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Multiple Temperature-Sensitive Spots Innervated by Single Nerve Fibers

Abstract. *Electrophysiological recordings were made from single nerve fibers which were specifically responsive to temperature changes of the skin of monkeys. Previous reports indicated that the receptive area on the skin of such preparations was a single small spot less than 1 millimeter in diameter. However, we found that the activity in a single thermally sensitive fiber increased when any one of eight individual spots on the skin was cooled. In other preparations two to six spots, each less than 1 millimeter in diameter, appeared to be innervated by a single fiber. The neural activity resulting from the cooling of one or several of these spots summed, and we suggest that this summation may be the neural analog of areal summation of thermal stimuli reported in psychophysical measurements.*

Although knowledge of the structural characteristics of cutaneous temperature receptors is lacking, it is desirable to describe their functional characteristics. These characteristics can be described in psychophysical or behavioral terms, and electrophysiological data can be obtained from measurements of changes in the activity of the peripheral nerve associated with changes in skin temperature. Correlations of the psychophysical and electrophysiological measurements of the effects of thermal stimulation provide information relevant to the nature of peripheral coding of thermal stimuli and to the processing of this information by the nervous system.

One functional characteristic of temperature reception which has been described in psychophysical terms is areal summation of thermal stimuli (*1*). As the area of skin stimulated is increased (up to about 1500 cm^2) the intensity of thermal stimuli required to produce a threshold sensation decreases. On the basis of these and other data concerned with summation, Hergert, Granath, and Hardy (*2*) have suggested that areal summation results from a convergence of sensory nerve activity at two different sites. Summation over small areas (less than 4 or 5 cm^2) results from endings whose branches converge near the periphery, whereas summation over large areas (greater than 4 or 5 to less than 1500 cm^2) results from convergence of axons on synaptic pools within the central nervous system.

Electrophysiological investigations in primates of peripheral thermally sensitive fibers (*3*) have failed to provide any evidence of the first type of convergence, and, to our knowledge, the problem of thermal summation in the central nervous system has not been investigated. In preparations in which such single specific peripheral fibers have been isolated, increased activity was induced by the cooling of only a single spot (not more than 1 mm in diameter) on the skin. Innervation of several sensitive spots by a single fiber has not yet been reported, even for the tongue and face of the cat (*4*).

We believe that we have discovered the neurological counterpart of small-area thermal summation determined by psychophysical methods. The data reported here are from one of eight preparations of single fibers taken from the radial and saphenous nerves of rhesus (*Macaca mulatta*) and stumptail (*Macaca speciosus*) monkeys. In these preparations a single thermally sensitive fiber (*5*) innervated two to eight spots on the skin. These spots were distributed over areas of up to 1.7 cm^2, and each spot in the cluster was no more than 1 mm in diameter. Twenty preparations have been obtained in which a single fiber innervated only one spot on the skin, but the data are insufficient to estimate the relative proportion of

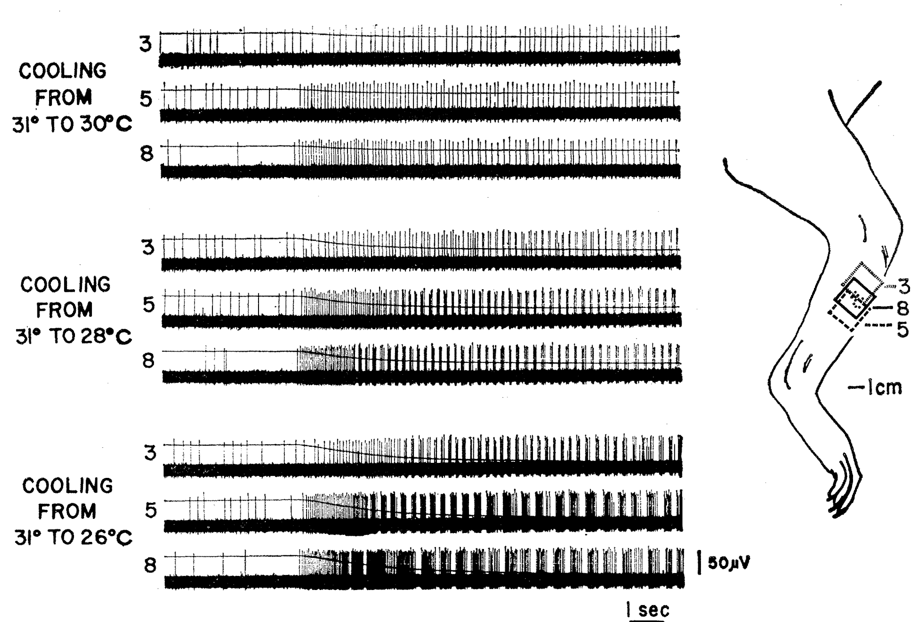

Fig. 1. The neural discharge of a single specific thermally sensitive fiber in response to cooling of the skin. Increased activity in the fiber was induced when any one of eight spots (shown to the right of the figure) was cooled with a small probe. Application of the probe to the skin between the spots failed to produce a response. Cooling first three, then five, and finally all eight of the spots by 1°, 3°, and 5°C with a large-area stimulator produced the neural activity shown here. The steady-state discharge, before the cool stimulus, was faster when three and five spots were stimulated than it was when all eight were stimulated. We attribute this to the fact that when the stimulator covered all eight spots, they are all maintained at 31°C. However, when only a portion of the spots were under the stimulator, the remaining ones were near skin temperature which, in this case, was 26°C. These few cooler spots were responsible for the higher steady-state frequency.

multiple-spot innervations by single fibers and single-spot innervations.

Records of neural activity were taken from a preparation of a single fiber from the saphenous nerve of a stumptail monkey anesthetized with sodium pentobarbital (Fig. 1). This particular fiber responded with increased frequency when any one of the eight spots shown in Fig. 1 was cooled. Cooling of the skin between spots by approximately the same amount failed to produce a change in the rate of discharge. No change in the response of the fiber could be induced when the spots were touched or pressed (5 to 10 g) with a thermally neutral wooden probe.

To determine if the sum of the activities induced by cooling each spot would equal the frequency observed when all spots were cooled at once, we placed a thermal stimulator, constructed from a Peltier cooler (*6*), so that it covered three spots, then the remaining five spots, and finally all eight spots (Fig. 1). At each position of the stimulator, the skin was adapted to 31°C for 5 minutes. It was then cooled by 1°, 3°, and 5°C (at an initial rate of about 0.6°C per second) and maintained for 20 seconds at each new temperature. At the end of each cool stimulus, the stimulator was returned to 31°C for a period of 5 minutes. It is clear that as more spots were involved in each cooling stimulus the frequency of activity in the single fiber increased (Fig. 1).

Figure 2 shows the change in frequency of neural activity resulting from stimulating three, five, and eight spots by cooling the skin 5°C. The characteristics of response shown here are typical of those obtained when less intense cool stimuli were used. There appears to be a linear relationship between the number of spots cooled and the peak frequency of activity. For example, in this preparation, the sum of peak frequencies resulting from stimulation of three and five spots approximated the peak frequency observed when all eight spots were cooled. This summation apparently holds only for the phasic increase in frequency associated with the onset of cooling. The frequencies of neural activity observed 10 seconds or more after cooling commenced when three and five spots were stimulated summed to a greater total frequency than that observed when all eight spots were stimulated. A second characteristic of these preparations is that the latency of the peak frequency is inversely related to the number of spots stimulated.

More quantitative statements concerning the way in which changes in neural activity occurred when three, five, or all of the eight temperature-sensitive spots were cooled are not warranted. Thermal gradients, both temporal and spatial, occurred at the edge of the thermal stimulator. When either three or five spots were covered by the stimulator, these gradients may have affected the neural activity produced at the spots not covered. The uncovered temperature-sensitive spots ranged from 1 to 5 mm from the edge of the stimulator. According to the measurements of Hensel (*7*), surface cooling by 5°C should reduce tissue temperature by as much as 2°C at 0.5 mm below the edge of the stimulator. The gradient should diminish so that there is no change 4 mm out from the edge. But time (about 20 seconds) is required to establish this gradient. In the 3 to 5 seconds after the onset of cooling (Fig. 2), during which the peak frequency of activity occurred, the thermal gradient should have been no more than a quarter of that attained 20 seconds after the onset of cooling. Although the thermal gradients beyond the edge of the stimulator may have produced some activity in those spots not covered by the stimulator, their effects are small; however, they may be sufficient to confound exact quantification.

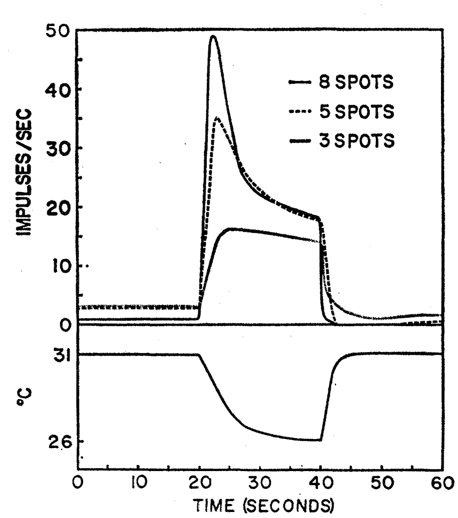

Fig. 2. The change in frequency in a single thermally sensitive fiber during cooling (by 5°C) of only three, the remaining five and, finally, all eight of the skin spots innervated by it (last three traces of Fig. 1). The sum of the phasic frequency increase (during the first 3 seconds of cooling) when three and five spots were cooled approximates the phasic peak frequency when all eight of the spots were cooled by the same amount. This statement does not hold for the frequencies of discharge following the phasic frequency increase (during the final 10 seconds of cooling).

It is interesting to speculate about the structural characteristics of the neural elements involved in the innervation of these preparations. On the basis of our current concepts (*8*) of the operation of terminals and branches of peripheral afferent neurons, we think it likely that in this preparation each spot was innervated by dendritic branches of the afferent primary neuron where generator potentials may summate, rather than by branches of the afferent neuron in which orthodromic impulses in collision with antidromic impulses would be annihilated. Were the latter true, one would expect the sum of the peak frequencies observed when three and five spots were stimulated to be greater than the frequency when all eight were stimulated simultaneously. It is also possible that some clusters of spots had both types of innervation. The results are not conclusive because the frequencies were low and the distances were small.

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