right part of the figure gives the response to simultaneous heating of spinal cord and hypothalamus. In spite of the low ambient air temperature the animal showed a marked increase in respiratory evaporative heat loss

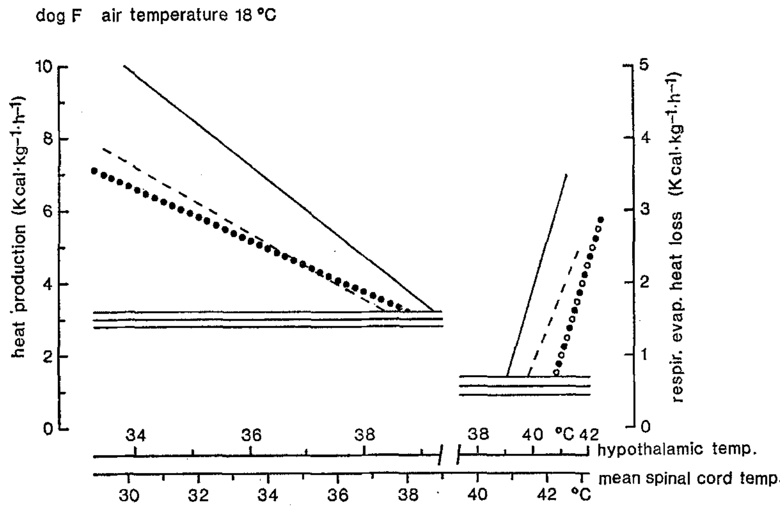


Fig. 3. Heat production and respiratory evaporative heat loss related to individual and simultaneous temperature changes of spinal cord and hypothalamus. Dog F, ambient air temperature 18° C.—Solid lines: Combined thermal stimulation of spinal cord and hypothalamus. Broken lines: Selective thermal stimulation of the spinal cord. Dotted lines: Selective thermal stimulation of the hypothalamus

of up to 3.5 Kcal/(kg · h) at a mean spinal cord temperature of 42.3° C and a hypothalamic temperature of 40.8° C.

Fig. 3 gives a comparison for dog F of the results of combined thermal stimulation as shown in Fig. 2 with those of selective stimulation of either spinal cord or hypothalamus. The abscissae of the figure represents the temperatures of spinal cord and hypothalamus. Their interrelationship is given by the linear regressions of Fig. 2 (lines A).—The two solid lines correspond to lines C of Fig. 2 and show the results of combined thermal stimulation to heat production (left side) and respiratory evaporative heat loss (right side). The broken lines for selective thermal stimulation of spinal cord and the dotted lines for hypothalamic stimulation were drawn from the results given in a previous paper[3]. Concerning heat production, the figure shows that the slope for the increase of heat production due to simultaneous cooling of spinal cord and hypothalamus exceeds that for individual cooling of either spinal cord or hypothalamus. Furthermore, the threshold temperature is elevated by about 0.5° C with respect to hypothalamic temperature and by 1.5° C for spinal cord temperature. By combination of these effects—elevation

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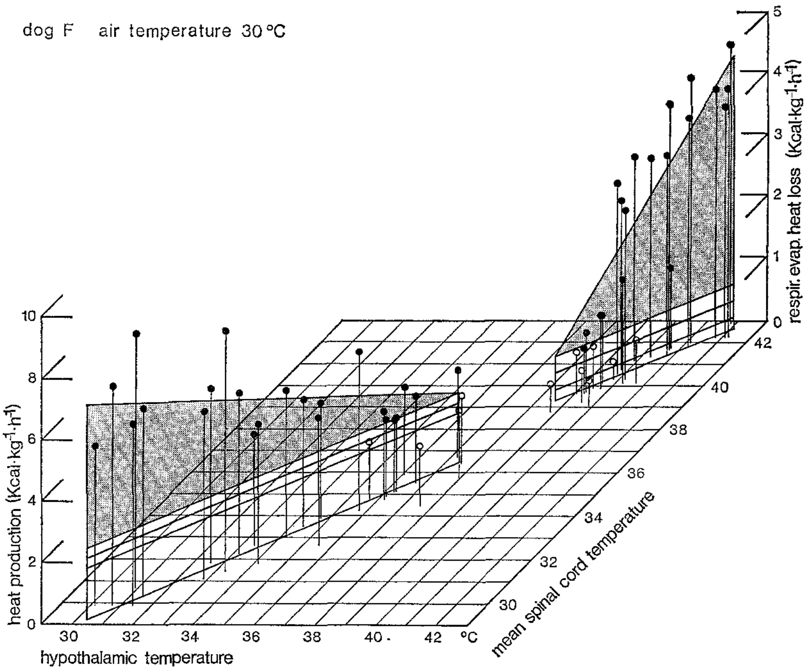


Fig. 4. Heat production and respiratory evaporative heat loss related to simultaneous temperature changes of spinal cord and hypothalamus. 52 stimulation periods in dog F at an ambient air temperature of 30° C

of threshold temperatures and increase of slope—the regression line for simultaneous cooling resembles the combination of the selective regressions. Thus, simultaneous cooling of spinal cord and hypothalamus appears to exert a drive for increasing heat production, which is the sum of the drives resulting from individual stimulation of either spinal cord or hypothalamus.

On the right side of Fig. 3, the responses to heating are plotted. As compared with selective heating of the spinal cord (broken line), simultaneous heating of both areas (solid line) resulted in a slightly steeper slope, starting at a lower threshold temperature (— 0.6° C). For individual hypothalamic heating, it was impossible to calculate the slope, whereas the threshold temperature was rather well defined at 40.80° C hypothalamic temperature. This hypothalamic threshold temperature was lowered by 1.70° C by additional spinal cord heating. In summarizing the results of combined spinal cord and hypothalamic heating, effects similar to those of combined cooling can be stated. Combination of the

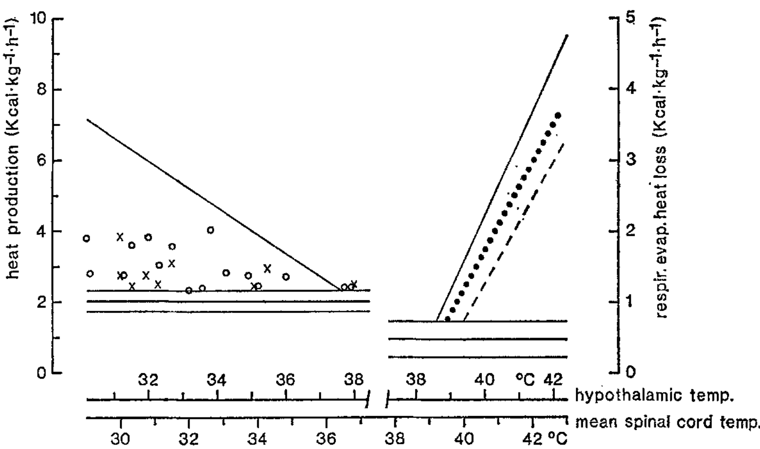


Fig. 5. Heat production and respiratory evaporative heat loss related to individual and simultaneous temperature changes of spinal cord and hypothalamus. Dog F, ambient air temperature 30° C.—Solid lines: Combined thermal stimulation of spinal cord and hypothalamus. Broken line and crosses: Selective thermal stimulation of the spinal cord. Dotted line and open circles: Selective thermal stimulation of the hypothalamus

two stimuli lowered threshold temperatures and, with regard to the spinal cord, slightly increased the slope.

Fig. 4 shows the results obtained in the same dog F at an ambient air temperature of 30° C. The series consisted of 52 stimulation periods. The arrangement of data and the construction of lines is the same as for Fig. 2. In spite of the warm ambient air temperature, combined cooling of spinal cord and hypothalamus initiated marked shivering with subsequent increase of heat production of up to more than 8 Kcal/(kg · h). This value is four times the resting heat production.—Owing to the elevated air temperature, the respiratory evaporative heat loss increased from a lower threshold value as compared with Fig. 2, namely at a hypothalamic temperature of 38.50° C and a mean spinal cord temperature of 39.20° C. The highest value of 4.5 Kcal/(kg · h) was obtained at a mean spinal cord temperature of 42.95° C and a hypothalamic temperature of 41.85° C. It is equivalent to a ninefold increase of the resting value.

Fig. 5 shows the relationship between the effects of simultaneous (Fig. 4) and individual thermal stimulation of spinal cord and hypothalamus. With regard to heat production, selective cooling of either

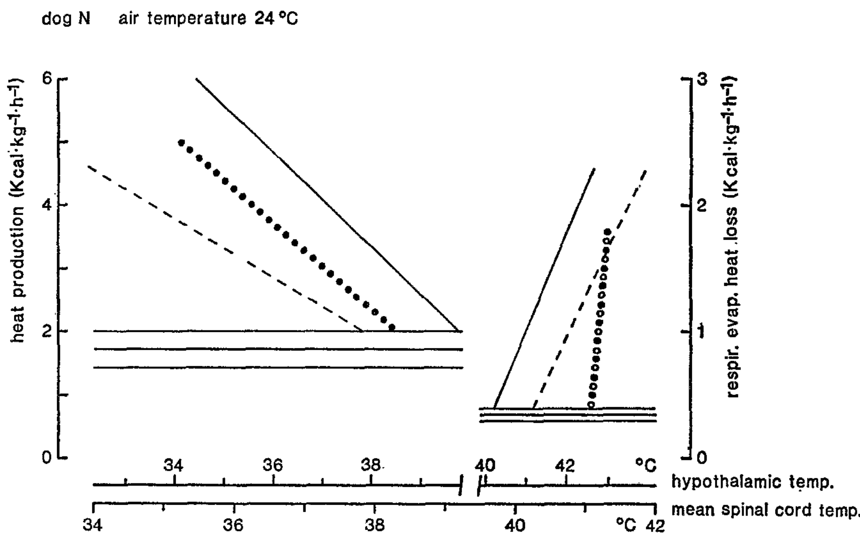


Fig. 6. Heat production and respiratory evaporative heat loss related to individual and simultaneous temperature changes of spinal cord and hypothalamus. Dog N, ambient air temperature 24° C.—Solid lines: Combined thermal stimulation of spinal cord and hypothalamus. Broken lines: Selective thermal stimulation of the spinal cord. Dotted lines: Selective thermal stimulation of the hypothalamus

spinal cord or hypothalamus did not elicit shivering in a reproducible and temperature-dependent manner. There were several periods with a marked increase of heat production, but in general, there was no definite relationship between the intensity of local cooling and the amount of heat production. It was impossible to calculate regressions, therefore the single periods are represented by single symbols.—On the contrary, combined cooling of spinal cord and hypothalamus regularly initiated shivering which was well correlated with the intensity of cooling (solid line). The effect of summation of shivering drives, originating in spinal cord and hypothalamus, is therefore clearly evident. On the right side, the responses to individual heating of the spinal cord (broken line) and hypothalamus (dotted line) are demonstrated. Compared with these results, the increase of respiratory evaporative heat loss due to combined heating started at a lower threshold temperature (hypothalamus —0.40° C; spinal cord —0.80° C).

In another animal (dog N) which, with regard to selective thermal stimulation of either spinal cord or hypothalamus had a higher thermosensitive capability of the spinal cord, 29 periods of combined cooling or warming of spinal cord and hypothalamus were carried out at an ambient air temperature of 24°C. The responses obtained in this series are shown in Fig. 6 by the solid lines. As in the previous figures, the regression lines for selective cooling or warming of either spinal cord or hypothalamus are also shown. Essentially, the results of this series resemble those obtained in dog F and confirm them.

## Discussion

### *I*

It was the aim of the present experiments to discern the nature of the central coordination of temperature signals originating in spinal cord and hypothalamus by comparing the responses to combined thermal stimulation with those obtained by selective stimulation of either spinal cord or hypothalamus. Single experiments have already shown a synergistic action of spinal cord and hypothalamic cooling in initiating shivering (Jessen, Simon, and Kullmann). Similar single results have been found with regard to panting in rabbits by Guieu and Hardy.

In discussing these data, some preliminary remarks appear to be necessary. As shown in a previous paper[4], the spinal cord and hypothalamus can be regarded in dogs as receptive fields providing temperature signals for a control system which converts the signals into drives for different effector systems. According to previous findings (Jessen, Meurer, and Simon), these effector systems come into play in a steplike sequence, which corresponds to different levels of temperature signals. For instance, a mild spinal cord warm stimulus will at first inhibit shivering initiated by any simultaneous peripheral cold stimulus. In a second stage, more intense spinal cord heating elicits cutaneous vasodilatation. Under the same condition, still more intense spinal cord heating leads to panting.

This sequence of activity of three different effector systems following different levels of one qualitatively uniform stimulus shows that the thermosensitive structures of the spinal cord, and likewise the hypothalamus, are not correlated to only one effector system. In this connection, spinal cord and hypothalamus have to be regarded as generators of temperature signals, which by themselves are fundamentally unrelated to one specific effector system. Type and activity of a single effector system, working at a given condition, depends solely on the *level* of temperature signals generated at the spinal cord, at the hypothalamus or at other thermosensitive areas. The graded pattern of effector systems implies that, changing the level of temperature signals by combination of spinal and hypothalamic thermal stimulation, has, on principle, to affect both the thresholds and the slopes of the effector systems as

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compared with selective thermal stimulation of either spinal cord or hypothalamus. With regard to shivering, which has a relatively moderate stimulus-response-relationship, slopes and thresholds may be influenced to the same extent. On the contrary, the panting response is generally characterized by its steepness. The temperature range between threshold and maximum response normally does not exceed 2°C in selective warming of either spinal cord or hypothalamus. Under these conditions, statements concerning the rate of increase become difficult so that the decrease of threshold temperatures may be expected as the predominant effect of combined warming.

Within the scope of these suggestions, the experiments described appear to support strongly the concept of additive action of temperature signals originating in spinal cord and hypothalamus. With regard to heat production, all three series gave consistent results. As compared with selective cooling of either spinal cord or hypothalamus, combined cooling of both areas led to steeper slopes and elevated threshold temperatures. The increase of heat production for a fixed degree of combined cooling resembles the sum of responses to selective stimulation of either spinal cord or hypothalamus.

Concerning respiratory evaporative heat loss, combined heating of spinal cord and hypothalamus slightly increased the slopes, but definitely lowered the threshold temperatures as compared with selective stimulation. In series N 24 especially, the decrease of threshold temperatures due to combined heating of spinal cord and hypothalamus became evident. In this instance, the threshold difference between selective and combined hypothalamic heating was 2.5°C hypothalamic temperature.

## *II*

The experiments described were also intended to obtain information about the magnitude of the combined thermosensitivity of spinal cord and hypothalamus in relation to the normal range of body core temperature. In the sequence of effector systems involved in temperature regulation previously mentioned, shivering and panting represent opposite effectors, between which finer adjustments to thermal loads are performed by variations in cutaneous blood flow. These variations in cutaneous blood flow represent the most sensitive indicator for evaluating the significance of temperature sensors. Vicariously, the difference between threshold temperatures for shivering and panting induced by combined thermal stimulation of spinal cord and hypothalamus provides some general information about the combined power of these thermosensitive areas.—As Figs. 3, 5, and 6 show, this difference did not exceed 1°C hypothalamic temperature in all three series with combined thermal stimulation of spinal cord and hypothalamus. This difference of 1° C hypothalamic temperature between thresholds for shivering and panting was valid also under the condition of 30° C air temperature, when a hypothalamic threshold temperature of 37.6° C for shivering was the lower limit of the range. Since the variation of cutaneous blood flow is controlled within the range, this finding indicates a high thermosensitivity of the combined spinal and hypothalamic sensors.

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