Cutaneous Slowly Adapting Mechanoreceptors in the Cat

Abstract. *Cutaneous mechanoreceptors have been anatomically delineated, and the physiological characteristics of the nerve fibers and receptor terminals have been studied. Frequency analysis of spike trains showed two rate processes associated with the rising and plateau phases of the mechanical stimulus. Natural stimulation is capable of evoking firing frequencies which saturate the carrying capacities of the fiber.*

In the course of experiments on cutaneous innervation in the skin of cats, I found discrete skin elevations associated with slowly adapting mechanoreceptor activity. These observations are in agreement with those recently reported by Iggo (*1*), who described a "tactile corpuscle" in the skin of cats, dogs, and primates. The present report, therefore, constitutes independent substantiation of Iggo's gross and microscopic anatomical findings and, in addition, presents data on the physiological characteristics of the tactile unit—the receptors and accompanying nerve fibers.

Nineteen slowly adapting tactile units were isolated and studied by dissection and recording from dorsal roots L-6, L-7, and S-1 in 39 adult cats. All the receptors of these units were located in hairless prominences of skin, 180 to 300 μ in diameter and 80 to 100 μ high (Fig. 1). The activity from a prominence could neither be elicited nor modified by moving or plucking adjacent hairs. A single unit encompassed no more than 1 cm^2 of skin area and consisted of from one to five terminal prominences per nerve fiber. Skin elevations of one unit did not intersect the area of another and only a single myelinated nerve was seen to ramify in each prominence. These observations suggest that the respective fields of the tactile units do not converge. Lack of peripheral convergence is unusual and should these observations be further substantiated, a re-evaluation of sensory spatial overlapping in the skin may be indicated.

The displacement sensitivity of the receptor was explored by a cylindrical stimulus probe (200 μ in diameter) driven by a loudspeaker. The movement of the probe was monitored by a photocell assembly. Displacements up to 400 μ could be obtained and pulse duration could be varied from 3 msec to several seconds. Threshold displacement was determined by using mildly damped 3-msec pulses for which the rise time (from base level to maximum displacement) was 2 msec. Application to the prominence of threshold or suprathreshold stimuli of this type elicited a single action potential (Fig. 2, top). Threshold displacements ranged from 9 to 58 μ. The mechanical-stimulus latency (transduction plus conduction times) was the longest upon threshold stimulation and decreased to a minimum value as the displacement was increased above threshold. In contrast to the behavior observed with the Pacinian corpuscle (*2*), a response could not be evoked by summation of several subthreshold displacements of short duration.

Typical slowly adapting firing patterns were produced when heavily damped, suprathreshold displacements of long duration were used (Fig. 2, middle). Frequency analysis of the pulse train shows that at least two rate processes are represented, one that is displacement-rate sensitive and coincident with the rising phase of the stimulus, and the other that is displacement sensitive and associated with the plateau. These output characteristics of the receptor resemble those of the "less rapidly adapting" tactile receptor of the toad's skin (*3*).

A single action potential was evoked by applying a short-duration, positive electrical pulse (*4*) to the tactile prominence (Fig. 2, bottom). Trains of action potentials could not be produced by increasing the stimulus duration. The stimulus was ineffective when applied between the elevations. The more peripheral portions of the nerve, in the prominence, were studied by dual electrical stimulation of one prominence or tandem stimulation of two prominences of the same tactile units. Absolute refractory periods of from 0.6 to 1.4 msec were measured. These values, characteristic of A-beta nerve fibers, coincide with the histological observations on the diameters of the myelinated nerves that innervate the skin regions. Changes in voltage threshhold of a second stimulus applied up to 100 msec after a threshold conditioning stimulus are shown in Fig. 3. Two threshold elevations are seen, one occurring from 0.6 to 2 msec that reflects the relative refractory period, and the second between 2 and 60 msec that has properties characteristic of the positive afterpotential. No measurable change in conduction time was observed beyond the relative refractory period.

When tandem electrical-mechanical stimulation sequences were used, mechanical threshold changes were found to correspond to those observed with

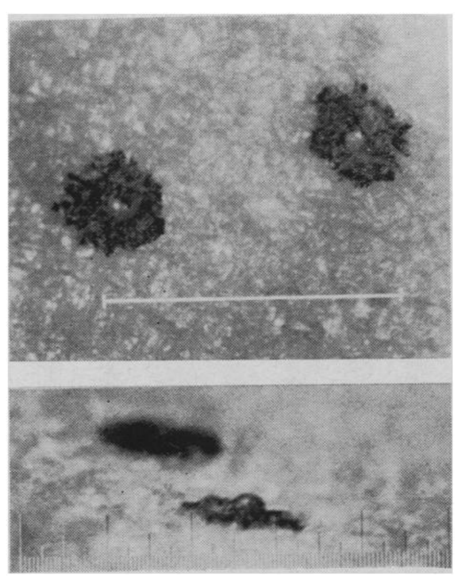

Fig. 1. (Top) Top view of two tactile prominences of a sensory unit; periphery shadowed with india ink. Distance, 5 mm. (Bottom) Side view; one division = 40 μ; hair removed from skin.

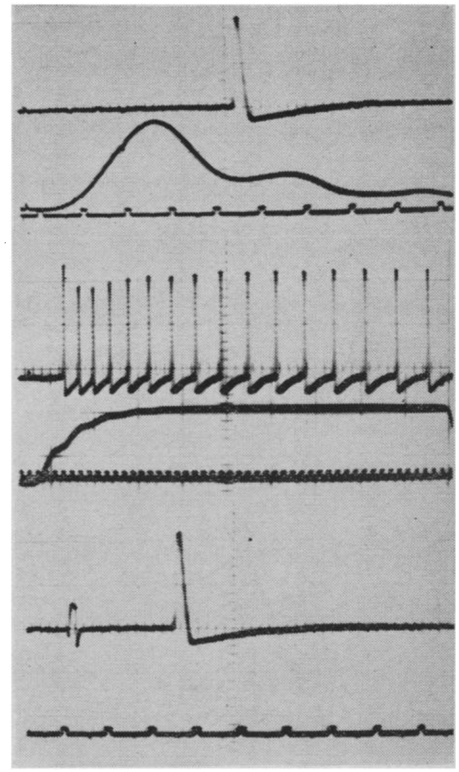

Fig. 2. (Top) Response to short mechanical stimulus. Displacement monitor. Time mark, 1000 cy/sec. (Middle) Response from sustained suprathreshold displacement. (Bottom) Response from short-duration electrical stimulus.

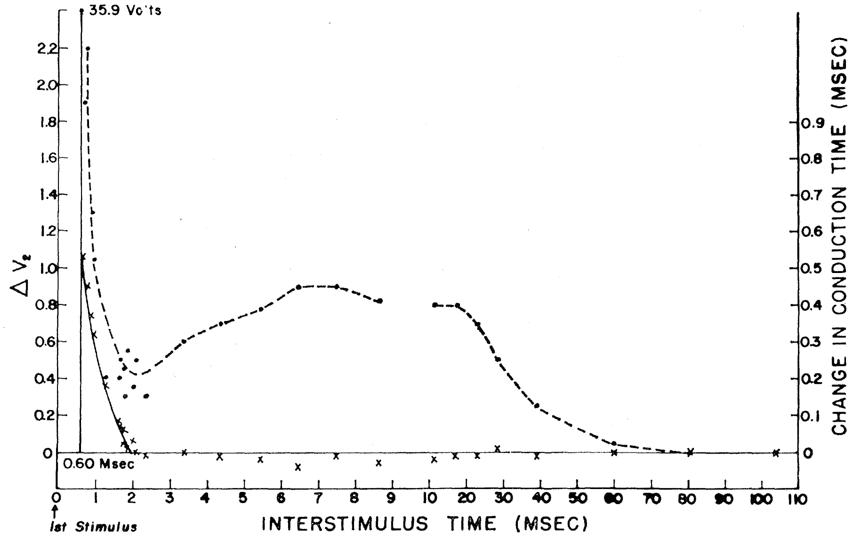

Fig. 3. Voltage threshold alterations for second stimulus after conditioning stimulus (•); change in conduction time of second evoked response (×).

dual electrical stimulation. In contrast to the latter, latency changes occurred beyond the relative refractory period, reflecting an increase in transduction time due to an elevated nerve fiber threshold close to the site of action potential initiation. A comparison of electrical and mechanical latencies showed a maximum mechanical transduction time of 1.3 msec and a minimum of 0.4 msec.

It appears that natural stimulation is capable of evoking firing frequencies that saturate the carrying capacity of the nerve fiber. The initial frequencies produced by sustained suprathreshold displacements (Fig. 2, middle) approach the maximum possible as determined by the absolute refractory period of the nerve and the recording site; the several spikes after the first are reduced in amplitude, indicative of the relative refractory period. Such high-frequency firing has also been observed from rapidly adapting hair receptors but stands in marked contrast to the lower frequencies naturally evoked by muscle receptors, the afferent fibers of which have equivalent or greater capacities (*5*).

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References and Notes

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2. W. R. Loewenstein, *Ann. N.Y. Acad. Sci.* **94**, 510 (1961).
3. U. Lindblom, *Acta Physiol. Scand.* **56**, 349 (1962).
4. Typical threshold stimulation parameters: 0.8 volt (+); 0.3 ma; duration, 0.1 msec; skin contact area, approximately 3×10^{-2} cm^2.
5. Supported in part by the Defense Atomic Support Agency, contract No. DA-49-146-XZ-058.

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Sarcomas in Cotton Rats Inoculated with Rous Virus

Abstract. *When newborn cotton rats were inoculated with Carr's strain of the Rous sarcoma virus, 50 percent of the rats developed sarcomas. The significance of this finding is discussed in relation to the pathogenicity of various strains of this virus in other mammals.*

A peculiar cystic hemorrhagic disease has been described simultaneously and independently in this laboratory (*1*) and elsewhere (*2*). The disease was induced in albino rats by inoculating the Rous sarcoma virus during the embryonic or neonatal period. It was also shown that some rats developed sarcomas long after this virus was injected (*3*). These experiments were later confirmed and extended (*4–7*). We suggest that further studies of chronic infections of albino rats with Rous virus, in which there are relapses and remissions, and which develop first as a cystic hemorrhagic disease and then as a sarcoma, might contribute to our knowledge of the general mechanisms of the pathogenic action of viruses at the level of the organism.

In this report we describe the data obtained in a preliminary study of the pathogenicity of the Rous virus in cotton rats (*Sigmodon hispidus hispidus*). Carr's strain of Rous virus was used. Newborn cotton rats, within the first 12 hours of life, were inoculated subcutaneously with 0.1 to 0.15 ml of a 30 percent homogenate of chicken Rous sarcoma (4×10^6 chick sarcomagenic units per milliliter) prepared as previously described (*1, 8*). The growth of the inoculated cotton rats was significantly retarded in comparison with that of controls. Tumors developed in 12 out of 23 of the inoculated cotton rats surviving until the age of 2 to 3 months. Histological examinations of the tumors showed them to be sarcomas. Most of the sarcomas were polymorphic with a prevalence of spindle-shaped and round cells and a significant amount of mucoid substance. In general, the histologic pattern of these tumors was similar to that of the original chicken Rous sarcoma. Fluid exuded from them on cutting, and they showed a tendency to hemorrhage, and they became rapidly necrotic in the central parts. Some of the tumors, however, were more solid and monomorphic with spindle-shaped cells. The sarcomas in cotton rats usually attained diameters of approximately 4 to 6 cm. One of these sarcomas was successfully transplanted to normal adult cotton rats.

Antigens of the chicken Rous sarcoma were not detected in extracts of the sarcomas from cotton rats when they were tested against highly active rabbit antiserum in the ring precipitation test.

These data show that cotton rats, as well as albino rats (*1–8*), and rabbits (*9*), are susceptible to the Carr's strain of Rous virus, although the question still remains as to whether the sarcomas are caused directly by conversion of cotton rat cells to a malignant neoplastic state by the Rous virus. Although, in albino rats, the Rous virus was isolated from sarcomas induced by this virus (*5, 8*), it is quite possible that only some of the sarcomas (especially those which were polymorphic and contained a large amount of mucoid substance) were caused directly by the Rous virus, whereas others might have developed as a result of secondary effects of the virus-induced condition (cystic hemorrhagic disease). Since the walls of the cysts consist of parallel rows of fibroblasts distended by liquid, the conditions here may be similar to those involved in the induction