

## Sensory Transmission of Spinal Heat and Cold Sensitivity in Ascending Spinal Neurons

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*Summary.* In anesthetized cats, mostly spinalized at C<sub>1</sub>/C<sub>2</sub>, the thoracic and lumbar sections of the vertebral canal were selectively heated or cooled. Single unit activity was recorded with steel microelectrodes from the spinal cord at the level of C<sub>2</sub> to C<sub>4</sub>. The positions of the electrode tips were determined by micromarking.

The existence of two groups of temperature dependent ascending spinal units was confirmed. One group of units was activated by spinal cord cooling below normal body temperature. The other group was activated by spinal cord heating. No temperature dependent neurons were found, so far, exhibiting maximum discharge rates at normal body temperature. A roughly proportional relation between discharge rate and vertebral canal temperature seemed to exist in both heat sensitive and cold sensitive units within a limited range of spinal hyperthermia or hypothermia respectively. Part of the units exhibited dynamic responses to changes of vertebral canal temperature in addition to their static responses.

As determined by micromarking, heat sensitive and cold sensitive ascending spinal units were conducted in the anterolateral tracts. Both types of units were observed also under neuromuscular blockage. It is concluded that the temperature dependent ascending spinal neurons are transmitting signals from basically afferent spinal thermosensitive structures existing as two functionally different sets, one heat sensitive and one cold sensitive.

*Key-Words:* Spinal Cord — Thermosensitivity — Anterolateral Tract.

The close involvement of spinal thermosensitivity in temperature regulation (Thauer, 1970) has underlined the significance of interconnections between spinal thermosensitive structures and the supraspinal parts of the central nervous thermoregulatory control system. The influence of spinal thermal stimulation on thermoregulatory effector activity mediated by spinal neurons may be explained by temperature effects on signal transmission in the *descending* thermoregulatory pathways. However, additionally required is the postulation of thermal influences on *ascending* spinal neurons, if the supraspinal effects of spinal thermal stimulation (Jessen, 1967; Kosaka *et al.*, 1969; Guieu and Hardy, 1970) are to be explained. Direct evidence for activation of ascending spinal neurons by spinal cord heating has been obtained in guinea pigs from extracellular micro-recording (Wünnenberg and Brück,

1968, 1970). Further, the existence of ascending units activated by spinal cold stimulation has been confirmed in cats (Simon and Iriki, 1970). The present investigation was carried out to further evaluate and to compare the properties of spinal heat sensitive and cold sensitive ascending spinal units in the same species under various degrees of spinal cord heating and cooling.

### Method

The presented results were obtained from 33 experiments in cats weighing 1.6 to 3.7 kg which were carried out between July 1969 and December 1970. Sodium pentobarbital was intraperitoneally administered at a dose of 40 mg/kg. If necessary, additional amounts of 10 mg/kg were given intravenously. With the exception of 7 animals, the spinal cord was transected at the level of C<sub>1</sub>/C<sub>2</sub>, and artificial ventilation was performed after cannulation of the trachea. Among the spinalized animals, 8 were investigated under neuromuscular blockage (continuous succinyl choline infusion of 200  $\mu$ g/(kg · min) in 3 cases; continuous D-tubocurarine chloride infusion of 30  $\mu$ g/(kg · min) in 3 cases; single intravenous injections of 0.5 and 1.0 mg/kg of D-tubocurarine chloride in 2 cases). The experiments were carried out at neutral to warm ambient conditions ( $T_a$  23–28°C). The animals were placed on a heating pad and were lightly covered with cotton cloth to prevent hypothermia in the spinalized preparations.

*Micro-Recording from the Cervical Spinal Cord.* The animals were mounted stereotaxically with the head and the cervical vertebral column fixed by means of ear bars and vertebra clamps. The arcs of the 2nd to 5th cervical vertebrae were removed and the dura was split. The spinal cord remained covered with cerebrospinal liquor and additional amounts of 0.9% saline solution. A ring made of silver sheet, 15 mm high and 25 mm in diameter was placed around the exposed parts of the spinal cord to allow access from the dorsal side of the preparation. This ring also served as the indifferent electrode. Single unit activity was picked up with monopolar stainless steel electrodes sharpened to less than 5  $\mu$  and coated with Insul-X. The impedances of these electrodes as determined with 800 Hz a. c. were, as a rule, 5 megohms or higher before the start of the experiments. As shown in occasional post-experimental controls, impedance decreased during the experiments to 600–1000 kilohms owing to the repeated penetrations of spinal cord tissue. The electrodes were inserted into the spinal cord, mostly at C<sub>3</sub>/C<sub>4</sub>, by means of a 3-dimensional micro-drive device. The potentials were amplified in a Tektronix 2A61 differential amplifier. The discharge rate of the recorded units was qualitatively controlled by means of an audio-monitor. During the first experiments, the discharges were directly displayed on a Tektronix 565 oscilloscope from which the discharges were photographed with a Tönnies camera. In subsequent experiments continuous recording on magnetic tape (VR-3200, Bell and Howell) was performed.

*Location of the Recorded Units.* A rough estimation was obtained from the coordinates of the electrode tip position in relation to the spinal cord dimensions. Further, in 22 units successful micromarking was carried out by applying weak anodic currents (about 2  $\mu$ Amp during 30 sec) to the electrodes. Iron deposits of about 200  $\mu$  in diameter were obtained which were stained by the ferro-cyanide method in frozen or paraffin embedded transverse sections.

*Thermal Stimulation of the Thoracic and Lumbosacral Spinal Cord.* A hairpin-like thermode of polyethylene tubing (Portex pp. 60) was inserted into the peridural space through an opening between the last lumbar vertebra and the sacral bone; it extended to the upper thoracic vertebrae. Four stages of vertebral canal cooling, an indifferent

stage, and 3 stages of heating were applied by perfusing the thermode at a constant flow rate of 30 ml/min with water of 14; 20; 26; 32; 38; 41; 44;  $47 \pm 0.5^\circ\text{C}$ , as a rule.

*Temperature Measurements.* Thermocouples, which were protected by thin polyethylene tubing, were connected to a Philips 12-channel servo recorder plotting at 4-sec-intervals. Two vertebral canal temperatures were measured within the lumbar peridural space about 5 cm rostral to the point of thermode insertion. One thermocouple was placed close to the thermode which was situated at the dorsal side of the spinal cord at this level. The 2nd thermocouple was placed at the ventral side of the spinal cord. Each vertebral canal temperature was plotted on the recorder every 12 sec. Further rectal temperature, air temperature and the temperatures of the ingoing and outgoing perfusion fluid were measured and were plotted every 48 sec.

*Exploration of Temperature Sensitive Single Units.* Whenever single unit activity was picked up, its response to changes of vertebral canal temperature was acoustically observed to find out a possible temperature sensitive unit among the numerous insensitive fibers. If an audible change of discharge rate was perceived, various cooling and heating periods of mostly either  $5 \times 48$  sec or  $10 \times 48$  sec were performed as long as the unit could be recorded. Every 48 sec and additionally every 24 sec after a change of perfusion temperature, discharge rate was determined over 2–10 sec. As a rule, the means of the discharge rates at 3 min and 12 sec and at 4 min after a change of perfusion temperature and the corresponding vertebral canal temperatures were evaluated to estimate the static response of the unit at a given stimulus intensity. If in an investigated unit more than one stimulation period had been carried out with the same stimulus intensity, final evaluation consisted in calculation of average responses and of average vertebral canal and rectal temperatures for these periods.

As reported in a preceding communication (Simon and Iriki, 1971), units activated by vertebral canal heating were found more often than units stimulated by vertebral canal cooling. In the present investigation equal numbers of heat and cold sensitive units were recorded in order to get comparable samples of observations.

## Results

### *Properties of Ascending Spinal Thermosensitive Single Units*

Fig. 1 demonstrates the discharge rate of a *heat sensitive ascending spinal unit* as influenced by variations of vertebral canal temperature. Three degrees of heating, perfusion with water at neutral temperature and slight cooling were alternately performed. This unit exhibited a mainly static type of response; only during strong heating a dynamic component became visible. The highest rate of steady discharge was achieved during strong heating. The course of vertebral canal temperature during the various stimulation periods of 4 min duration is demonstrated by the peridural temperature measured close to the thermode. An approximately exponential change of temperature with time occurred during the single stimulation periods. This temperature course was, in principle, the same in all experiments, since the same perfusion rates and the same temperature steps of cooling and heating were applied. However, the absolute levels of the corresponding vertebral canal temperatures varied to some extent from case to case according to slightly varying distances between thermode and thermocouple.

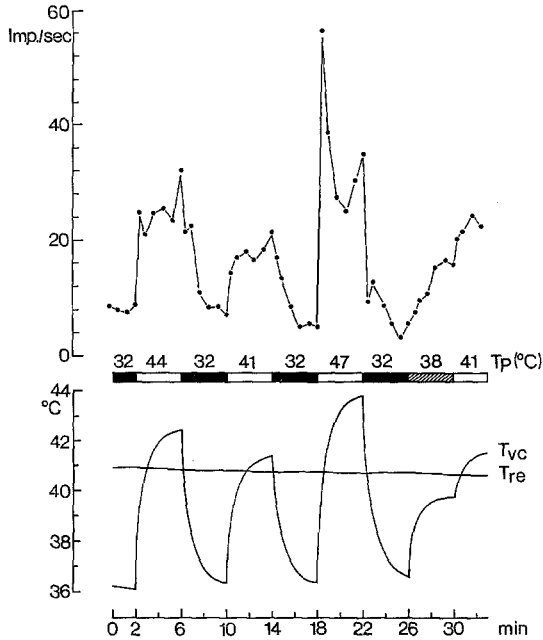


Fig.1. Heat sensitive ascending spinal unit as influenced by changes of vertebral canal temperature.  $T_p$ : periods of 4 min duration with cold (black bars), warm (white bars) and neutral (hatched bar) perfusion of vertebral canal thermode (with perfusion temperatures). Upper curve: discharge rate; lower curves: vertebral canal temperature ( $T_{vc}$ ) and rectal temperature ( $T_{re}$ ); ambient air temperature  $24^\circ\text{C}$

Fig.2 shows a *cold sensitive ascending spinal unit*. It represents another type of response to changes of vertebral canal temperature, namely a combined dynamic and static response. The dynamic component led to an “overshoot” during the early phase of spinal cord cooling—as during strong heating in the heat sensitive unit described above. However, additionally a corresponding “undershoot” of activity during the early phase of rewarming occurred in this case. On the whole, the response of this fiber resembled that of a peripheral cold receptor.

As determined from the *static components* of the responses to thermal stimulation of the spinal cord, 20 units could be classified as heat sensitive and further 20 units as cold sensitive. Among all observed units which showed a definite susceptibility to changes of vertebral canal temperature, no one unit was found, so far, exhibiting a maximum discharge rate at normal body temperature.

A *dynamic component* of the response to thermal stimulation was observed in 9 out of the 20 heat sensitive units. As shown in Fig.1, this

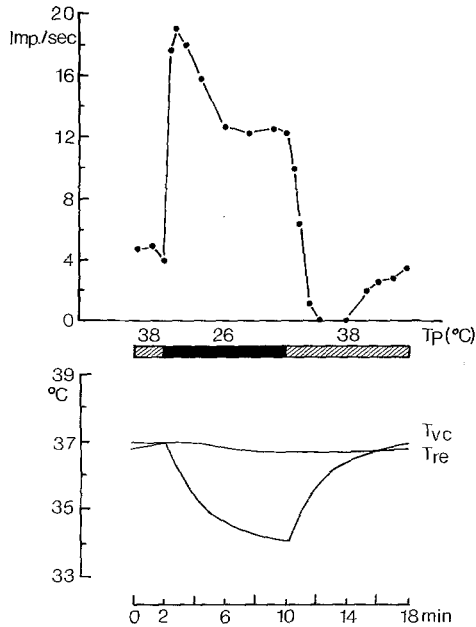


Fig. 2. Cold sensitive ascending spinal unit as influenced by vertebral canal cooling of 8 min duration.  $T_p$ : cold (black bar) and neutral (hatched bars) perfusion of vertebral canal thermode (with perfusion temperatures). Upper curve: discharge rate; lower curves: vertebral canal temperature ( $T_{vc}$ ) and rectal temperature ( $T_{re}$ ); ambient air temperature 25°C. Unit investigated under continuous succinyl choline infusion of 200  $\mu\text{g}/(\text{kg} \cdot \text{min})$

component was in most cases clearly visible only during strong heating and was restricted to the phase of increasing vertebral canal temperature. Only in 2 cases an “undershoot” of discharge rate during the phase of rapidly falling vertebral canal temperature was observed. Among the 20 cold sensitive units a dynamic component of the response was seen in 6 cases and could be observed at all degrees of cooling. However, like in the heat sensitive units, an “undershoot” of response during rewarming occurred only in 2 units.

*Several other features* of the investigated thermosensitive units are mentioned briefly: In some cold sensitive and, to an even higher degree, in heat sensitive units an apparently irregular waxing and waning of discharge rate was observed which seemed to be unrelated to changes of spinal cord temperature. Similar variations have been observed in thermosensitive hypothalamic and brain stem units (Cabanac and Hardy, 1969; Nakayama and Hardy, 1969). Further, a few of the cold sensitive and heat sensitive units showed rhythmic variations of discharge rate associated with the rhythm of artificial ventilation. Discharge rate partly increased during lung

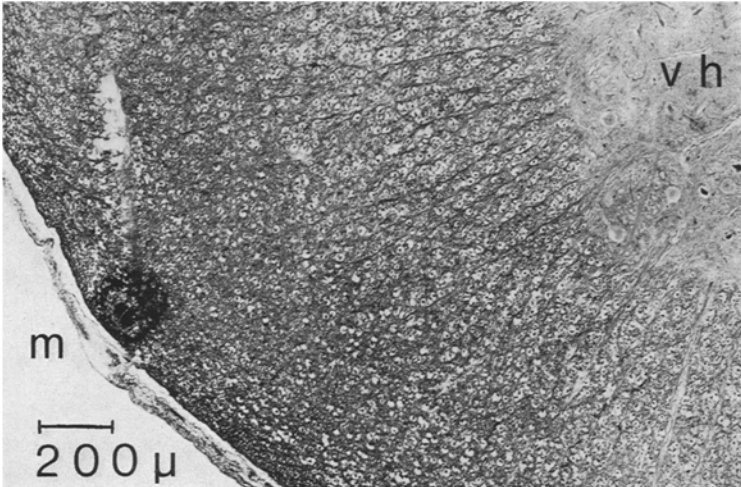
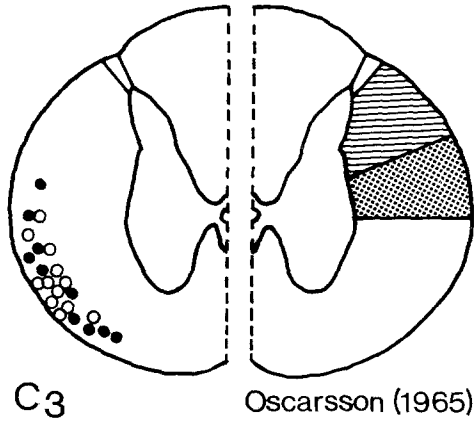


Fig. 3. Location of heat sensitive (○) and cold sensitive (●) ascending units in the anterolateral tract of the spinal cord as determined by micromarking [left side of the diagram; the right side shows the location of the spinocerebellar tracts according to Oscarsson (1965)]. The microphotograph demonstrates a transverse section from the 3rd cervical spinal segment with a micromark (*m*); ventral horn (*vh*)

inflation and in other cases during lung deflation. Superficial receptors do not seem to have induced this rhythm, because occasional testing did not reveal a sensitivity to touch; however, this question was not systematically investigated.—At strong heating (perfusion temperature of 47°C) an unexpected change of discharge rate was occasionally observed. One heat sensitive fiber showed a very great dynamic increase of activity (up to more than 100/sec) with subsequent drop to zero during further heating. In another heat sensitive unit, discharge rate dropped to zero during

the first minute of strong heating; thereafter the discharge reappeared and reached a level of frequency higher than at normal body temperature but lower than during thermode perfusion with water of 44°C. In one cold sensitive unit a sudden jump of discharge rate to high values occurred during strong heating (see Fig. 4). In a further cold sensitive unit, in which discharge rate was zero at slight heating, a temporary increase of activity occurred in the beginning of strong heating, however, during further heating activity again fell to zero within 2 min.

*The location of the ascending spinal thermosensitive units* within the anterolateral tracts of the spinal cord was suggested by the coordinates of the recording points as referred to the dimensions of the spinal cord. This was confirmed by micromarking which gave successful results in 10 cold sensitive and 12 heat sensitive units. As shown by Fig. 3, the units were confined to the marginal area of the anterolateral tract. At the level of C<sub>3</sub>, where most of the thermosensitive units were recorded, both spinocerebellar tracts have a dorsal position in the cat (Oscarsson, 1965). Therefore, the identified—and most probably all other recorded thermosensitive fibers—were conducted in the spinothalamic tracts.

#### *Static Responses of Thermosensitive Ascending Spinal Units*

Since under natural conditions only slow changes of body temperature, or of spinal cord temperature respectively, may be expected, evaluation of the static responses of spinal thermosensitive units was of special interest for the elucidation of their possible role in thermoregulation. As shown by the unit in Fig. 2, in which a cooling period of 8 min duration was performed, a contribution of the dynamic component to the level of discharge rate could be perceived only during the first minutes. This was confirmed in several other experimental periods of 8 min duration both in heat sensitive and cold sensitive units exhibiting an initial dynamic response. Therefore, the discharge rates during the 4th min of stimulation could be regarded as a reliable estimation of the static response as related to the measured vertebral canal temperature or, respectively, to the given stimulus intensity. The discharge rates of 20 cold sensitive and 20 heat sensitive units determined in this way are plotted in Figs. 4 and 5 according to the corresponding stimulus intensities.

All *cold sensitive units* tested with perfusion temperatures of 26°C and 38°C had higher discharge rates at the lower perfusion temperature. In 9 out of 10 investigated units higher discharge rates were observed at 26°C perfusion when compared with 32°C perfusion. However, if the discharge rates at perfusion temperatures of 20 and 14°C on one side were compared with those at 26°C perfusion temperature on the other side, 6 units showed an increase and 4 units a decrease of activity with falling temperature. In the hyperthermic range, elevation of per-

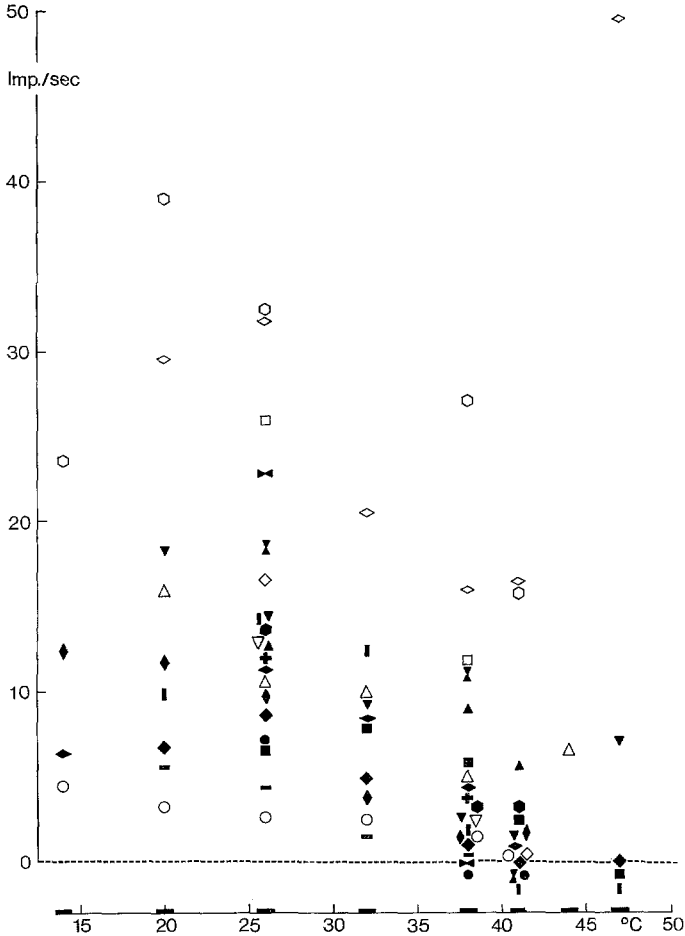


Fig. 4. Steady discharge rates of 20 cold sensitive units in relation to the applied stimulus intensities. The various steps of perfusion temperature are indicated by the small black bars at the abscissa. Open symbols: units recorded in paralyzed animals; ( $\nabla$ ,  $\Delta$ ,  $\diamond$ ) succinyl choline infusion of  $200 \mu\text{g}/(\text{kg} \cdot \text{min})$ ; (O, o) curare infusion of  $30 \mu\text{g}/(\text{kg} \cdot \text{min})$ ; ( $\diamond$ , n) single curare injections of 0.5 and 1.0 mg/kg 3 and 8 min before cooling

fusion temperature from  $38^{\circ}\text{C}$  to  $41^{\circ}\text{C}$  further reduced the discharge rate with the exception of 2 units in which discharge rate remained presumably constant. Between normal body temperature and stronger heating (perfusion temperatures of  $44$  and  $47^{\circ}\text{C}$ ) activity decreased in 1 case and increased in 3 cases. The mean steady discharge rates calculated for the cold sensitive units at the various steps of thermal stimulation



are shown in the Table. The data indicate that the relation between unit activity and stimulus intensity was, on the whole, non-linear. Only within the range between 26°C and 41°C perfusion temperatures a roughly proportional relation seemed to exist. A rather flat maximum was presumably reached somewhere around a perfusion temperature of 20°C. This assumption is based on the divergent behaviour of the single cold sensitive units tested at the higher cooling intensities. In the hyperthermic range a minimum value of average activity at slight heating can be assumed, whereas during stronger heating a "paradoxical" rise of activity (Dodt and Zotterman, 1952) must be expected.

The plot of the static responses of *heat sensitive units* in Fig. 5 shows that all units investigated with perfusion temperatures of 38°C, 41°C and 44°C increased their discharge rates with increasing stimulus intensities. However, if the results obtained at 41°C perfusion temperature are compared with those at 47°C, a decrease of activity can be stated in 4 cases and a further increase in 6 cases. Between perfusion temperatures of 44 and 47°C, a decrease of activity was found in 3 cases and a further increase in 8 cases. In the hypothermic range there was always a decrease of discharge rate when perfusion temperature was lowered from 38°C to 32°C or from 38°C to 26°C. However, within the range of the various steps of cooling, there was a tendency towards a stable discharge level or even towards an increase of discharge rate with increasing cooling intensity. As in cold sensitive units, the mean values calculated for the heat sensitive units indicate a non-linear relation between stimulus intensity and discharge rate (Table). A steep and roughly proportional rise of discharge rate with rising temperature seems to exist between perfusion temperatures of 32°C and 41°C. Above this range the slope of the response curve decreased. A maximum of average unit activity must be assumed somewhere around a perfusion temperature of 47°C as indicated by the rapid fall of discharge rate in some cases. In the hypothermic range unit activity seemed to reach a minimum value different from zero at a rather slight degree of cooling. At lower temperatures no further drop of average activity could be confirmed.

The Table further contains the mean values of rectal temperature and of two vertebral canal temperatures, one measured close to the thermode and the other at a more distant position, during the 4th min of stimulation. Since in both heat and cold sensitive units the same steps of heating and cooling were applied in general, common mean values were calculated for all investigated units. On the basis of the two peridural vertebral canal temperatures an estimation of the average *static sensitivities* may be carried out. For the greatest change of average discharge rate with temperature in cold sensitive units, i.e. between perfusion temperatures of 32°C and 26°C, a sensitivity of  $-2.2$  (Imp/sec)/°C results, if calcu-

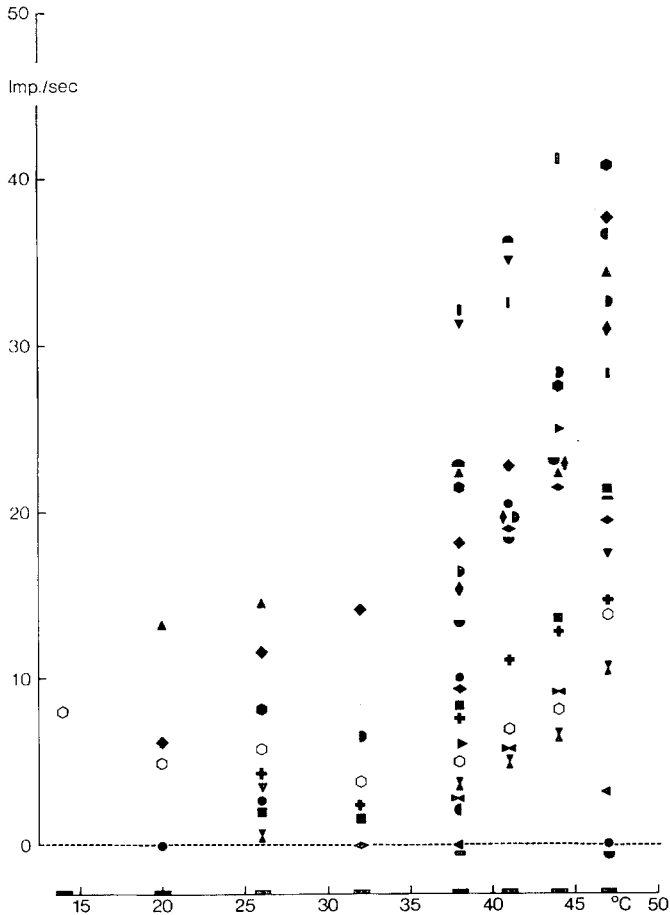


Fig. 5. Steady discharge rates of 20 heat sensitive units in relation to the applied stimulus intensities. The various steps of perfusion temperature are indicated by the small black bars at the abscisa. Open symbol: unit recorded in an animal paralyzed by curare infusion of  $30 \mu\text{g}/(\text{kg} \cdot \text{min})$

lation is based on that vertebral canal temperature measured close to the thermode. A sensitivity of  $-4.4 (\text{Imp}/\text{sec})/^\circ\text{C}$  results, if the second vertebral canal temperature is used for calculation. Correspondingly, average maximum sensitivities of  $+3.9 (\text{Imp}/\text{sec})/^\circ\text{C}$  and of  $+6.1 (\text{Imp}/\text{sec})/^\circ\text{C}$  result for the heat sensitive units between perfusion temperatures of  $38^\circ\text{C}$  and  $41^\circ\text{C}$ . The courses of single unit activity and of the two vertebral canal temperatures in many experiments indicated, however, that the discharge rate rather followed vertebral canal temperature measured close to the

Table. Average steady discharge rates of 20 cold sensitive and 20 heat sensitive ascending spinal units with corresponding average rectal and vertebral canal temperatures at the various steps of spinal thermal stimulation (thermode perfusion). Vertebral canal temperatures: I. measured close to the thermode at the dorsal side of the lumbar spinal cord; II. measured at a more distant position at the ventral side of the lumbar spinal cord.  $n$  = number of stimulation periods,  $\bar{x}$  = mean values,  $S_{\bar{x}}$  = standard deviations of mean values

Perfusion temp. °C	14	20	26	32	38	41	44	47
Cold sensitive units	$n$	4	9	20	10	19	14	5
	$\bar{x}$	11.70	15.53	14.53	8.09	5.72	3.53	6.50
	$S_{\bar{x}}$	4.28	3.94	1.84	1.76	1.58	1.50	9.64
Heat sensitive units	$n$	1	4	9	6	20	13	17
	$\bar{x}$	8.00	6.10	5.84	4.67	12.52	19.52	20.16
	$S_{\bar{x}}$	—	2.72	1.54	2.11	2.19	2.91	3.20
Temperatures:								
Rectum	°C	5	13	29	16	39	27	22
	$S_{\bar{x}}$	38.00	38.07	38.67	38.58	38.68	38.64	38.94
		0.45	0.50	0.25	0.40	0.21	0.24	0.39
Vertebral canal (I)	°C	21.62	27.96	31.64	34.64	38.65	40.46	43.10
	$S_{\bar{x}}$	1.18	0.66	0.36	0.36	0.16	0.19	0.34
Vertebral canal (II)	°C	28.90	31.69	34.20	35.66	38.27	39.42	40.96
	$S_{\bar{x}}$	2.25	0.79	0.35	0.35	0.19	0.27	0.50

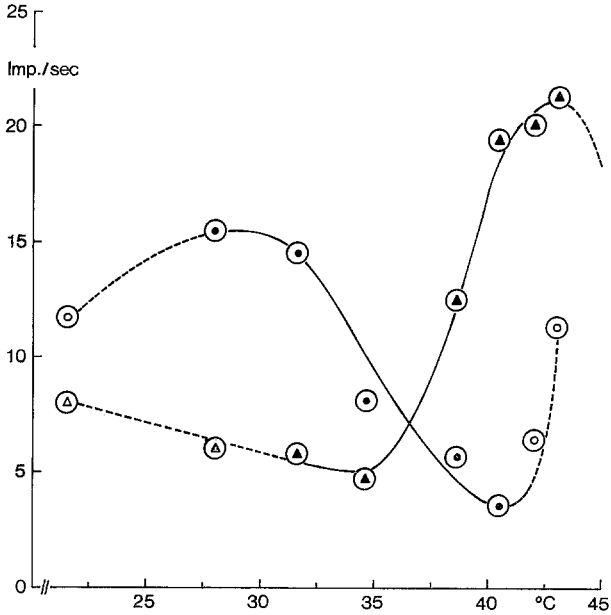


Fig. 6. Average responses of cold sensitive (circles) and heat sensitive (triangles) ascending spinal units as related to vertebral canal temperature measured close to the thermode. The open symbols indicate values obtained from less than 6 units

thermode. Therefore, estimations based on this temperature seemed more reliable.

Consequently, the *interrelations between spinal cold and heat sensitivity* were evaluated by plotting the mean discharge rates of both groups of units against vertebral canal temperature measured close to the thermode. As shown in Fig. 6 the response curves intersected with their steepest parts at a temperature slightly below normal body temperature at the given experimental conditions. The diagram suggests that a reasonable "measuring" of vertebral canal temperature could be achieved by the cold sensitive units for the range between 32°C and 40°C and by the heat sensitive units for the range between 36°C and 42°C.

#### *Thermosensitive Units in Paralyzed Animals*

Temperature susceptibility of spinal structures with a basically afferent function is indicated by the finding that spinal thermosensitive units were conducted in the spinothalamic tracts. Theoretically, there exists an alternative possibility that changes of  $\alpha$ - and  $\gamma$ -motoneuron

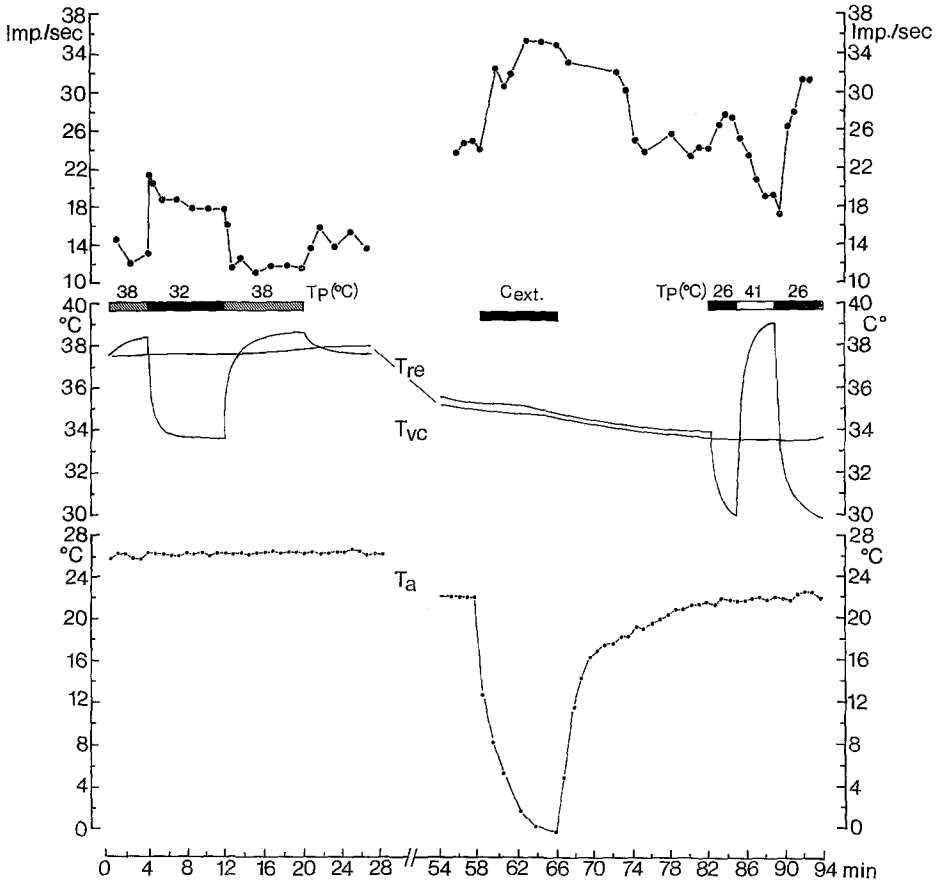


Fig. 7. Ascending spinal unit activated by spinal cord cooling and by external cooling.  $T_p$ : cold (black bars), warm (white bar) and neutral (hatched bars) perfusion of vertebral canal thermode (with perfusion temperatures);  $C_{ext}$ . external cooling (black bar). Upper curves: discharge rate; lower curves: vertebral canal temperature ( $T_{vc}$ ), rectal temperature ( $T_{re}$ ), ambient air temperature ( $T_a$ ). Unit investigated under continuous succinyl choline infusion of  $200 \mu\text{g}/(\text{kg} \cdot \text{min})$

activity induced by spinal thermal stimulation might influence muscle spindle discharge and consequently also ascending spinal unit activity. To the degree that this alternative is plausible, it presumably applies only to spinal cold stimulation (Klussmann, 1969). Therefore, experiments were performed in animals paralyzed with succinyl choline or curare, which drugs are known to suppress or greatly to alter muscle spindle responses to motoneuronal influences. Fig. 4 contains 7 cold sensitive

units found under these conditions. The discharge rates of 2 units (one under succinyl choline and one under curare infusion) were above the range of the units observed in non-paralyzed animals; 4 other units were within this range. Heat sensitive units were also observed in paralyzed animals on several occasions. Since, however, the demonstration of this finding seemed not to be necessary for the interpretation of the present experimental results, only one unit was recorded (see Fig.5).

Demonstration of both heat and cold sensitive units was difficult during continuous curare infusion. However, not only thermosensitive units but also any other spontaneous activity in ascending tracts appeared to be definitely reduced. This coincides with observations of Mountcastle *et al.* (1957) concerning a depressing effect of curare on sensory transmission.

#### *Effects of Peripheral Cold Stimulation*

Two units activated by spinal cord cooling in which the effect of peripheral thermal stimulation was tested showed an increase of activity during peripheral cooling. In the case demonstrated in Fig.7, unit activity was investigated at first by spinal cord cooling at warm ambient conditions ( $T_a$  26°C). Uncovering of the animal and lowering of air temperature to 22°C led to a gradual fall of core temperature and presumably also of skin temperature which resulted in a considerable increase of the discharge rate. Further rapid lowering of ambient temperature at a nearly constant rectal temperature induced a further substantial rise of discharge rate within a few minutes. When ambient temperature was reestablished to its former value, discharge rate gradually returned towards its previous level. As further shown by the diagram, this discharge rate could be increased by spinal cooling and was reduced by spinal cord heating.—In the 2nd investigated unit sensitive to spinal and peripheral cooling, a local external cold stimulus was applied. Cooling of the contralateral thoracic region resulted in increased discharge rate, whereas no activation was seen, when the skin of the contralateral hind leg or of the homolateral side of the trunk was cooled.

#### **Discussion**

As indicated by the coordinates of the recording sites and by the micromarks, the investigated thermosensitive fibers were conducted in the spinothalamic tracts. Therefore, the nature of the thermosensitive sites driving the spinothalamic neurons seems to be basically afferent. Whether thermosensitivity is constituted by thermal susceptibility of synaptic processes (Pierau and Klussmann, 1971) or by special thermosensitive structures acting on ascending neurons remains to be elucidated. It may further be assumed that these primary thermosensitive sites are, in both cases, localized within or at least in close proximity to the spinal cord.

With special respect to cold sensitive ascending units, several considerations and the observations in paralyzed animals largely preclude that these neurons were driven by muscle spindle afferents excited by way of motoneuron activation: Ascending fibers conducting muscle spindle activity should preferably be found within the spinocerebellar tracts. However, no such activation was observed in the dorsolateral quadrants, where these fibers should be expected according to Oscarsson (1965). Further,  $\alpha$ -motoneurons cannot have caused an appreciable muscle spindle excitation, since in the spinalized animals only weak shivering occurred (Kosaka and Simon, 1968). On the other hand,  $\gamma$ -motor efferents exhibit, as a rule, maximum discharge rates only at moderate degrees of spinal cord cooling (Klussmann, 1969) and probably could not account for activation of ascending neurons at more severe degrees of spinal hypothermia. Finally, in curarized animals, in which blockage of  $\alpha$ - and  $\gamma$ -motor influences on muscle spindles may be assumed (Hunt, 1952; Granit *et al.*, 1953), cold sensitive units could be recorded. This was the case also in animals treated with doses of succinyl choline great enough to excite muscle spindle afferents to discharge rates considerably higher than those observed in the cold sensitive units at normal body temperature (Brinling and Smith, 1960).

The present investigation has shown that, with respect to the static sensitivities, the thermally susceptible ascending spinal neurons can be classified as either heat or cold sensitive. However, the single units within each group could differ distinctly from each other with respect to the existence of a dynamic component in their responses and to the presence of a respiratory rhythm. The significance of these differences remains open to discussion.

Presence or absence of the dynamic response in the recorded ascending neurons could depend on the number of interneurons intercalated at the segmental level between the primary thermosensitive sites and the recorded fibers. To the degree that recordings were made from multisynaptically driven spinothalamic neurons (Oscarsson, 1964), convergence of neurons mediating different modalities (Kolmodin and Skoglund, 1960; Christensen and Perl, 1970) would explain the observation that some units exhibited thermosensitivity and susceptibility to other, presumably mechanical stimuli. However, receptors might exist in the vertebral canal which are susceptible to mechanical and thermal stimulation as it is known from cutaneous receptors (Witt and Hensel, 1959). Both, convergence (Kolmodin and Skoglund, 1960; discussion to Szentagothai, 1964) and susceptibility to different modalities (Christensen and Perl, 1970), do not necessarily preclude a specific function of these neurons. Further experimental evaluation, especially of the properties of the primary thermally susceptible structures, is necessary to outline definite criteria for a possible specific sensory function.

The static responses of the investigated thermosensitive units give no support for the assumption that in thermally susceptible afferent spinal neurons the maxima of the discharge rates are statistically distributed over a wide range between hypothermic and hyperthermic spinal cord temperatures. The fact that two clearly separated sets of thermosensitive units exist may be regarded as an argument in favour of a specific sensory function of these neurons. This suggestion is supported by the

finding that the average static sensitivities of spinal ascending heat and cold sensitive units were of the same order of magnitude as those of the hypothalamic temperature sensors. This applies also to the heat sensitive units described in guinea pigs (Wünnenberg and Brück, 1970).

Heat sensitive hypothalamic units showed mean static sensitivities of  $+4.2$  (Imp/sec)/ $^{\circ}\text{C}$  (cat—Nakayama *et al.*, 1963) of  $+7$  (Imp/sec)/ $^{\circ}\text{C}$  (dog—Hardy *et al.*, 1964), of  $+3.5$  (Imp/sec)/ $^{\circ}\text{C}$  (dog—Cunningham *et al.*, 1967) and of  $+4.9$  to  $+2.1$  (Imp/sec)/ $^{\circ}\text{C}$  (rabbit—Hellon, 1967). In cold sensitive hypothalamic units, static sensitivities of  $-1$  (Imp/sec)/ $^{\circ}\text{C}$  (dog—Hardy *et al.*, 1964), of  $-3.3$  (Imp/sec)/ $^{\circ}\text{C}$  (dog—Cunningham *et al.*, 1967) and of  $-0.8$  (Imp/sec)/ $^{\circ}\text{C}$  (rabbit—Hellon, 1967) were found. Thus, in spinal thermosensitive units as well as in hypothalamic thermosensors heat sensitivity appears to be more pronounced than cold sensitivity. Further, it seems to be common for both hypothalamic (Hardy *et al.*, 1964) and spinal (Simon and Iriki, 1971) neuronal thermosensitivity that cold sensitive fibers were less frequently observed.

If a specific sensory function of ascending spinal thermosensitive fibers is presupposed for the present considerations, the described courses of the average response curves mean that each set of units can “measure” body temperature only within a limited range. For instance, degrees of central hypothermia below  $36^{\circ}\text{C}$  could not be perceived by heat sensitive units. Therefore, if heat sensitive spinal units behave similarly in other species, e.g. in dogs, pigeons and rabbits, the graded responses of these animals to vertebral canal cooling with greater intensities would require the existence of cold sensitive units. Conversely, cold sensitive units would fail to “measure” body temperatures higher than  $40^{\circ}\text{C}$ . However, both systems together would cover a range extending from approximately  $32^{\circ}\text{C}$  to  $42^{\circ}\text{C}$ .

In the present investigation the average response curves of heat and cold sensitive units intersected with their steepest parts (Fig. 6), i.e. at a point, where a maximum of combined sensitivities was achieved. Under the given experimental conditions, i.e. at a presumably warm skin, this point corresponded to a spinal temperature  $1-2^{\circ}\text{C}$  below normal body temperature in cats. If one speculates about the stimulating effect of peripheral cooling observed in the two cold sensitive units, one might suggest that the cold unit response curve would be displaced towards higher levels of discharge rate by external cooling. This would imply that under external cold conditions the point of intersection of the average response curves of heat and cold sensitive units would be shifted to a higher body temperature.

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