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TEMPERATURE RECEPTORS IN THE CENTRAL NERVOUS SYSTEM

Jack A. Boulant and Jay B. Dean

Department of Physiology, The Ohio State University, Columbus, Ohio 43210

INTRODUCTION

For half a century, it has been known that thermosensitive regions of the rostral brain stem are important in thermoregulation (61). Figure 1 indicates that a variety of thermoregulatory responses can be elicited by changing the temperature of the preoptic area and anterior hypothalamus (PO/AH). PO/AH warming evokes heat-loss responses, and PO/AH cooling evokes heat-production responses. If PO/AH temperature is changed slightly above or below normal, there are changes in heat-retention responses such as skin blood flow and thermoregulatory behavior. Figure 1 also describes the synaptic organization of PO/AH thermosensitive neurons (4). While most neurons are temperature insensitive, warm-sensitive neurons have firing rates that increase with warming or decrease with cooling. Conversely, the firing rates of cold-sensitive neurons increase with cooling or decrease with warming. Many central thermosensitive neurons also receive synaptic inputs from skin and spinal thermoreceptive pathways (4, 7). This indicates that such neurons are capable of thermal integration, and it increases the likelihood that these neurons function in thermoregulation. As summarized in Figure 1, the evidence for central thermosensitivity comes from thermoregulatory studies during thermal stimulation of discrete neural areas and from electrophysiological studies of temperature-sensitive neurons. In this review, these studies are presented first as an overview of the comparative aspects of central thermosensitivity in vertebrates. The second half of this review focuses on the properties and synaptic organization of PO/AH thermosensitive neurons.

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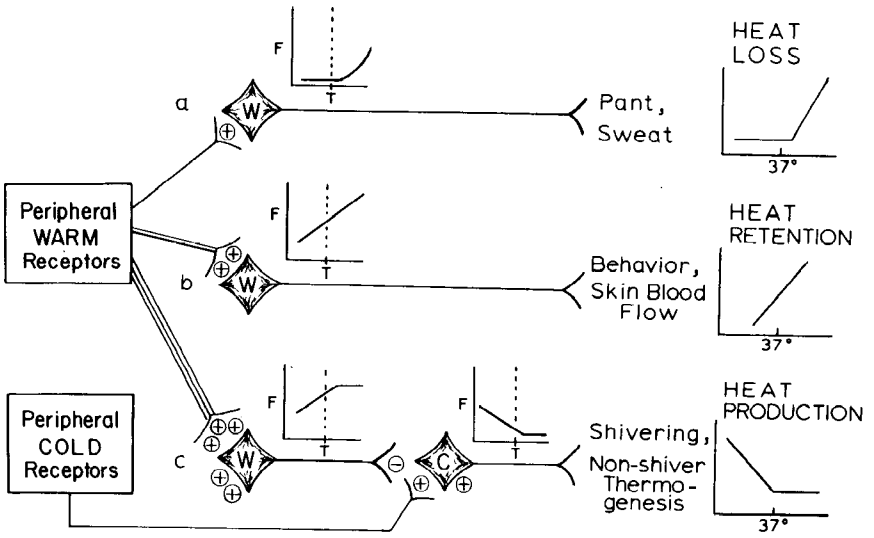

Figure 1 A model showing the hypothalamic neuronal control of various thermoregulatory responses. *W*=warm-sensitive neuron; *C*=cold-sensitive neuron; (+)=excitatory input; (−)=inhibitory input. Hypothalamic thermoresponse curves of different neurons and thermoregulatory responses are shown. *F*=neuronal firing rate; *T*=hypothalamic temperature; *dashed line*=thermoneutral temperature. (Redrawn from Boulant; Reference 4).

COMPARATIVE STUDIES OF CENTRAL THERMAL STIMULATION

Mammals

If local warming and cooling of a neural area induces appropriate thermoregulatory responses, then it is usually concluded that the neural area contains central thermoreceptors that function in thermoregulation (4, 6, 37, 93). The best example of such an area is the PO/AH in mammals. In the rabbit, for example, PO/AH cooling elicits a profound increase in metabolic heat production due to shivering. This response is quickly reversed during PO/AH warming, which also increases panting and skin blood flow. Cooling of the mammalian PO/AH may also elicit nonshivering thermogenesis, metabolic endocrine release, piloerection, and a host of behavioral thermoregulatory responses. During PO/AH warming certain mammals show sweating, saliva spreading (i.e. evaporative cooling), and other behavioral responses (4, 37).

In mammals, other neural areas have been shown to respond to thermal stimulation. The posterior hypothalamus differs from the PO/AH in that it lacks an appropriate thermosensitivity for autonomic responses (75); however, posterior hypothalamic thermal stimulation produces appropriate behavioral re-

sponses in squirrel monkeys (1). Local warming of the medulla (11) increases respiratory frequency, while thermal stimulation of the spinal cord sometimes elicits a variety of thermoregulatory responses comparable to those induced by manipulation of PO/AH temperature (93).

Birds

It has been suggested that birds display interspecies differences in terms of their predominant sites for central thermoreception (88). In some birds the spinal cord appears to be a primary thermoreceptive structure, especially in determining heat production. These species include the pigeon (28, 77), penguin (33, 97), quail (100), and duck (62, 96, 99). Even in these birds, appropriate heat loss and heat retention responses can be evoked by subtle changes in PO/AH temperature (97, 99, 100). During more drastic temperature changes, however, particularly during PO/AH cooling, thermoregulatory responses are often inappropriate or weak. In contrast, the hypothalami of other birds are highly thermosensitive and respond in a manner similar to that observed in mammals. Rostral brain stem thermal stimulation induces both appropriate heat-loss and heat-production in the emu (53), goose (36), and house sparrow (64). Moreover, spinal thermosensitivity was found to be of little significance in the goose (36). In the duck, thermal stimulation of the lower midbrain and upper pons produced effective thermoregulatory responses (62, 96, 98). It is important to emphasize that any divergence of avian thermoreception appears to exist only for physiological responses, not for behavioral responses. The avian rostral hypothalamus still remains highly thermosensitive in terms of controlling behavioral thermoregulatory responses (83–86).

Ectotherms (Reptiles, Amphibians, and Fishes)

Rostral brain stem thermal stimulation elicits appropriate behavioral thermoregulatory responses in lizards (32, 66), turtles (65), and fishes (13–15, 34) placed in thermal gradients. Brain stem warming causes these animals to exit from a warm environment at a lower body temperature than would normally elicit this response. Brain stem cooling produces the opposite response, with the exception of the brown bullhead, which apparently lacks appropriate central thermosensitivity in the hypothermic range (15). Amphibians have also been shown to behaviorally thermoregulate in response to extrahypothalamic thermal stimulation. In the frog, spinal cord (18) or intra-abdominal warming (9) causes behavioral selection of cooler environments. In some cases physiological responses are affected by rostral brain stem thermal stimulation. Evaporative heat-loss (panting) is directly related to brain temperature in turtles (65, 80) and lizards (12, 102). One study investigated brain thermosensitivity indirectly in the bullfrog by radiant heating of the head. It was found that head warming

increased cutaneous mucus discharge, which impedes desiccation during basking (60).

Summary of Vertebrate Thermal Stimulation

The combined evidence from these studies supports the concept that the rostral brain stem serves a thermoregulatory function in all vertebrates. Behavioral thermoregulation predominates and is often recruited before physiological responses, even in species with well-developed autonomic thermoregulation (4). Satinoff (81) suggests that behavioral and autonomic thermoregulatory neuronal networks are functionally and anatomically distinct. Adair's (1) research on mammals and some avian studies (62, 83–86, 96, 98) support this concept. Caputa (10) further proposes that avian differences in the control of autonomic responses may be related to the development of flight. In some flying birds PO/AH thermosensitivity is apparently reduced such that brain temperature is maintained lower than body temperature. Since thermal fluctuations of the head could be great during flight, hypothalamic thermosensitivity might not be as appropriate as deep-body thermosensitivity (10, 100). Accordingly, in some species the neural control of autonomic thermoregulation may have shifted down the neuroaxis to the lower midbrain (62, 96, 98) and spinal cord (93).

ELECTROPHYSIOLOGY OF THERMOSENSITIVE NEURONS

Criteria for Neuronal Thermosensitivity

Table 1 shows the locations and proportions of thermosensitive neurons observed in many of the recent electrophysiological studies. Table 1 also indicates that there are no uniform criteria for classifying neuronal thermosensitivity. Earlier studies used either the neuronal Q_{10} or the slope of the thermoresponse curve as a criterion (4). Studies of neuronal integration have preferred slope because this criterion can be applied to a neuron's local temperature and to the peripheral temperature affecting the neuron's afferent input. Generally, minimum Q_{10} criteria include values significantly greater than 2.0 for warm-sensitive neurons and values less than 0.5 for cold-sensitive neurons. Minimum criteria for slopes or regression coefficients are 0.8 impulses/sec/°C for warm-sensitive neurons and −0.6 impulses/sec/°C for cold-sensitive neurons (4). It is also important that these values be determined over at least a 2–3°C temperature range. As evidenced by Table 1, recent publications show a disturbing trend towards classifying neurons based on values far below previously accepted minimums. Even more disturbing is the fact that many recent studies give no criteria at all. As a result, the proportions of thermosensitive neurons are probably overestimated in some recent studies.

Table 1 Recent single unit studies showing locations and proportions of neurons tested for local thermosensitivity.

Species	CNS location[a]	Neurons: Warm (%)	Neurons: Cold (%)	Neurons: Insensitive (%)	*n*	Criteria warm[b]	Criteria cold[b]	Reference
cat	PO, AH	9	40	51	57	—	—	72
kangaroo rat	PO, AH	47	27	26	40	> 0	< 0	22
rabbit	PO, AH	43	11	46	28	> 0	< 0	21
rabbit	PO, AH	31	31	38	45	—	—	26
rabbit	PO, AH	38	24	38	53	—	—	25
rabbit	PO, AH	28	28	42	21	+0.4	—	23
rabbit	PO, AH	40	25	35	97	—	—	24
rat[c]	PO, AH	22	6	72	139	+0.7[d]	−0.6	38
rat[c]	PO, AH	47	23	30	56	+0.7[d]	−0.7[d]	89
rat[c]	PO, AH	19	2	79	640	+0.1[d]	−0.1[d]	50
rat[c]	PO, AH	35	10	55	140	—	—	49
rat[c]	PO, AH	37	15	48	188	+0.7	−0.7	42
rat[c]	PO, AH	39	13	48	286	+0.7	−0.7	41
rat[c]	PO, AH	45	24	31	55	—	—	43
rat[c]	PO, AH	32	13	55	62	$Q_{10} > 2$	$Q_{10} < 0.5$	2
rat[c]	PO	33	12	55	112	—	—	56
rat[c]	PO	43	16	41	56	—	—	63
rat[c]	PO	34	10	56	145	+0.7[d]	−0.7[d]	57
rat[e]	PO, AH	32	6	62	117	+0.8	−0.6	87
rat[e]	PO, AH	73	0	27	22	$Q_{10} > 2$	$Q_{10} < 0.5$	47
rat[e]	PO, AH	30	10	60	138	+0.8	−0.5	55
rat[e]	PO, AH	17	15	68	48	+0.8	−0.6	54
rat[e]	PO, AH	17	8	75	86	$Q_{10} > 2$	—	44
rat[e]	PO	35	10	55	167	+0.8	−0.6	90
rat[e]	PO	37	8	55	180	+0.8	−0.6	91
rat[e]	PO	29	6	65	256	—	—	45
rat[e]	PO	61	7	32	60	—	—	67
rat[e]	AH	34	1	65	75	+0.1[d]	−0.1[d]	46
guinea pig[e]	PO, AH	43	13	44	53	+0.8	−0.6	8a
guinea pig[e]	PO	43	12	45	110	+0.8	−0.6	8b
rat[f]	PO	24	10	66	95	$Q_{10} > 2$	$Q_{10} < 0.5$	3
mouse[f]	PO, AH	28	4	68	54	—	—	51
cat[c]	PH	19	16	65	98	$Q_{10} > 2$	$Q_{10} < 0.5$	19
rabbit[c]	PH	15	2	83	155	—	—	104

Table 1 *(continued)*

Species	CNS location[a]	Neurons: Warm (%)	Neurons: Cold (%)	Neurons: Insensitive (%)	n	Criteria warm[b]	Criteria cold[b]	Reference
cat[c]	rMB	10	8	82	99	$Q_{10} > 2$	—	16
cat[c]	cMB	72	11	17	72	$Q_{10} > 2$	—	16
rabbit[c]	MB	8	19	73	204	+0.8	−0.8	39
rabbit[c]	MB	10	27	63	51	—	—	48
rat[c]	MB	58	0	42	24	$Q_{10} > 2$	—	40
rabbit[c]	MD	21	26	53	187	—	—	52
duck	HY	49	14	37	35	$Q_{10} > 1$	$Q_{10} < 1$	94
sunfish[c]	PO	17	2	81	276	+1.0[d]	−1.0[d]	70
trout[c]	TH, MB	18	1	81	140	$Q_{10} > 4$	$Q_{10} < 0.25$	29

[a] HY = hypothalamus; PO = preoptic area; AH = anterior hypothalamus; PH = posterior hypothalamus; TH = thalamus; MB = midbrain; MD = medulla; r = rostral; c = caudal.
[b] Unless designated as Q_{10}, values are the minimum slope criterion in impulses/sec/°C used to access warm and cold thermosensitivity.
[c] Anesthetized preparation
[d] Also used $Q_{10} > 2$ or < 0.5 to access warm or cold sensitivity, respectively.
[e] Tissue slice preparation
[f] Tissue culture preparation

Neuronal Proportions and Locations

Thermosensitive neurons have been recorded in several species at various locations and in different types of preparations, including anesthetized and unanesthetized animals, and in vitro tissue slices (55) and tissue cultures (68). Only recent studies (primarily 1980–1985) that used local thermal stimulation to determine the proportions of warm-sensitive, cold-sensitive, and temperature-insensitive neurons are included in Table 1. Early single unit studies (1961–1980) (4, 37) indicate that in the mammalian PO/AH neuronal population approximately 30% of the neurons are warm sensitive, 10% are cold sensitive and 60% are temperature insensitive. A similar trend can be seen in Table 1, if one considers only recent studies with relatively large sample sizes (i.e. $n > 100$). The recent studies using anesthetized animals find that 31% of the PO/AH neurons are warm sensitive, 10% are cold sensitive, and 59% are temperature insensitive. Recent PO/AH tissue slice studies report that 34% of the neurons are warm sensitive, 9% are cold sensitive, and 57% are temperature insensitive. The two tissue culture studies found a slightly lower proportion of thermosensitive neurons: 26% warm sensitive, 7% cold sensitive, and 67% temperature insensitive. In Table 1, the studies using unanesthetized whole-animal preparations had smaller sample sizes (i.e. $n < 100$) and showed consistently higher percentages of cold-sensitive PO/AH neurons (26%). This

may be due to the absence of any anesthetic suppression of synaptic activity impinging upon the cold-sensitive neurons, as depicted in Figure 1. It may also be attributable to the lack of any rigid cold-sensitivity criterion in these experiments, which could cause overestimation of this neuronal population.

Thermosensitive neurons are found in the PO/AH in all vertebrates studied (Table 1). In addition to those CNS locations indicated in Table 1, thermosensitive neurons have been identified in mammalian (92, 95, 103) and avian (27, 69, 76) spinal cords. Conversely, Gorke (27) explored the reptilian spinal cord and found no thermosensitive neurons. Recently, tissue slice studies have mapped the locations of temperature-sensitive neurons in the mammalian hypothalamus. Frontal preoptic slices show that warm-sensitive neurons are located primarily in the central and lateral portions of the medial and lateral preoptic areas and that cold-sensitive neurons are localized mainly in central portion of the medial preoptic area (90, 91). Horizontal slices passing through the entire hypothalamus show that cold-sensitive neurons are found in the preoptic area, lateral and posterior hypothalamus, mammillary nuclei, and nucleus reuniens. In addition to these regions, warm-sensitive neurons are found in the paraventricular, ventromedial, and anterior hypothalamic nuclei (17).

SYNAPTIC ORGANIZATION OF PREOPTIC THERMOSENSITIVE NEURONS

Neuronal Functional Specificity

Do both thermosensitive and temperature-insensitive neurons function in thermoregulation? In some neuronal models, synaptic inputs from temperature-insensitive neurons serve as steady-state reference signals to set-point interneurons (30, 31, 35). According to these models the interneurons simply compare synaptic inputs from warm-sensitive neurons with antagonistic synaptic inputs from temperature-insensitive neurons. Another model holds that while neurons may be temperature-insensitive in terms of their firing rates (i.e. impulses/sec), some are actually thermosensitive in terms of their interspike intervals (78). Thus, the coding of thermal information may not be limited to firing rate alone.

In describing the role of temperature-insensitive neurons we should consider other functional roles of a particular neural area. In addition to thermoregulation the PO/AH regulates body water, metabolite and hormonal levels, and sexual behavior; PO/AH neurons have been shown to be sensitive to osmotic pressure, blood glucose levels, and the levels of circulating reproductive steroids, testosterone and estrogen (90, 91). It has been suggested that the PO/AH neurons have functional specificity (4), i.e. that the thermosensitive neurons function in thermoregulation and the majority of the temperature-

insensitive neurons constitute the osmosensitive, glucosensitive, and steroid-sensitive neurons, which control other regulatory systems. However, some studies suggest interrelationships between thermoregulation and these other regulatory systems (90, 91).

With the advent of tissue slice studies it is now possible to characterize individual neurons according to their sensitivities to a variety of endogenous factors. The evidence obtained from such studies belies any strong functional specificity among PO/AH neurons (90, 91). Figure 2 shows the proportions of preoptic temperature-sensitive and temperature-insensitive neurons that respond to various experimental perfusion media. Approximately half of the thermosensitive neurons are affected either by low glucose and hyperosmotic media or by testosterone and estradiol media. In contrast, these media affect a much smaller proportion of the temperature-insensitive neurons. Also, while most of the osmosensitive neurons are also affected by low glucose media, this is not the case with the testosterone- and the estradiol-sensitive neurons; these two steroids rarely affect the same neuron.

The important finding of these studies is that the population of temperature-insensitive PO/AH neurons does not contain the majority of the osmosensitive, glucosensitive, and steriod-sensitive neurons. Rather, most of these neurons constitute the population of thermosensitive neurons. This emphasizes that the observation of thermosensitivity in a neuron does not guarantee that it has a functional role in thermoregulation. However, these studies do indicate a neuronal basis for the interactions between different regulatory systems. For

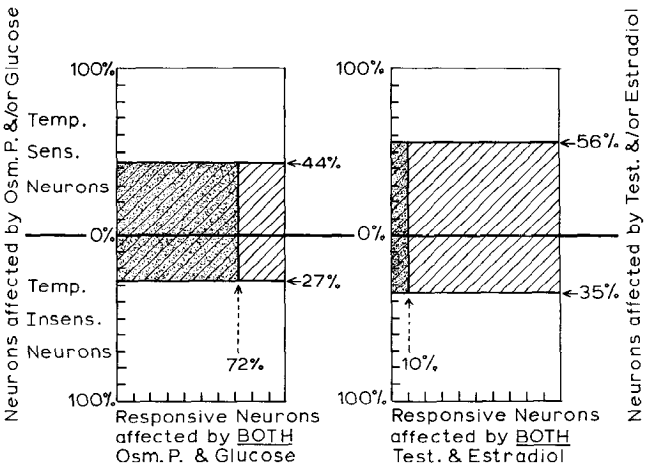

Figure 2 Proportions of temperature-sensitive and temperature-insensitive preoptic neurons affected either by hyperosmotic or hypoglucose media and by testosterone or estradiol media (hatched areas). Shaded areas show the proportions of osmosensitive neurons affected by glucose and the proportions of testosterone-sensitive neurons affected by estradiol. (Summarizes References 90 and 91.)

thermoregulation in particular the evidence shows that a central thermoreceptor can be affected by a variety of endogenous factors, in addition to synaptic inputs from afferent pathways. Moreover, it shows that temperature can affect the regulation of other homeostatic systems.

Influence of Afferent Input on Neuronal Thermosensitivity

Some studies make clear distinctions between "thermoreceptors" and set-point interneurons (20, 30, 35). Thermoreceptors are often defined as neurons whose thermoresponse curves are exponential or linear over wide temperature ranges. The thermoresponse curves of interneurons are thought by some to be nonlinear and limited to narrow temperature ranges. Under rigid definitions, thermoreceptors are viewed as neurons that are only sensitive to local temperature and that receive no afferent or local synaptic input (30, 35). These definitions of thermoreceptivity are not used in this review because there is nothing to preclude an inherently thermosensitive neuron from receiving synaptic input either from a nearby thermosensitive neuron or from a peripheral afferent pathway.

Warm-sensitive neurons may control several thermoregulatory responses. The model shown in Figure 1 proposes that a neuron's range of thermosensitivity indicates its most likely role in thermoregulation. It has been shown that low-firing warm-sensitive neurons are thermosensitive in the hyperthermic range but high-firing warm-sensitive neurons are thermosensitive in the hypothermic range (4). The higher-firing warm-sensitive neurons receive the greatest proportion of afferent input from peripheral thermoreceptor pathways (5, 7). Accordingly, this model (Figure 1) suggests that some warm-sensitive neurons (*a*) receive relatively little synaptic input, and therefore have low firing rates. Since these low-firing neurons are primarily thermosensitive above 37°C, they probably control heat-loss responses. Another group of warm-sensitive neurons (*b*) have medium firing rates and receive a moderate amount of afferent input. Since these neurons are equally thermosensitive both above and below 37°C, many are probably involved in heat-retention responses, such as changes in behavior and skin blood flow. A third group of warm-sensitive neurons (*c*) have high firing rates, presumably because they receive the greatest amount of afferent input. Since these neurons are primarily thermosensitive below 37°C, they probably control heat-production, possibly by inhibiting nearby interneurons that appear to be cold-sensitive. Figure 1 also suggests that these cold-sensitive neurons are synaptically driven by excitatory inputs, both from afferent pathways and from nearby neurons.

Neuronal Thermosensitivity in Tissue Slices

Recent tissue slice studies have improved our understanding of the synaptic organization of the preoptic neuronal network. Since tissue slices are devoid of afferent inputs, they provide a means to test predictions of the model in Figure 1.

Hypothalamic tissue slices contain the same proportions of warm-sensitive, cold-sensitive, and temperature-insensitive neurons as recorded in intact animals (Table 1). Most neurons in tissue slices, however, have low spontaneous firing rates, presumably due to the removal of afferent input (55). Figure 1 predicts that deafferentation will produce a homogeneous population of low-firing warm-sensitive neurons that are primarily thermosensitive above 37°C. Indeed, nearly all (87%) of the warm-sensitive neurons in tissue slices display their greatest thermosensitivity in the hyperthermic range (4, 54, 55). Cold-sensitive neurons in tissue slices also have low firing rates and are sensitive primarily to temperatures above 37°C. This finding suggests that the thermosensitivity of cold-sensitive neurons results from inhibitory input from nearby warm-sensitive neurons.

Synaptic Blockade of Thermosensitive Neurons

In addition to deafferentation, tissue slices offer certain advantages not afforded in whole-animal experiments. No anesthetic is used, and exact locations of recording sites are guaranteed. In addition, tissue slices can be alternately perfused with a normal nutrient medium and a medium containing an agent for synaptic blockade. In this way the firing rate and thermosensitivity of individual preoptic neurons can be determined before, during, and after synaptic blockade. One such study (54) found that synaptic blockade alters the firing rates of some warm-sensitive neurons but has no effect on other warm-sensitive neurons. Regardless of the firing rate effect, however, nearly all PO/AH warm-sensitive neurons retain their thermosensitivity during synaptic blockade, which suggests that warm-sensitive neurons possess an intrinsic thermosensitivity. In many cases, it appears that this sensitivity can be accentuated by local synaptic input, possibly from reverberating circuits of warm-sensitive neurons.

This same study (54) also showed that thermosensitivity is lost in cold-sensitive neurons during synaptic blockade. This observation supports the hypothesis that neuronal cold sensitivity is due to inhibition from nearby warm-sensitive neurons. This point remains controversial, however, since two other in vitro studies report the existence of cold sensitivity during synaptic blockade (3, 45). Unfortunately, the criteria used for cold sensitivity differ considerably, and it is likely that many of the cold-sensitive neurons in these later studies would be considered temperature-insensitive in the former study.

Intracellular Recordings of Thermosensitive Neurons

A study of the intracellular activity of preoptic neurons in fish has found two basic types of thermosensitive neurons (71). One type is warm sensitive, and displays pacemaker-like depolarizations with no evidence of synaptic input. It has firing rates that are exponentially thermosensitive. The other neuronal type

includes both warm-sensitive and cold-sensitive neurons. This type of cell is strongly dependent on synaptic input, and the extent to which it is inherently thermosensitive is not known. As predicted in Figure 1, however, the cold-sensitive neurons in fish receive both inhibitory and excitatory synaptic potentials. This observation implies that cold sensitivity is synaptically derived. Another recent study (73) recorded the intracellular activity of preoptic thermosensitive neurons in the anesthetized rat. In this study the warm-sensitive neurons received much thermosensitive excitatory synaptic input, which appeared to accentuate an inherent thermosensitivity. This suggests that there are local networks of reverberating circuits among the warm-sensitive neurons. Again, the cold-sensitive neurons receive both inhibitory and excitatory synaptic potentials. In this rat study neuronal cold-sensitivity was directly dependent upon this synaptic input; local warming decreased the frequency of excitatory potentials and increased the frequency of inhibitory potentials.

Intracellular studies have been conducted on spinal motoneurons that increase their firing rates during cooling (58, 59, 74). Cooling increases membrane resistance, often followed by a slight depolarization. This depolarization appears to be due to decreases in the K:Na permeability ratio rather than decreases in the electrogenic pump (58). In addition, the increased membrane resistance causes an increase in the amplitude and duration of excitatory and inhibitory synaptic potentials (74). Both the decrease in membrane potential and the increase in the excitatory synaptic potential appear to contribute to the increased firing rate during cooling. While the thermal dependence of membrane resistance does provide a basis for neuronal cold-sensitivity, the cooling enhancement of firing rate appears to depend primarily on the postsynaptic membrane's response to excitatory synaptic input.

SUMMARY OF THERMORECEPTOR ELECTROPHYSIOLOGY

Although no uniform criteria exist for classifying neuronal thermosensitivity, various studies indicate that 40% of the PO/AH neurons are temperature-sensitive. Thermosensitivity per se does not guarantee that a neuron has a functional role in thermoregulation. In fact, many thermosensitive neurons are osmo-, gluco-, and steroid-sensitive, which suggests that there are interactions among various regulatory systems. PO/AH thermosensitive neurons also receive much thermal afferent input, indicating an integrative role in thermoregulation. Peripheral stimulation and tissue slice studies imply that this afferent input determines both neuronal firing rate and thermosensitivity range. Since the range of thermosensitivity suggests the function of a neuron, it is intriguing to speculate that the development of afferent input could determine a neuron's functional role in thermoregulation.

For warm-sensitive neurons, distinctions between thermoreceptors and synaptically driven interneurons remain debatable. Intracellular studies suggest that some warm-sensitive neurons receive much synaptic input, while others are independent of this input. Synaptic blockade shows that most synaptically driven PO/AH warm-sensitive neurons are inherently thermosensitive. This supports the concept that reverberating networks of warm-sensitive neurons reinforce neuronal thermosensitivity. The inherent thermosensitivity of cold-sensitive neurons is controversial. Intracellular studies of spinal motoneurons show that cold-sensitivity depends primarily on postsynaptic responses to excitatory input. Presumably, such thermosensitivity would disappear during synaptic blockade. While some studies suggest that PO/AH neuronal cold-sensitivity exists during synaptic blockade, other studies indicate that cold-sensitive neurons lose their thermosensitivity during blockade. These latter studies are supported by intracellular recordings which show that neuronal cold-sensitivity is due to synaptic rather than inherent activity.

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