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WARM RECEPTORS IN THE NASAL REGION OF CATS

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SUMMARY

1. Specific warm receptors in the nasal region of cats were studied by recording afferent impulses from single units dissected from the infra-orbital nerve. In addition, a few cold fibres from the same region were examined.

2. Numerous warm fibres with spot-like receptive fields were found on the back of the nose. They were not excited by mechanical stimulation.

3. Multi-fibre strands serving this area responded to moderate warming with an increase of the integrated discharge.

4. At constant temperatures from 30° C on, single warm fibres showed a steady discharge with a regular sequence of impulses, the frequency of which rose steeply with temperature and reached a maximum between 45 and 47° C. At higher temperatures the frequency fell to zero.

5. Rapid warming caused a dynamic overshoot, rapid cooling a transient inhibition of the warm fibre discharge. The highest dynamic frequencies of single fibres were 200 impulses/sec.

6. For a large population of single warm fibres the average maximum of static activity was 36 impulses/sec at 46° C, whereas the cold fibre population had a maximum of 9 impulses/sec at 27° C.

INTRODUCTION

Afferent impulses elicited by warming the skin have been recorded from various cutaneous nerves in mammals (Hensel, Iggo & Witt, 1960; Iriuchijima & Zotterman, 1960; Hensel, 1968*a*, *b*; Iggo, 1969). However, our present knowledge of warm-sensitive receptors is rather fragmentary, in spite of their possible importance for temperature regulation and behaviour. In this respect, the skin area supplied by the *infra-orbital nerve* deserves special interest. A summary of behavioural experiments shows that in cats the face is much more sensitive to warming than are other parts of the furred skin, such as thigh or back (Kenshalo, Duncan & Weymark, 1967). These results were in conflict with the general opinion, based on electrophysiological evidence (Hensel, 1952; Boman, 1958; Iriuchijima & Zotterman, 1960; Kenshalo, 1968), that the number of warm fibres in the infra-orbital nerve is very much smaller than the number of cold fibres.

Recent systematic investigations, however, have revealed a sensory field in the nasal region of cats with a high density of warm receptors (Hensel, 1968*a*, *b*). A typical feature of this area was that on warming a marked increase in the integrated activity of multi-fibre preparations could be obtained which was in striking contrast to the behaviour of all cutaneous nerves hitherto investigated, including infra-orbital branches. Single warm-sensitive fibres from the nasal area had spot-like receptive fields and were not excited by mechanical stimulation. Their static discharge covered a temperature range from 30 to 48° C, the average maximum frequency being approximately at 45° C (Hensel, 1968*b*). Another cutaneous field with a high density of warm receptors was recently found in the scrotum of the rat (Iggo, 1969).

The present work was carried out to obtain more quantitative information about the properties of infra-orbital warm fibres from the nasal area and to add to our limited knowledge of cutaneous warm receptors in general. Some occasional results on cold receptors in the same region of the skin have been included in this study.

METHODS

The cats used were anaesthetized with I.P. sodium pentobarbitone or with I.M. chloralose (60 mg/kg) and urethane (250 mg/kg). A tracheal cannula was inserted and the head fixed. After exposure of the infra-orbital nerve at the infra-orbital foramen, the branch serving the apical part of the back of the nose was isolated and dissected into fine filaments. Afferent impulses were picked up either by platinum electrodes under paraffin oil or by wick electrodes soaked with Ringer solution. In most animals the thin hair coat of the receptive field was left intact; in a few cases it was removed from the skin by a chemical depilatory. This procedure had no significant effect on the properties of thermoreceptors.

Two methods of thermal stimulation were used: (1) Infra-red radiation from a small d.c. heating coil was directed towards the receptive field. Heating current and distance of the heat source could be controlled. A fine thermocouple of 0·1 mm diameter with polished surface was brought into close contact with the skin and covered with a thin layer of Vaseline. Thus the temperature of the thermocouple was influenced mainly by heat conduction from the skin and less by direct absorption of radiant heat. Shielding the skin from heat radiation with small strips of aluminium foil of various width allowed a localization of the receptive fields. (2) A water-circulated thermode of 10 mm diameter was placed on the skin. Thermal conduction between thermode and skin was improved by paraffin oil. The water was supplied from five thermostats set at various constant temperatures (± 0·02° C) and selected by a multi-way tap. Temperature was recorded with a small thermistor mounted to the copper plate on the bottom of the thermode. The amplified impulses and thermal deflexions were displayed on oscilloscopes for monitoring and recording.

RESULTS

Receptive fields. The receptive area with the highest density of cutaneous warm receptors was situated on the apical part of the back of the nose (Fig. 1). It could easily be distinguished from the surroundings by its very thin fur coat and axial direction of hairs. This area is limited laterally by the naso-labial sulcus and apically by the glabrous part of the snout.

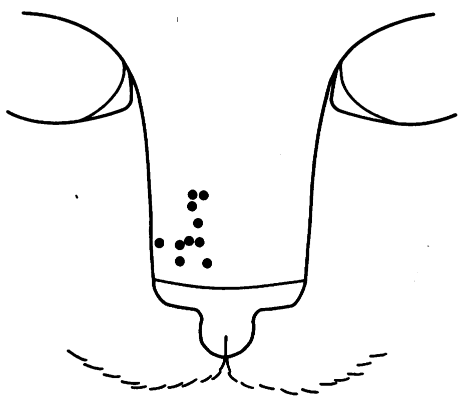

Fig. 1. Receptive fields of ten single warm fibres from the right infra-orbital nerve in various cats.

By shielding the skin with small aluminium strips of various width and position (cf. Fig. 4), the receptive fields of single warm fibres could be localized with an accuracy of about 1 mm. In the preparations investigated a single warm fibre was found to innervate one peripheral spot not exceeding 1 or 2 mm in diameter; the large majority of sensory fields being situated in the described area. The same held true for the occasional single cold fibres that were encountered.

Response of multi-fibre preparations. A typical feature of the warm-sensitive area on the cat's nose was that in most cases a rise in temperature caused a marked increase in the integrated discharge of multi-fibre strands. Figure 2 shows an example. Starting from 'neutral' skin temperatures between 32 and 34° C, a temperature rise of 2–3° C was sufficient to elicit a vigorous multi-unit discharge which disappeared as soon as the skin temperature was falling again. The density of impulses is clearly dependent on the amount of warming.

When the nasal temperature was kept constant at levels above 30° C, a persistent discharge of warm-sensitive units was observed, the frequency of which increased steeply as a function of temperature (Fig. 3). In twenty-one few-fibre preparations the total frequency reached its maximum discharge rate at temperatures above 45° C.

Besides this type of discharge, impulses in other afferent fibres could be elicited from the nose by cooling or by mechanical stimulation.

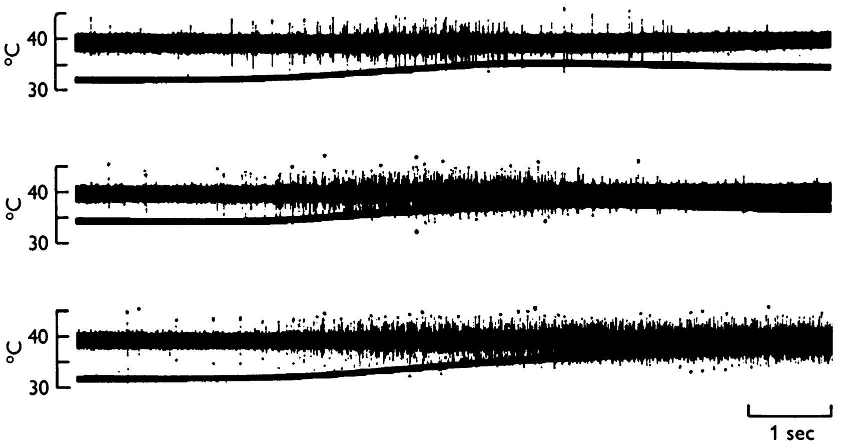

Fig. 2. Afferent discharge of a multi-fibre preparation and skin temperature when applying heat radiation.

Response of single fibres. Thirty-three single units excited by moderate warming were investigated. The definition of these units as 'warm' receptors was based on the following criteria: (1) steady discharge at constant temperatures between 30 and 48° C and temperature dependence of the discharge frequency, (2) increase in frequency on sudden warming, (3) no response on sudden cooling, if the fibre was silent, or a decrease in frequency of the steady discharge, (4) no response to mechanical stimulation (Hensel, Iggo & Witt, 1960; Hensel, 1961). Conduction velocities were not measured in these experiments but size and shape of the spikes suggest that the infra-orbital warm receptors are served by small myelinated as well as by non-myelinated fibres.

In the experiment illustrated in Fig. 4 the steady discharge of a single warm fibre was maintained by heat radiation. A strip of aluminium foil 1·5 mm wide was used to shield the receptor from the heat source. When the strip was moved over the skin surface without touching it, the discharge stopped abruptly at a certain position and started again when the strip was shifted to either side by 1 or 2 mm. Repeating this procedure in two co-ordinates allowed the site of the receptor to be localized with an accuracy of about 1 mm. Individual warm fibres were found to innervate single spot-like fields of not more than 1 or 2 mm in diameter.

A few preparations contained a single warm unit as well as a single cold unit. In these cases the units had different receptive fields and could be stimulated separately. As shown in Fig. 5, isolated shielding of the warm spot stops only the warm fibre activity, whereas shielding both the warm and cold spot causes a simultaneous inhibition of the warm receptor and an excitation of the cold receptor. The opposite occurs when the shield was removed and the skin warmed-up.

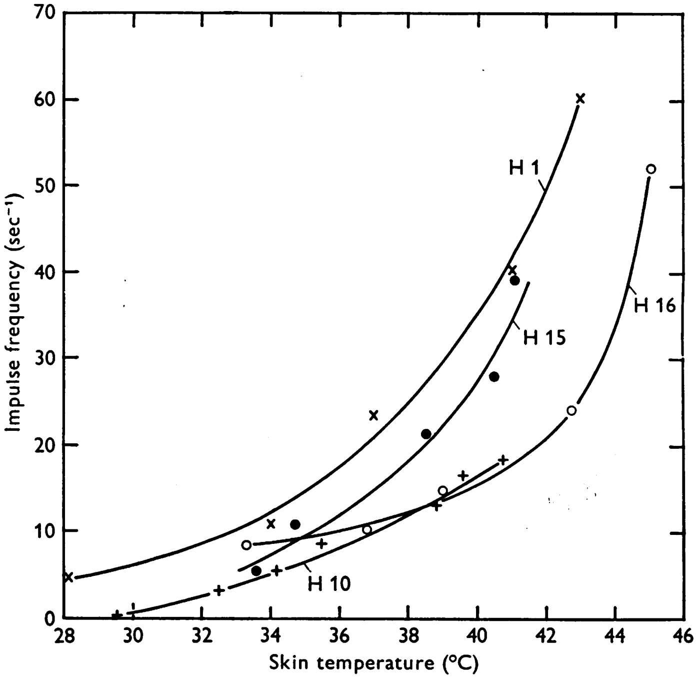

Fig. 3. Static impulse frequencies of multi-fibre strands as a function of skin temperature using an infra-red stimulator to provide constant heat radiation to the skin.

Touching the skin or pressing a wooden rod against the receptive field had no effect on the warm fibre discharge, provided the object did not influence the skin temperature (Fig. 6). Even strong local pressure on warm spots (3·5 N/cm^2) that deformed the whole nose was ineffective, whereas slight warming acted as an adequate stimulus. Thus the infra-orbital warm receptors are highly selective or specific to thermal stimuli.

Rapid temperature changes between constant levels caused a typical *dynamic response* (Fig. 7). On sudden warming to a higher level the warm receptors reacted with an overshoot in frequency, followed by adaptation to a new steady state. A temperature jump to the initial level led to a transient inhibition and a return of the discharge to the initial frequency.

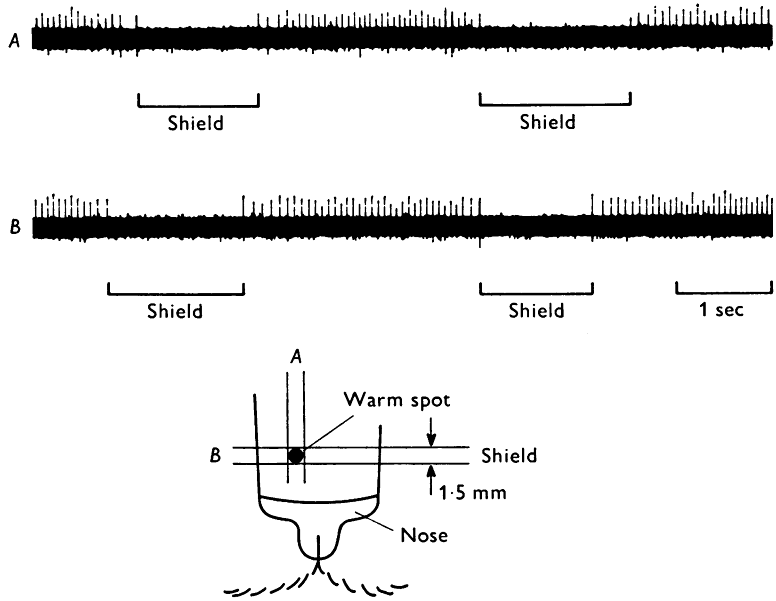

Fig. 4. Afferent impulses of a single warm fibre when applying constant heat radiation to the skin. Shielding the skin from heat radiation by a small strip of aluminium foil in the dimensions *A* and *B* was used to localize the receptive field.

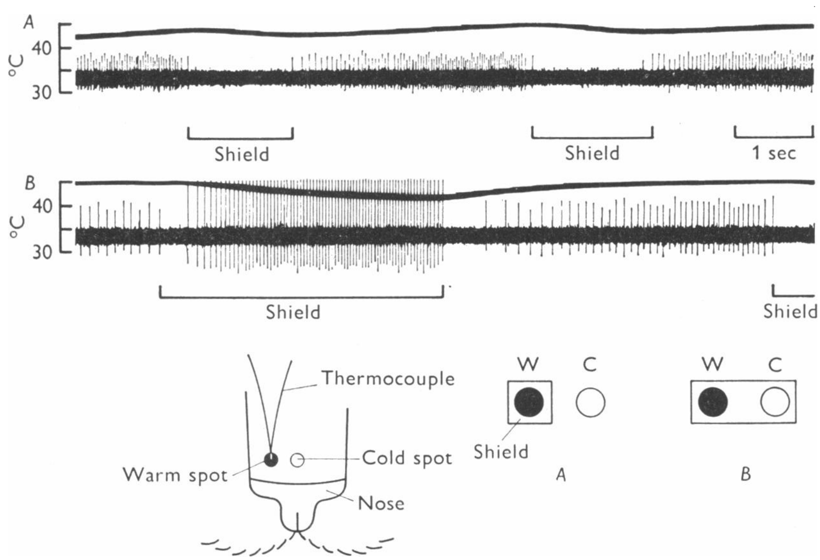

Fig. 5. Afferent impulses from a preparation containing a single warm fibre and a single cold fibre. *A*, when the warm spot is shielded from heat radiation the warm fibre discharge stops. *B*, simultaneous shielding of warm (W) and cold (C) spots causes inhibition of warm fibre and excitation of cold fibre.

For the most sensitive receptors, warming by a few tenths of a degree from neutral skin temperature was sufficient to cause a marked frequency rise. When the skin was heated with a rate of 2·5° C/sec, starting from an adapting temperature of 30° C, 80 % of all fibres which had been silent at

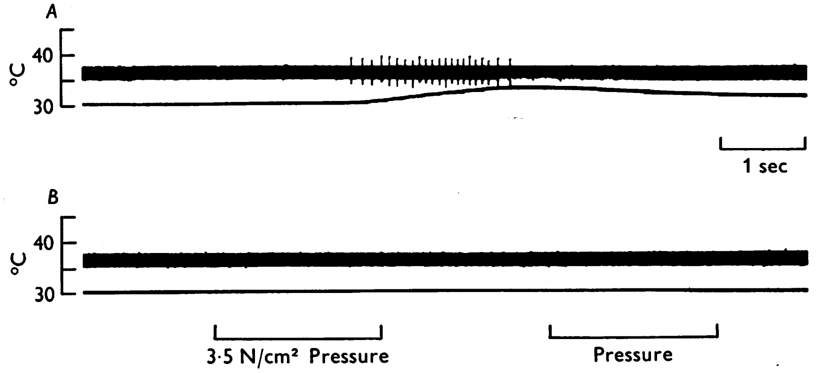

Fig. 6. Afferent impulses of a single warm fibre and temperature of the skin when applying thermal and mechanical stimuli. *A*, warming the skin. *B*, strong pressure on the skin at 30° C does not excite the warm fibre.

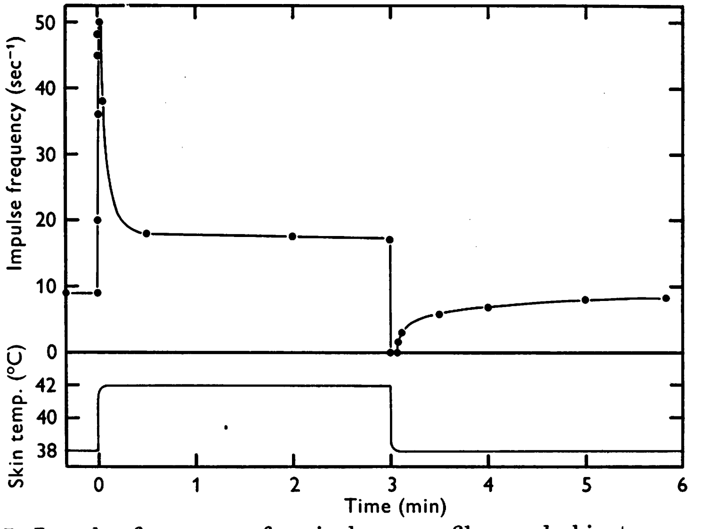

Fig. 7. Impulse frequency of a single warm fibre and skin temperature when applying temperature jumps between 38 and 42° C.

30° C were firing at temperatures below 35° C. The dynamic response of warm receptors is further characterized by the maximum frequency reaching 200 impulses/sec in some cases and by the dynamic sensitivity amounting to + 70 impulses/sec per °C for the most sensitive fibres.

An example of the *static response* of a single warm fibre is shown in Fig. 8. At constant temperatures between 40 and 45° C the receptor fires regularly with a frequency that increases steeply with temperature. The static discharge is a function of absolute temperature irrespective of whether the level was reached from higher or lower temperatures. The warm fibres from the infra-orbital region exhibited a regular sequence of impulses throughout the whole static and dynamic activity range, whereas some

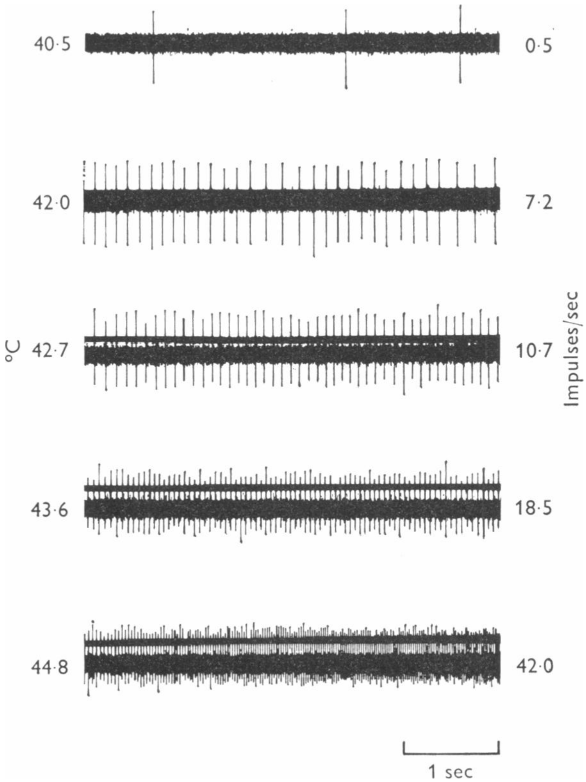

Fig. 8. Static discharge of a single warm fibre at various constant temperatures of the skin, using constant heat radiation as the stimulus.

of the infra-orbital cold fibres showed regular discharges as well as periodic bursts of impulses interrupted by silent periods. Such bursts have been described for cold fibres in the lingual nerve of cats (Hensel & Zotterman, 1951; Dodt, 1952) and were particularly seen in the discharge of cutaneous cold receptors in primates (Iggo, 1963, 1969; Kenshalo & Gallegos, 1967).

When the temperature exceeded that at which activity was maximal, the impulse frequency soon fell to zero. In some cases, as in Fig. 9, the discharge was cut off sharply at its maximum, whereas in other cases the inhibition was preceded by a short drop in frequency. This inhibition was completely reversible provided that the skin was not maintained for a long time at noxious temperatures. As we tried to avoid skin injury, no systematic studies were made at temperatures above 48° C. We observed, however, that higher skin temperatures sometimes led to a vigorous discharge of small impulses associated with nociceptive reflexes in the lightly anaesthetized animal, such as withdrawing the head or struggling with the legs.

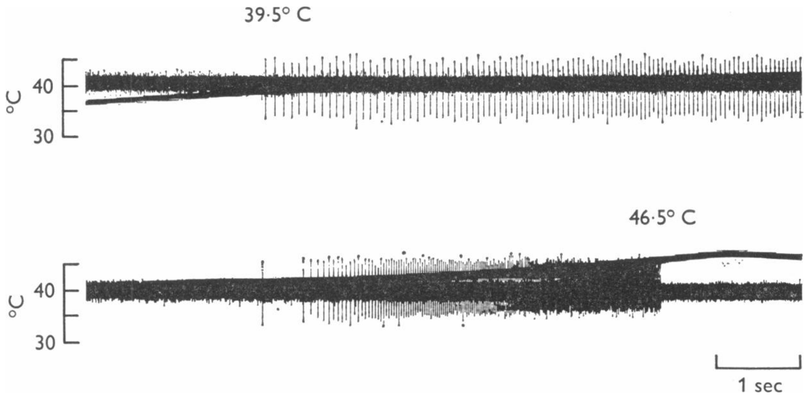

Fig. 9. Response of a single warm fibre and skin temperature when applying heat radiation of various intensity to the receptive field.

With respect to static sensitivity, the population of infra-orbital warm receptors is surprisingly homogeneous (Fig. 10). The curves depicting static impulse frequency as a function of temperature are similar in shape, and the maximum discharge for various warm fibres covers the narrow range between 45 and 47° C.

During our investigations of warm fibres we also tested several cold fibres serving the nasal area (Fig. 11). At temperatures between 30 and 45° C there was usually a regular discharge without bursts. The frequency of the static cold fibre discharge decreased at higher temperatures, the upper limit of persistent activity being 43° C.

Figure 12 shows the average static frequencies of single warm and cold fibre populations in the infra-orbital nerve as a function of skin temperature. The average maximum of the static warm fibre discharge is at 46° C, the maximum of cold fibre activity at 27° C. There is some overlap in the temperature ranges of both groups, the curves crossing near 37° C. A summary of quantitative data for populations of cold and warm receptors in the nasal area of cats is given in Table 1. The group of infra-orbital cold receptors seems to be less homogeneous than the group of warm receptors, in that the temperatures of the static maxima of individual cold fibres varied from 18 to 34° C, whereas the maxima of the warm fibre discharge were found to be in the range between 45 and 47° C.

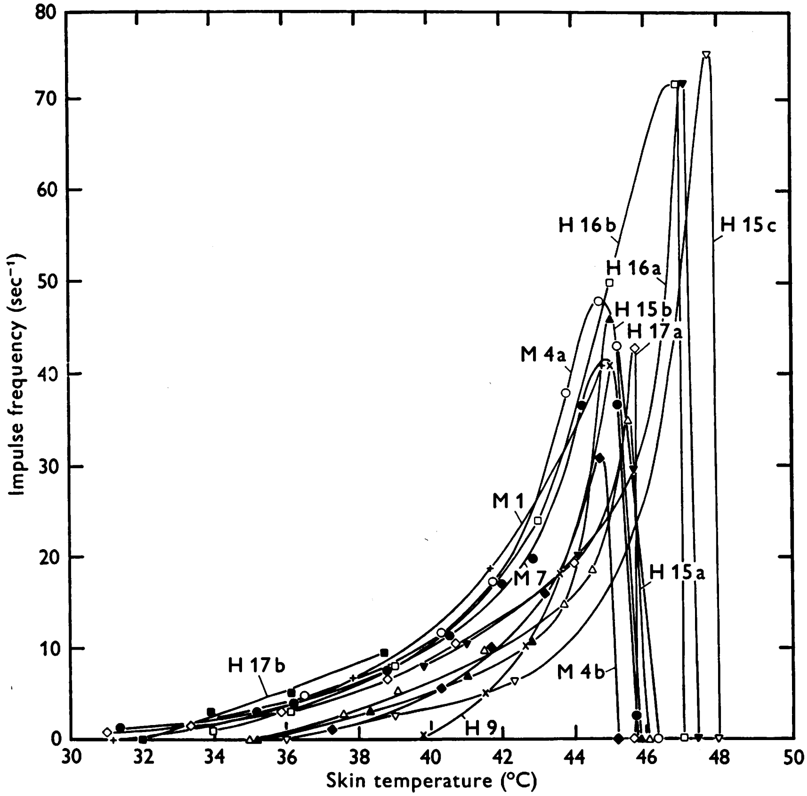

Fig. 10. Static impulse frequencies of single warm fibres as a function of skin temperature, using constant heat radiation (H) or water-circulated metal thermodes (M) of constant temperature as the stimulus.

DISCUSSION

The results presented in this paper confirm previous reports on a receptive field in the nasal area served by numerous warm fibres and on the quantitative properties of these fibres (Hensel, 1968*a*, *b*). The nasal warm receptors represent an example of functionally specialized nerve endings in some areas of the skin even if the morphological basis of their specificity might be too subtle for our present investigative methods.

Non-myelinated nerve fibres with high selective sensitivity to warming have been found in the saphenous nerve of cats (Hensel *et al.* 1959, 1960), in the infra-orbital nerve of cats and dogs (Iriuchijima & Zotterman, 1960), and in the scrotal nerve of rats (Iggo, 1969). The limited amount of quanti-

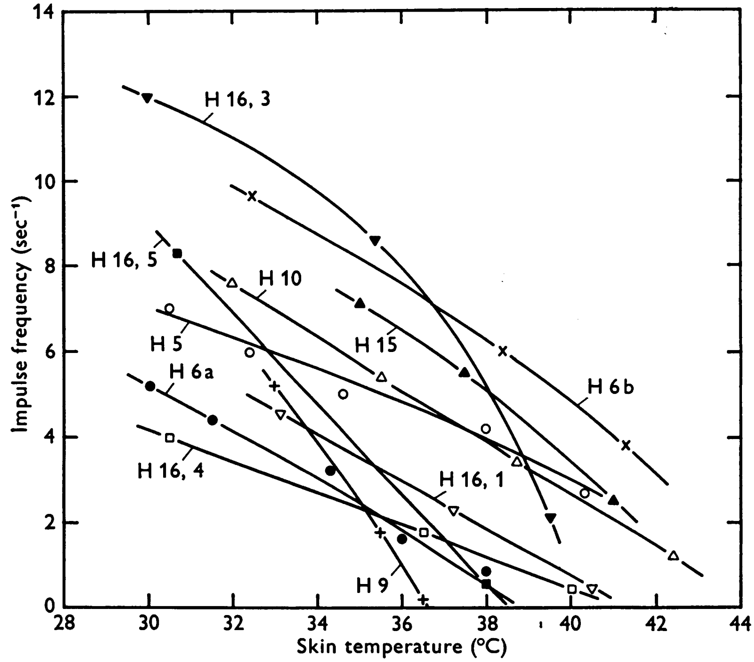

Fig. 11. Static impulse frequencies of single cold fibres as a function of skin temperature, using constant heat radiation as the stimulus.

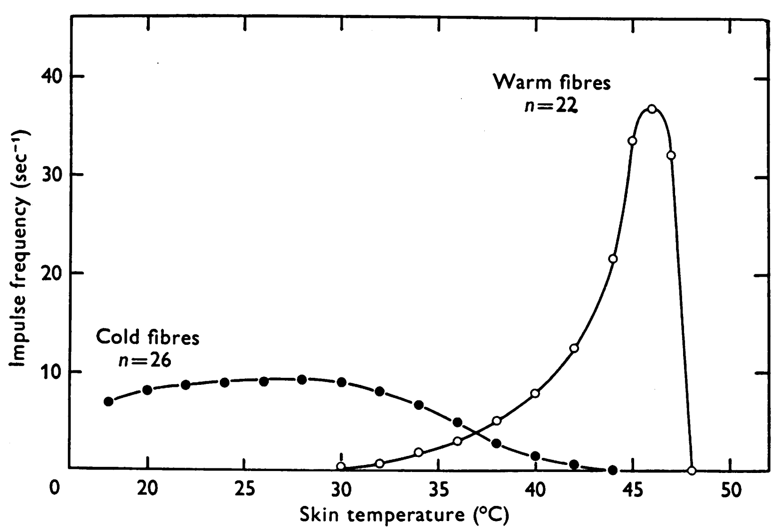

Fig. 12. Average frequency of the static discharge as a function of temperature for warm and cold fibre populations (part of the data for cold fibres drawn from Hensel & Wurster, 1969).

tative data for these fibres does not allow a detailed comparison with the warm receptors in the nasal region. With respect to static activity as a function of temperature one single unit has been examined so far in the saphenous nerve (Hensel *et al.* 1960) and another unit in the scrotal nerve (Iggo, 1969). The static curves of both units were almost identical, the non-myelinated warm fibre in the saphenous nerve having a sensitive range from 38·5 to 43° C and a sharp maximum at 41·2° C, whereas the respective data for the unit in the scrotal nerve were 37 to 45° C and 42° C.

TABLE 1. Properties of cold and warm fibres from the nasal area

Property	Cold fibres*	Warm fibres
Number of units	26	22
Static temperature limits	5...43° C	30...48° C
Maximum static frequency (average)	9 impulses/sec	36 impulses/sec
Temperature of static maximum (average)	27° C	46° C
Maximum static sensitivity (average)	− 1 impulses/sec °C	+ 14 impulses/sec °C
Highest dynamic sensitivity	− 50 impulses/sec °C	+ 70 impulses/sec °C
Highest dynamic frequency	240 impulses/sec	200 impulses/sec

* Part of the data for cold fibres drawn from Hensel & Wurster (1969).

In a multi-unit preparation from the scrotal nerve the values were found to be about 1° C higher. If these findings were representative for the warm fibre populations, then the activity range of saphenous and scrotal fibres, amounting to 7° C from the onset of discharge up to the maximum, were narrower than that of the infra-orbital warm fibres which was 16° C for a larger group.

There are several reports dealing with non-myelinated cutaneous fibres in the leg of cats excited only by intense heating (Iggo, 1959; Hensel *et al.* 1960; Perl, 1968). The large majority of these 'heat' fibres had thresholds above 46° C, sometimes as high as 55° C, and responded also to strong mechanical stimuli. This receptor population can rather clearly be distinguished from the group of infra-orbital warm fibres since most of the 'heat' receptors, besides being mechanically sensitive, were active at temperatures at which the warm fibres had ceased to discharge. Our present results indicate that similar 'heat' fibres exist in the infra-orbital nerve but more experiments are necessary in this direction.

In the present state of investigation it is difficult to comment on our results in terms of behaviour and sensation. Since no direct comparisons have been made between warm fibre discharge and behavioural responses in animals, or between warm fibre activity and temperature sensation in human subjects, any conclusion in this direction must remain more or less hypothetical. The quantitative properties of infra-orbital warm fibres fit quite well into our present knowledge of behavioural responses in cats to warming the face. They would also be in good agreement with the facts of human temperature sensation, provided that the properties of warm receptors in cats and in human subjects are comparable. It seems worth mentioning that the average maximum of the warm fibre discharge is near 46° C and thus close to the threshold for non-adapting pain and nociceptive reflexes (Hardy, 1953). In other words, the warm fibres would gradually stop discharging at temperatures at which heat pain begins.

On the basis of previous experiments revealing a surprisingly small number of infra-orbital warm receptors (Hensel, 1952; Boman, 1958; Iriuchijima & Zotterman, 1960; Kenshalo, 1968) the hypothesis was put forward that behavioural responses to warming as well as warm sensations might be due to an inhibition of cold fibres rather than to an excitation of warm fibres. The data presented here do not fit into this concept as far as the number of warm receptors is concerned. They do not disprove, of course, the possibility of cold fibre inhibition being involved in warm sensations. It might be the case that both sets of receptors are acting together in a certain range, particularly at temperatures associated with sensations such as 'less cold', 'neutral' and 'slightly warm'.

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