The Usefulness and Limitations of Single Neuron Recordings in Evaluating the Neural Control of Temperature Regulation

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This paper deals with the possible significance that single neurons, which respond to local or remote temperature stimuli, may have in thermoregulatory control. Recordings of single neurons that appear to be involved in temperature regulation are easy to interpret as long as a functional association can be demonstrated. The processing of afferent thermal signals at different levels of the neuraxis exhibits differences in degree, depending on the location of the receptive field. Descending control of afferent temperature signals is already apparent at the segmental level of the spinal cord. It seems promising to search for central primary thermodetectors in the spinal cord rather than in those regions of the central nervous system where the principles of structural organization are largely unknown. In the hypothalamus, it is difficult to correlate neuronal responses to temperature with regulatory output, even in conscious animals. Characterization of thermoresponsive neurons by their sensitivity to biogenic amines might be used to establish a functional association. In vitro recordings from temperature-responsive neurons in the hypothalamus of rats and ducks indicate that a differentiation of intrinsic and synaptically induced thermosensitivity per se is not relevant to functional characterization.

The regulation of body temperature in warm-blooded animals is mainly achieved by the integrative function of the nervous system, in that it processes the temperature information from different sites in the body and generates appropriate signals to control the different effector mechanisms for heat production or heat conservation. There is no doubt that recordings from single neurons at different levels of the central nervous system (CNS) have contributed tremendously to our current understanding of temperature regulation. A correct and significant interpretation of observations obtained by single neuron recording techniques appears to be possible only if the functional role of a neuron under investigation can be determined (i.e., in neurons which clearly belong to either the afferent or efferent temperature control pathway). This situation is illustrated in the present paper by examples obtained from neurons of the afferent thermal pathway.

In the case of "integrative" neurons which receive a vast synaptic input, additional criteria are necessary to unravel their possible position in the thermoregulatory control network. This condition is particularly true for hypothalamic neurons, which may respond both to temperature change of one or more sites in the body, outside the hypothalamus, as well as to the temperature of the hypothalamic area itself. Attempts to resolve this problem have been made in several directions. One method has been to record from the hypothalamic neurons of unanesthetized, unrestrained animals and correlate the observed neural activity pattern with the concomitantly observed...
thermoregulatory effector responses. Another method has been to record from hypothalamic slices in vitro, so as to eliminate most of the synaptic connections, in order to reveal the intrinsic neuronal response to local temperature changes. Both approaches will be delineated and critically discussed.

Studies of the ascending thermal pathway in the spinal cord [1–9], the brain stem [10–14], and the thalamus [13,15–19] have already revealed differences in the processing of temperature signals from two skin areas which are particularly rich in temperature receptors—the facial skin and the inguinal region. The temperature response characteristics of neurons which respond to facial skin temperature changes, in both the trigeminal nuclei and the thalamus, simply reflect the static and transient response characteristics of peripheral temperature receptors, indicating that, apart from some convergence of ipsilateral receptive fields, these neurons relay only the afferent signal. The temperature signals from the inguinal region, however, are already processed at the spinal segmental level. Many dorsal horn neurons (DHN) responding to scrotal temperature changes, demonstrate either purely static or transient responses. Bursting patterns of activity, frequently observed in the primary afferent temperature-sensitive fibers, are completely absent in DHN. Most strikingly, the majority of DHN responding to scrotal thermal stimulation do so with abrupt changes in activity over relatively small ranges of temperature (0.5°C–4°C) from either minimum to maximum firing rates, or vice versa. The result of this response is conversion of the bell-shaped curve for the activity-temperature relation of peripheral pudendal fibers into abrupt, switch-like sigmoid curves (Fig. 1).

In the brain stem and thalamus, essentially all neurons which react to inguinal temperature changes demonstrate this switching type of response, but the temperature range in which these supraspinal relay neurons operate is usually less than 1°C. The dramatic narrowing of the operating range appears to occur in the nucleus raphe magnus. A combination of thalamic recording with spinal or brain stem lesions, and brain stem recording in decerebrate animals has indicated that the thermoafferent pathway from the scrotal skin is in fact spino-raphe, rather than spino-thalamic. From the nucleus raphe magnus, the information ascends either directly to the thalamus and hypothalamus [12,13] or indirectly via the dorsal raphe and medial forebrain bundle [20]. The differences in the central processing of the thermal afferent pathways from the facial and inguinal regions may well be a reflection of the different physiological roles of the thermal information. Whereas the input from the facial skin has a profound effect upon behavioral thermoregulation and is obviously important in cognitive discrimination, the input from the inguinal region provides an extremely powerful drive to the autonomic thermoregulatory network. Neither hypothalamic nor brain stem neurons which respond to skin temperature changes are subject to descending control from the cortex. A proportion of the sensory thalamic neurons do, however, depend upon an intact cortical synaptic connection. The role and hypothalamic function of this small class of neurons is unknown.

There is some controversy about the nature of supraspinal control of spinal cord neurons which respond to skin temperature changes. A reversible blockade of signal transmission in the rat’s cervical cord could either increase or decrease the tonic activity as well as the reaction to scrotal skin temperature changes of DHN (Fig. 2). This suggests that brain stem neurons can exert excitatory, inhibitory, or even no influence on the spinal neurons, although it is not known what factors invoke the descending control [5]. It has been shown that, of the anterolateral tract neurons which
receive both peripheral and spinal cold inputs, only the peripheral input was subject to supraspinal control [21]. This fact might indicate a mechanism for providing a weighting factor to the different components of the ascending thermal signal.

A problem that is central to any interpretation of electrophysiological data showing activity changes of neurons in response to local temperature changes is the question of whether these neurons are part of the afferent or efferent pathway or are "primary" temperature sensors. While anatomical considerations are useful in assessing the role of spinal and thalamic neurons, the neurons of the brain stem or the hypothalamus could conceivably be either afferent or efferent. This question can be resolved for brain stem neurons by experiments in acutely decerebrate animals, but this method is patently not possible for hypothalamic neurons. A particularly fruitful field for possible future research has been opened by the discovery of spinal neurons which possess an intrinsic thermosensitivity [21]. These neurons possess axons which project through the anterolateral quadrants and can be excited by thermally stimulating the spinal cord without influencing core temperature. Different populations of neurons respond to warming or cooling the cord in a manner similar to the peripheral receptors, and they can drive the appropriate thermoregulatory response, even when the dorsal roots are cut (Fig. 3). Future research should, perhaps, be directed at determining the precise origin of the ascending anterolateral fibers which appear to convey information from these spinal cold and warm sensors.

Regarding supraspinal "primary" thermostors, interpretation of single neuron studies is possible only where the principles of structural organization are known, as they are in the spinal cord. Although the local temperature sensitivity of hypothalamic neurons is not in doubt, it is impossible to determine whether any single hypothalamic

![Diagram of response curves for a warm-reactive and a cold-reactive dorsal horn neuron in rats for a range of different constant scrotal temperatures. Operating range: 1°C in the warm- and 0.5°C in the cold-reactive neuron. From [5].]
neuron is part of the afferent input, whether it comprises part of the intrinsic regulatory network, or whether it is directly responsible for driving the autonomic effectors.

The application of single-unit recording in unanesthetized animals was proposed in order to unravel the hypothalamic neuronal network controlling body temperature [22]. The obvious advantage of this preparation is that the elimination of the depressant effect of anesthetics allows recording of thermoregulatory effector responses concurrently with single neuronal activity. An attempt to correlate the effector output of the intact regulatory system with the response of single hypothalamic neurons to temperature changes within the hypothalamus was made in conscious unrestrained goats [23]. It was assumed that hypothalamic neurons involved in mediating receptor responses would show similar changes in activity to alterations of two or more locally thermosensitive sites known to evoke such responses. Local

FIG. 2. Rate meter recordings of the activity of two different warm-reactive dorsal horn neurons (A, B) of rats in response to periodic changes of scrotal temperature before, during, and after the cervical cord was effectively blocked by cooling to 5°C. While only the tonic activity but not the temperature reaction is suppressed in one neuron (A), all activity ceased after effective blockade of the cervical cord. From [Tuschiya, Pierau: unpublished].
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FIG. 3. Temperature characteristics of discharge rates of spinal anterolateral tract neurons in cats stimulated by either warming or cooling the spinal cord itself. The afferent function of these neurons was confirmed by histological verification of the recording sites. Upper part (A and B): combined dynamic static responses to changes of spinal canal temperature (T_sc), while core temperature (T_c, measured in the colon) remains virtually constant. A: warm sensitive neuron; B: cold-sensitive neuron. Lower part (C): average static temperature/frequency relationships of 20 cold-sensitive and 20 warm-sensitive spinal anterolateral tract neurons recorded in cats.

temperature stimulation was applied to the hypothalamus and the spinal cord by means of the appropriate thermodes. Out of 53 units from which stable recordings were obtained, nine neurons were classified as hypothalamic warm-sensitive, two as hypothalamic cold-sensitive, and one as warm-sensitive to spinal cord temperature changes. In all locally temperature-sensitive neurons, the autonomic response and the firing rates closely followed hypothalamic temperature, as is demonstrated in Fig. 4. The firing rate of all recorded hypothalamic neurons demonstrated a great variability, which appears to be characteristic for the neuronal activity of this brain area in unanesthetized animals. Although in all experiments the thermoeffector activity was affected by alterations of hypothalamic and spinal cord temperature, the firing frequency of each unit followed temperature changes from only one or the other of these two sites, with the exception shown in Fig. 5.

It is obvious that the results of this study do not fulfill the criteria introduced for the characterization of hypothalamic neurons involved in the control of autonomic responses. This objection does not seem to apply to the technique used, which appears to be adequate. Further studies on this preparation would probably gather an appropriate number of neurons which react to temperature changes in more than one local site. It might prove impossible, however, to approach the functional identification
of effector neurons in this manner, since convergence of different temperature-sensitive areas onto afferent neurons should result in activity changes similar to those expected from neurons integrated in the control circuit of autonomic responses. More work has to be done to enable a final decision on whether similar approaches can serve to identify the function of single neurons in the hypothalamic neuronal circuitry which controls temperature regulation. Exact determinations of the latency between neuronal responses and the related effector response may help to discriminate between neurons belonging to the afferent or efferent pathway.

Another possibility for accomplishing a functional characterization of neurons in complex circuits is their association with the effect of putative transmitter substances. The basic suggestion is that neurons which belong to a particular functional system should react in a uniform way, thus allowing them to be associated with a previously identified functional pathway. For example, two pathways relevant for the control of body temperature, which ascend to the hypothalamus, are thought to fulfill these
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FIG. 5. Time course of an experiment demonstrating a warm-sensitive hypothalamic neuron which also reacts to spinal cord warming. From top to bottom: rectal temperature (Trec); metabolism (M) in W/kg; respiratory evaporative heat loss (REHL) in W/kg; ear skin temperature (Ts) in °C; inlet perfusion temperature for the hypothalamus (solid line) and the spinal cord (dashed line); and neuronal firing rate. From [Mercer, Jassen, Pierau: unpublished].

criteria [24]. One is noradrenergic and comes from the dorsomedial reticular formation; the other one is serotonergic and originates from the nucleus raphe magnus.

Correlation of the response of a neuron with local temperature changes and iontophoretically applied biogenic amines in anesthetized rabbits revealed a predominantly stimulating effect of 5-hydroxytryptamine (5HT) on warm-sensitive neurons, whereas cold-sensitive neurons were often inhibited [25]. The opposite effect was produced by the iontophoretic application of noradrenaline (NA), which is in accordance with similar studies on anesthetized cats and rats [26]. It was rather surprising that a large number of temperature-sensitive neurons did not respond to any of the applied drugs. This fact might be due to the suppressing effect of general anesthetics. To overcome this problem, it might be more promising to apply microiontophoresis to the hypothalamic neurons of conscious animals.

In experiments on unanesthetized Pekin ducks [27], a number of putative transmitter substances were iontophoretically applied to temperature-sensitive hypothalamic neurons. While all temperature-sensitive neurons were inhibited by GABA and excited by glutamate, the majority of cells was also excited by ACH. Different effects on cold- and warm-sensitive neurons (total, 27) but only 50 percent of the warm-reactive (total, 34) were facilitated by 5HT, while the other half of the warm units was depressed. These two sets of warm-responsive neurons reacted differently to NA: all neurons which were inhibited by 5HT were also inhibited by NA, but the NA facilitated and inhibited almost equal numbers of those neurons which were facilitated by 5HT. In this respect the reaction of the population of warm-sensitive neurons resembled that of the cold-sensitive neurons of this study. The results suggest that iontophoretic administra-
tion of putative transmitter substances in unanesthetized animals may be a promising approach to a more complete functional differentiation of temperature-sensitive neurons in the hypothalamus. This approach might be particularly fruitful if additional criteria such as the neurons' response to remote temperature stimulation are used in combination with the techniques just described.

The previously described approaches were designed to confirm the functional significance of temperature-sensitive hypothalamic neurons under conditions in which the neuronal circuitry of the hypothalamus as well as its ascending and descending connections were intact and not depressed by narcotics or influenced by other drugs. An entirely opposite approach is the physical separation of hypothalamic neurons using in vitro techniques that employ hypothalamic cell cultures [27] or thin slices of hypothalamic tissue [28–32]. The latter preparation has the advantage that the effect of temperature on the neuronal circuit can be investigated in the absence of any synaptic input from other brain areas. Two additional possibilities are that the neurons under investigation can be subjected to manipulations of the ionic composition of the bath solutions and to localized neurochemical manipulations. These in vitro studies have demonstrated that the composition of the populations of various hypothalamic neurons in vitro are similar to those observed in vivo, and that the properties of the thermoresponsive neurons are essentially the same in both kinds of preparation.

Evidence has been produced [34] that the early criteria of linearity or non-linearity of their temperature response in vivo [22] do not suffice in discriminating between neurons with intrinsic thermosensitivity (primary thermodetectors), and neurons whose temperature sensitivity is based on a temperature effect on synaptic currents. The slice technique was therefore used to distinguish between inherent thermosensitivity and thermosensitivity dependent on local synaptic input. This was done by using a reversible inhibition of the local synaptic activity in the tissue slice by decreasing the Ca++ and increasing the Mg++ concentrations in the perfusion medium [31,33]. The results obtained from two such studies differ in some respects. In one study [33], in six out of seven warm-responsive neurons the response to temperature changes was preserved during synaptic blockade, while the remaining neuron lost its warm sensitivity. All of the seven cold-responsive neurons, however, lost their responsiveness to temperature changes during synaptic inhibition. In the other study [31], in 18 out of 23 warm-responsive neurons, the temperature response remained during synaptic inhibition but was lost in the five remaining neurons. The temperature response also remained during synaptic blockade in three out of four cold-responsive neurons. The remaining one ceased firing in Ca++-free/high Mg++ solution.

It appears uncertain whether these inconsistent results permit the conclusion that the temperature sensitivity of warm-responsive hypothalamic neurons is almost entirely intrinsic, while the temperature sensitivity of cold-responsive neurons stems from synaptic activity [33], as proposed by the neuronal model which predicts that the activity of hypothalamic cold-sensitive neurons is controlled by the input from hypothalamic and peripheral warm detectors [34,35].

Differences in the slice and recording techniques might be the cause for the discrepancy observed in the two studies. The possibility has been discussed by Kelso and Boulant [33] that the preservation of cold sensitivity in the study by Hori et al. [31] might be due to an effective synaptic blockade, since the concentration of Mg++ might have been too low. The applied solution (0 Ca++; 6.5 mM Mg++), however, has proved adequate to abolish the synaptic fraction of the potential evoked by electrical
stimulation of hypothalamic slices [Nakashima: unpublished]. Suppression of the thermosensitivity of five warm-responsive neurons in 0 Ca++/6.5 mM Mg++ solution [31] also indicates that synaptic inhibition was effective under this condition, but not before ten minutes of incubation. It might also be suggested that the Mg++ concentration of 9 mM used by Kelso and Boulant [33] was too high under the given conditions, since the spontaneous activity of almost all of the recorded temperature-sensitive neurons was significantly depressed in low Ca++/high Mg++ solution. This result conceals the danger that, after returning to normal solutions, recordings were made from neurons which were not the original control neurons that were observed prior to synaptic blockade.

The higher proportion of warm-sensitive neurons which lost their response to temperature during synaptic blockade in the study of Hori et al. [31] appears to suggest that there might be a statistical sampling problem and that the probability of finding intrinsic as well as synaptically induced thermosensitivity increases with the number of neurons that are observed. It should also be added that in explant cultures of rat medial basal hypothalamus and preoptic area, synaptic inhibition of low Ca++/high Mg++ left temperature sensitivity intact in both warm- and cold-sensitive neurons [28]. Although the two different in vitro preparations are not completely comparable, these results would suggest an equal probability of intrinsic temperature sensitivity for both warm- and cold-responsive neurons.

Independent of the question of whether the properties of hypothalamic warm- and cold-responsive neurons are different, the functional significance of either type of thermosensitivity still remains undefined. The association of a temperature-responsive neuron with inherent or synaptically induced temperature sensitivity per se cannot prove or disprove whether hypothalamic temperature sensitivity (and consequently the control of body temperature) is achieved by neurons possessing inherent temperature responsiveness, by neurons in which the temperature response is synaptically induced, or by an interaction of a number of neurons from both categories. This opinion concurs with Boulant’s view [34] that “the thermosensitivity of synaptic events (i.e., the effect of temperature on the release, diffusion, binding, breakdown, and reuptake of neurotransmitters) or the thermosensitivity of local reverberating circuits (in which the moderate thermosensitivity of individual neurons in a pool of mutual excitatory neurons can render each neuron highly thermosensitive) may be more important than the local thermosensitivity of an individual neuron, free from synaptic inputs.”

A possible way of elucidating the relevance of inherent and synaptically induced temperature responsiveness of hypothalamic neurons is to compare the properties of temperature-sensitive neurons of two species in which the sensitivity of the hypothalamus to local temperature changes has developed to a different degree. In contrast to that of mammals, the thermosensory function of the hypothalamus in birds is slight. While the thermoregulatory responses to preoptic/anterior hypothalamic (PO/AH) warming are moderate to weak, but nevertheless appropriate, PO/AH cooling causes insignificant or even inappropriate thermoregulatory effector responses ([36], for review). As in a mammal, however, the bird’s hypothalamus acts as the dominant site of signal integration and effector control in the temperature regulation (37,38). In spite of the different contribution of hypothalamic thermoresponsiveness to avian and mammalian temperature regulation, previous in vivo studies on the Pekin duck have revealed that hypothalamic neurons in the PO/AH region exhibit thermal characteristics that are indistinguishable from those observed in mammals [39,40].
The slice technique offers an ideal opportunity for comparing the thermosensitivity of mammalian and avian PO/AH neurons under identical conditions. PO/AH slices were obtained from Wistar rats (170–250 g), and from ducks (1.0–3.2 kg), employing the preparation procedure previously used in rats [30,31]. Extracellular recordings were obtained conventionally, using glass micropipettes in a temperature-controlled chamber perfused with solutions as previously described [31]. The only difference was that the 0 Ca++/high Mg++ solution, used for synaptic inhibition, contained Mg++ in a concentration of only 3.1 mM; at higher concentrations of Mg++, the spontaneous activity of duck neurons ceased completely. During the search for spontaneously active neurons, the bath temperature was maintained at a constant level of 37°C for rat slices and 38°C for slices of duck PO/AH. To avoid unknown bias which might influence the results, experiments were performed on rats or ducks on alternate weeks. Neurons responding to temperature changes with a temperature coefficient (F/T) > 0.6 imp. s⁻¹°C⁻¹ and Q₁₀ > 2 were classified as warm-responsive. Cold-responsive neurons had a negative temperature coefficient of < –0.6 imp. s⁻¹°C⁻¹ and Q₁₀ < 0.1.

Table 1 demonstrates that the proportion of warm-responsive, cold-responsive, and temperature-insensitive neurons is similar in both species, although the number of cold-response neurons is considerably lower than in comparable preparations of rats [41] and ducks [39] in vivo, and rats in vitro [30,31,32]. This might be due to the relatively high bath temperature employed during the search period, which might have caused some cold-sensitive neurons to cease firing. During synaptic blockade, similar proportions of warm-responsive neurons retained their temperature sensitivity in both species (Fig. 1B). The temperature response of a warm-responsive neuron from a PO/AH slice of a duck which preserved its temperature sensitivity in 0 Ca++/3.1 mM Mg++ is demonstrated in Fig. 5. The non-linear response curve, indicating a temperature sensitivity only in the hypothermic range, is characteristic for the majority of warm-responsive neurons in both species. During synaptic blockade, the spontaneous activity of the neuron was increased. This was the case in five of the neurons subjected to 0 Ca++/high Mg++, while spontaneous activity was reduced in the other five neurons and not changed in the remaining three. The response of the spontaneous activity was similar to that in warm-sensitive neurons of rats.

Independent of the effect of 0 Ca++/high Mg++ on the spontaneous activity, the temperature coefficient of those units which preserved their temperature sensitivity increased in three neurons, decreased in three others, and was converted to a negative coefficient in the hyperthermic range in the remaining neuron (Fig. 6B). This same kind of conversion was observed in a warm-sensitive neuron in a rat PO/AH slice (Fig. 6A). Both neurons responded again with a positive temperature coefficient after being returned to the control solution (Fig. 6A, B). This would imply that the conversion of the temperature coefficient was produced by a direct effect of the 0 Ca++/high Mg++ solution, rather than by any change of the neuronal response over time. Alternatively, the two warm-responsive neurons might have received a strong synaptic inhibition from nearby cold-sensitive neurons (in the hypothermic range) as well as an excitatory synaptic input from warm-sensitive neurons (in the hyperthermic range). The release of the synaptic influence during synaptic inhibition might then explain the conversion of the temperature coefficient from a positive to a negative one.

Of the two cold-responsive neurons subjected to 0 Ca++/high Mg++ solution (Fig. 8), one lost its temperature response during synaptic inhibition, but the other reacted to cooling with an increased spontaneous activity, although the fluctuation of the
TABLE 1
Comparison of Proportion of Neuron Types in Hypothalamic Slices from Rats and Ducks

|        | warm responsive | cold responsive | unresponsive | total |
|--------|-----------------|-----------------|--------------|-------|
| duck   | 24              | 3               | 14           | 41    |
| rat    | 17              | 1               | 12           | 30    |

A Number of PO/AH neurons recorded in hypothalamic slice preparations of ducks and rats; classification according to the response to local temperature changes.

B Numbers of warm-responsive PO/AH neurons (see A) from ducks and rats, which were subjected to 0 Ca++/3.1 mM Mg++ to block synaptic activity; classification according to retained or not retained temperature response during synaptic inhibition.

discharge was greater than in the normal solution. As is illustrated in Fig. 7, the threshold-type temperature response curve became linear during synaptic inhibition, but it remained linear after being returned to the control solution. Certainly the number of recorded cold-responsive neurons is too small to draw any definite conclusions. Taken together with the results previously discussed [28,31], these results

![Diagram A](image1)

FIG. 6. A: Rate meter recordings of the activity of a warm-responsive PO/AH neuron in a duck hypothalamic slice preparation during periodic temperature changes of the perfusion chamber in normal solution (0.9 mM Ca++/1.3 mM Mg++) 0 Ca++/high Mg++ (0 Ca++/3.1 mM Mg++), and subsequent normal solution. Time interval between recordings indicated as minutes. B: Frequency/temperature relation of the same neuron derived from the appropriate data in A. Linear regressions were calculated separately for the hypo- and hyperthermic temperature range.
A 0.9 mM Ca++, 1.3 mM Mg++; 0 Ca++, 3.1 mM Mg++; 0.9 mM Ca++;

B 0.9 mM Ca++, 1.3 mM Mg++; 0 Ca++, 3.1 mM Mg++; 0.9 mM Ca++;

FIG. 7. Frequency/temperature relation of a warm-responsive PO/AH neuron from hypothalamic slice preparations of a rat (A) and a duck (B) in normal solution ①; during 0 Ca++/high Mg++ ②; and subsequent normal solution ③, demonstrating conversion of the temperature coefficient during synaptic inhibition ②.

do not indicate the existence of a basic difference between warm- and cold-responsive PO/AH neurons in regard to the proportion of inherent or synaptically induced temperature sensitivity.

The comparison of temperature-sensitive neurons of the PO/AH of rats and ducks has demonstrated similar properties of those neurons in regard to average firing frequency, temperature coefficients, and Q10 values, the proportion of linear and non-linear response curves, and the proportion of warm-, cold-, and temperature-sensitive neurons. Furthermore, the proportion of temperature-responsive neurons which lost or retained their responses to temperature changes during synaptic inhibition by 0 Ca++/high Mg++, was similar in both species; as were the changes of the average frequency, the temperature coefficients, and the temperature/frequency relations under these conditions. In the context of the differing significance of local hypothalamic responsiveness in birds and mammals, these similarities at the level of single neurons suggest that any differentiation into inherent and synaptically induced temperature sensitivity in hypothalamic neurons has no functional significance. This concept would not mean that recordings from single neurons are unnecessary for the evaluation of the central control of temperature regulation, but rather that investigators should be aware of the obstacles before drawing any conclusions about function.

Studies of single neurons in parts of the CNS which have a highly integrative function, but no precisely defined morphological organization, always mean that the neuron under investigation belongs to a complicated neuronal circuitry in which mutual interaction is the dominant principle. Consequently, functional predictions and
neuronal modelling should only be inferred from single neuron studies with suitable caution. Future electrophysiological studies of the functional role of hypothalamic neurons in the control of body temperature would certainly require multi-unit recording in conscious animals as well as in the in situ preparation. Intracellular recordings are urgently required to study the membrane properties responsible for neuronal temperature sensitivity. The two examples of intracellular recordings of rat's hypothalamic neurons demonstrated by Dr. Boulant during this meeting seem to point in the right direction. Finally, combining studies of local neuronal thermoresponsiveness and the response to temperature changes of remote receptive fields at the surface or in the core of the body in conscious animals with micro-iontophoretic application of putative neurotransmitter substances may also help to elucidate the functional principles of the hypothalamic controller.

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