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A QUANTITATIVE STUDY OF C-MECHANORECEPTORS IN HAIRY SKIN OF THE CAT

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SUMMARY

1. Single C-mechanoreceptor afferent units were examined by recording from fibres dissected from the saphenous nerves of cats anaesthetized with chloralose. The receptive fields, averaging 4 × 3 mm when 10–50 × threshold stimuli were used, were in the hairy skin of the leg and foot.

2. The extent and excitability of receptor terminals was tested by two- and three-point field studies. The excitability of terminals in one part of the field of a unit could be depressed without affecting the excitability of terminals elsewhere in the field.

3. The afferent units could be excited by both inward and outward movement of the stimulus probe, in appropriate conditions; that is, there was non-directional sensitivity.

4. After-discharge was found to depend on restorative movements of the skin, not on a persistence of the response of the receptor to the original movement.

5. The response to mechanical stimulation was slowly adapting with two time constants and the stimulus–response relationship was exactly described by a power function, with exponents ranging from 0·6 to 1·3.

6. The C-mechanoreceptors could be depressed by rapidly repeated or prolonged mechanical stimulation and the effect was confined to the excited terminals.

INTRODUCTION

Non-myelinated afferent fibres supplying hairy skin innervate a diversity of receptors, varying in sensitivity from those excited by gently moving the hairs or by small temperature changes, to those which require either severe mechanical or thermal stimuli (Zotterman, 1939; Douglas & Ritchie, 1957; Iggo, 1959, 1960, 1969; Douglas, Ritchie & Straub, 1960; Hensel, Iggo & Witt, 1960; Iriuchijima & Zotterman, 1960; Witt & Griffin, 1962;

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Bessou & Perl, 1969; Bessou, Burgess, Perl & Taylor, 1971; Hensel & Iggo, 1971; Iggo & Ogawa, 1971; Beck, Handwerker & Zimmermann, 1974; Zimmermann, 1975; Handwerker & Neher, 1976). Single unit studies have established that several distinct categories, based on quantitatively controlled peripheral stimuli, can be made. In the present paper we have restricted our attention to the sensitive C-mechanoreceptors – the class readily excited by low intensity mechanical deformation of the skin and which can also be excited briefly by sudden lowering of the skin temperature (Iggo, 1960; Bessou *et al.* 1971; Hahn, 1971; Zimmermann, 1975). They are abundant in the hairy skin of non-primate mammals (Sassen & Zimmermann, 1971). Particular attention has been given to the characteristics of the receptive field, to a quantitative evaluation of the stimulus–response relationship and to the depression of sensitivity of the receptors induced by a repetition of mechanical stimulation.

METHODS

Ten adult cats, weighing 2·5–4·0 kg, anaesthetized with I.V. α-chloralose (80 mg/kg) after induction with ethyl chloride and ether, were used. Afferent fibres, dissected from the saphenous nerve as single units and identified by methods developed for work on C-fibres (Iggo, 1956, 1958, 1960; Brown & Iggo, 1967), innervated hairy skin on the lower inner leg, ankle and foot. For the purposes of these experiments it was necessary to be able to record from one unit for several hours, and this was possible under the conditions that were used.

Mechanical stimulators of the kind described by Brown & Iggo (1967) were used. With them the stimulus probe could be positioned with an accuracy of ± 10 μm in the plane parallel with the skin surface and the vertical position of the probe adjusted both electrically and mechanically to within ± 5 μm, using a digital voltmeter calibrated in μm to read the final electrical adjustment of position. Stimulus parameters (stimulus velocity, amplitude, duration, repetition interval) were controlled by a digital clock (Digitimer – Devices Ltd.) and by voltage wave-form generators. A more detailed description of the apparatus is given by Chambers, Andres, von Duering & Iggo (1972).

Design of the experiments. An important factor in experiments designed to establish a stimulus–response relationship for the sensitive C-mechanoreceptors is the depression of response following mechanical stimulation (Iggo, 1960; Bessou *et al.* 1971; Hahn, 1971). In the present trials a uniform response was obtained when an interval of 90 sec to 3 min was allowed between successive indentations, each of which was not greater than 600 μm in amplitude, nor longer than 10 sec in duration. As the Results will show, complete recovery from a single stimulus may take as long as 5 min, but nevertheless a reproducible standard response, adequate for our purposes, was obtained in the series we ran using the shorter intervals. An overriding consideration was the total time required to run a sequence of trials. A randomized trial at six given intensities repeated ten times with a 3 min inter-trial interval required a minimum of 3 hr. Since units could not be held with any certainty for longer periods, the 3 min interval was the maximum used. The data were plotted, using logarithmic co-ordinates and regression lines were calculated, using the method of least squares.

Receptive field interactions. The interdependence of receptor elements within the receptive fields of individual C-mechanoreceptors was examined by first defining the

area of the field (usually about 4 × 3 mm), then selecting two or three points within the field not more than 2 mm apart. The two conditioning points and the test point were stimulated mechanically, using round Perspex probes, 1·00 mm diameter or a small-tipped metal probe ($d \approx 100\ \mu m$).

Electrical stimulation. The saphenous nerve, exposed in the same pool as for recording, was stimulated through Ag/AgCl wire electrodes, 6–10 mm apart, placed beneath the nerve and isolated by dissection from the subjacent muscle, for conduction velocity measurements (Brown & Iggo, 1967) and to test the effect of antidromic impulses on the responses to 'natural' stimuli.

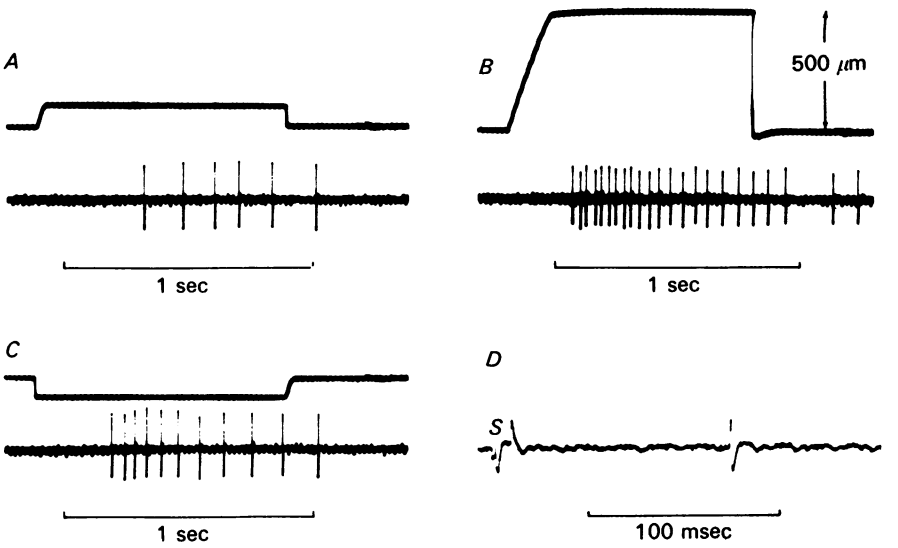

Fig. 1. Responses of a single C-mechanoreceptor (16117–4) to mechanical (*A*, *B*, *C*) and electrical (*D*) stimulation of the skin. In *A–C* the upper traces show the indentation delivered to depilated skin, using a probe (d = 1 mm), and the lower traces show the afferent responses. The long latencies of response are due to the conduction time from the receptor terminals to the recording electrodes. This is illustrated in *D*, where the receptor was stimulated electrically at *S* and an action potential was recorded 120 msec later. The conduction velocity was 0·8 m/sec. In *C* the probe tip slightly indented the skin at rest and the receptor was excited by withdrawal of the probe – an example of non-directional sensitivity.

RESULTS

The thirteen C-mechanoreceptors reported in this paper were similar to those previously studied in this (Iggo, 1960), and other (Bessou *et al.* 1971; Hahn, 1971) laboratories, and were all in hairy skin. They were excited by moving hairs, touching the skin (Fig. 1 *A–C*), quickly lowering skin temperature, had thresholds (von Frey hair) less than 50 mg wt. and axons conducting at less than 2·5 m/sec (Fig. 1 *D*) in the saphenous nerve in the mid-thigh.

Receptive fields. Receptive fields for liminal stimuli, using standard pulses, had a small region of maximal sensitivity surrounded by a larger area of lower sensitivity. (For technical reasons, afferent units with receptors in hairy skin on the medial aspect of the leg were selected for these tests.) The fields, for stimuli of about 100 μm delivered to depilated skin, were 2–5 mm by 1–3 mm and were oriented with the long axis parallel to the long axis of the limb. The fields, when tested by stroking the skin or hairs appeared to be larger than this, due to transmission of the deformation through the skin by stretching, or by displacements transmitted through hairs. Each unit ended in one small field of maximal sensitivity, even though the skin surface was extensively explored for additional fields, and within each field there was no indication of discontinuities of responsiveness, i.e. the fields were not spotty.

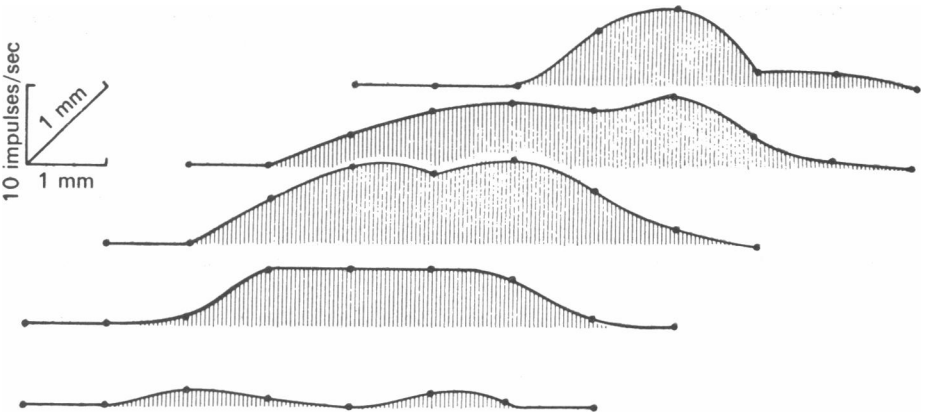

Fig. 2. Receptive field profiles, on a 1 mm grid, for a C-mechanoreceptor (1697–2). The field in depilated skin was plotted using standardized mechanical indentations (240 μm). The area of the field was *ca.* 25 mm^2.

The results for unit 1697–2 are given in Fig. 2 for a stimulus strength of 240 μm using a smooth-tipped probe 1 mm in diameter. Threshold displacement, tested immediately before the field study, was about 10 μm, and the receptor responded linearly, at least up to 500 μm displacement, so that the test-stimulus was within the normal intensity range of the unit. Maximum sensitivity was restricted to an area of less than 4 × 3 mm and fell sharply within a further 2 mm. Another receptor tested with a sharp-tipped metal probe had a field at 30 μm indentations (4 × threshold) of 2 × 1 mm which enlarged to a field of 3·5 × 2·5 mm for a 240 μm displacement. The maximum response was elicited from an area 2 × 2 mm. When 500 μm indentations were used, the average receptive field size was 4 × 3 mm. The apparent field also depends on stimulus intensity, since the

receptor terminal can be activated by deformation transmitted through the skin, like the SA II mechanoreceptor (Chambers *et al.* 1972), and in contrast to the SA I mechanoreceptors which are insulated from remote stimuli (Iggo & Muir, 1969). If stimulus spread is a factor it would be expected that not only would the number of impulses discharged be less when the stimulus was away from the receptor terminals, but also the latency of the first impulse in the discharge would be longer. Both these effects were seen when the two intensities of mechanical stimulation were tested, 40 and 240 μm.

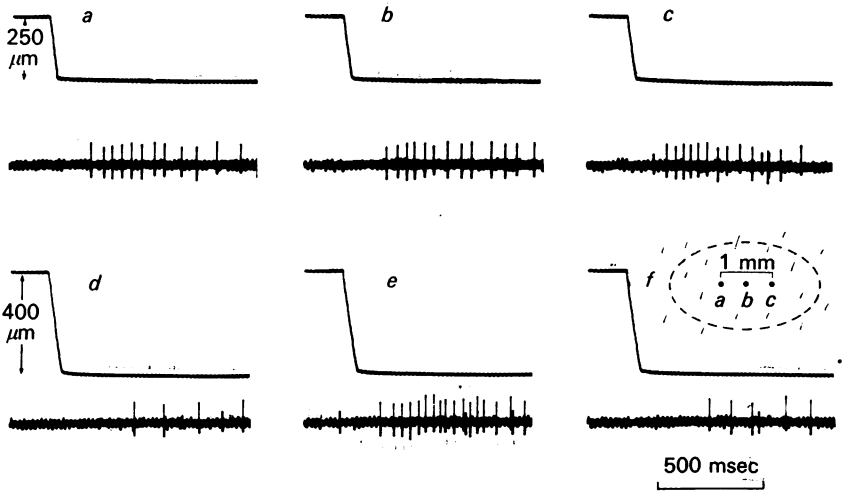

Fig. 3. Test for receptive field interactions in a C-mechanoreceptor (1697–2). The skin was indented separately at three points (*a*, *b*, *c*), in the receptive field, as shown in the inset at *f*. *a*–*c*, test responses before repetitive indentation at *a* and *c* at 10 sec intervals. Ninety seconds after *a*, the test stimuli were repeated at 1·6 × the original intensity. The responses at the outer points (*d* and *f*) are reduced by about 80 % whereas at *e* the response at the mid-point was reduced by only 20 % (after making allowance for the larger indentation in *d*–*f*).

A further test of the extent of the nerve terminal distribution was the use of two and three point stimulation of the receptive field. As is described more fully on page 559, the mechanical sensitivity of the C-mechanoreceptors is temporarily reduced by repeated mechanical stimulation. Using the experimental arrangement shown in Fig. 3, the spatial extent of this depression of sensitivity was tested. In a two-point test the responsiveness of one point (*a*) in the receptive field was depressed by 85 % using a 1 mm probe and repeating a standard stimulus five times at 5 sec intervals. The sensitivity tested at an adjacent locus (*c*) 1 mm away was almost

unaffected. Reversal of the test procedure, i.e. (*c*) before (*a*), gave a similar result. When the two points, *a* and *c*, 1 mm apart, were depressed by rapid alternate stimulation with 1 mm diameter probes, the intermediate point *b* was depressed by 40 %. The receptive field thus comprised a spread of receptor terminals extending at least 1 mm in the long axis of the limb. In order to test more exactly the terminal distribution the experiment was repeated using a metal probe with a small tip. The outer points (*a*, *c*) were again separated by 1 mm, but the stimulus probe used to condition the outer points this time did not make contact with the middle point. Mechanical stimuli at each of these points, tested separately, excited the receptor (Fig. 3*a–c*). After alternating mechanical stimulation (nine standard stimuli at each point, at 10 sec intervals) had depressed the outer points, *a* and *c*, to about 25 % of the control value, the intermediate point *b* had a less diminished sensitivity – seventeen instead of twenty-two impulses (Fig. 3*d–f*).

Directional sensitivity. The normal test procedure for the C-mechanoreceptors was to start with the stimulus probe at, or just above, the skin surface, and to test the receptor by an inward displacement of the skin. The typical responses in these circumstances are shown in Fig. 1*A,B*. At low intensities of stimulation there is the usual dynamic and static response. At high intensities there may also be an 'off-response' or 'after-discharge'. If, however, the probe indented the skin at rest there could be a response to outward movement of the probe (Fig. 1*C*). The C-mechanoreceptors can therefore be excited by both inward and outward movement of a stimulating probe, or by displacement and restoration of the skin surface.

After-discharge. A characteristic feature of the C-mechanoreceptors is a discharge that can persist following the end of a mechanical stimulus – the *after-discharge* (Zotterman, 1939) which is particularly conspicuous if the skin is stroked, and may be absent when the skin is indented with a probe (Iggo, 1960). In the present experiments using probes, an after-discharge was usually absent with small ($< 250\ \mu$m) skin displacement, but was often present after larger ones (400–500 μm), although it was short-lasting, $< 0{\cdot}5$ sec (Fig. 1*A,B*). Microscopic observation of the skin during the after-discharge, following a stroke of the skin with a smooth glass rod, revealed small restorative movements of the epidermal surface that coincided with the after-discharge. Since the various parts of the receptor terminals respond independently (see 'Receptive fields'), it is possible that the after-discharge was caused by the summation of small excitatory responses during these restorative movements, especially since the C-mechanoreceptors are not directionally sensitive (see 'Directional sensitivity').

It is not necessary to postulate a long-lasting reaction within the terminals of the receptors that continues after the stimulus has been withdrawn to account for the after-discharge. On the hypothesis that it is caused by restorative movements of the epidermis, following removal of the stimulus, it would be expected that there should be a null point in the receptor discharge on withdrawal of the stimulus and before the after-discharge starts. A typical example is illustrated in Fig. 1*B* in which there is a silent period of 190 msec. In Fig. 1*B* the silent period appears to begin about 140 msec after withdrawal of the probe. This apparent delay is due to the conduction time in the afferent fibre – 120 msec in Fig. 1*D*, from the receptor terminal to the recording electrodes. If, on the other hand, the after-discharge was due to a long time constant in the receptor terminals, the expectation would be that the flow of impulses would gradually cease following withdrawal of the stimulus. Such is not the case.

The sensitive C-mechanoreceptors can be excited by small (10–20 μm) movements of both guard and down hairs. With the stimulus probe attached to one guard hair and several down hairs, a small movement (45 μm) was sufficient to cause the discharge of 5 impulses in 1 sec. Hair movements can therefore also contribute to the after-discharge, especially when the skin is stroked. The removal of hairs from the skin surface by depilation reduced, but did not abolish, after-discharge, and slow epidermal movements in depilated skin probably account for the remaining after-discharge.

Response to a standard stimulus. The normal mechanical stimulus used in these experiments was an indentation produced by a smooth-tipped probe, orientated normal to the skin surface, with a maximum indentation of 600 μm. The base-line position of the probe was adjusted, under binocular microscopic control, so that the tip was just in contact with the skin surface. In these conditions there was no resting discharge from the afferent unit. The probe was then advanced at a linear velocity, varying from 3 to 5 μm/sec in different trials, until it reached the pre-set amplitude at which it remained for one second until it was removed abruptly. The C-mechanoreceptors exhibited both a dynamic and a static response (Fig. 1*A*,*B*). The critical slope of the dynamic response was low, as has also been reported by Bessou *et al.* (1971), although unlike the SA II mechanoreceptors, which also have very low critical slopes, there was no resting discharge. One factor responsible for these low critical slopes of the C-mechanoreceptor may be a summation of responses within the receptive field; when two simultaneous weak stimuli were delivered close together to the receptive field of a single C unit the discharge was greater than for either alone. Presumably there is either a summation of generator depolarization or a confluence of abortive spikes at conducted-spike initiation sites in the terminal arborization of the afferent unit (Chambers *et al.* 1972).

The response to an indentation of the skin maintained for 5–10 sec (static response) was a discharge of impulses that continued for several seconds. The lengths of interspike intervals were fairly regular, with a progressive increase in length during a steady maintenance of the stimulus.

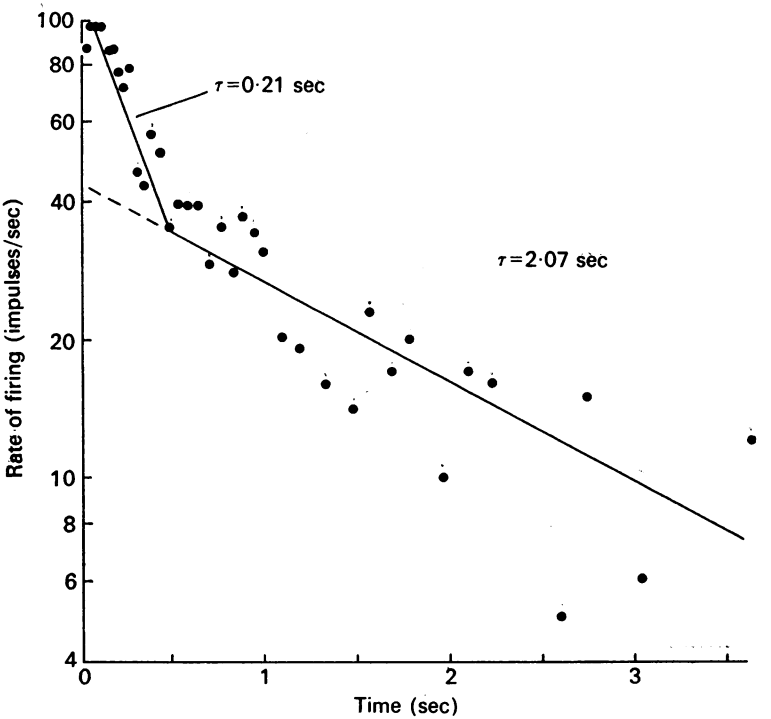

Fig. 4. Adaptation of a C-mechanoreceptor (1197–1) to a skin indentation of 476 μm. The rate of firing fell continuously from a maximum of 100 impulses/sec and when plotted on semilogarithmic co-ordinates, two time constants could be fitted, using the relation $f = f_0 e^{-t/\tau}$, where f_0 is the original firing frequency, f is the firing frequency, t is the time after stimulus onset and τ is the time constant of the exponential decline in firing rate (see Gottschaldt *et al.* 1973).

This aspect of the discharge pattern has been attributed in myelinated slowly-adapting cutaneous mechanoreceptors (SA II) to a single, or dominant, conducted-spike initiation site (Chambers *et al.* 1972) and a similar argument holds for the C-mechanoreceptors, that is, the generator currents at different points in the receptor arborization are integrated or summed at one or a few spike-initiation sites. The adapting discharge of the C-mechanoreceptor has at least two time constants (Fig. 4), an early, rapid one of about 200 msec, and a second, slower one of 1·4–2·1 sec. In

order to obtain these long time constants it was necessary to leave an interval of several minutes between successive stimuli, and even then the discharge did not persist longer than 3 or 4 sec. At short intervals between mechanical stimuli, the discharge was abbreviated.

Stimulus-response relation. This was measured quantitatively in eight C-mechanoreceptors by a series of up to ten given indentations within the range 25–500 μm delivered in random order and repeated up to 100 times. The stimulus duration was fixed in any set of trials and only the amplitude

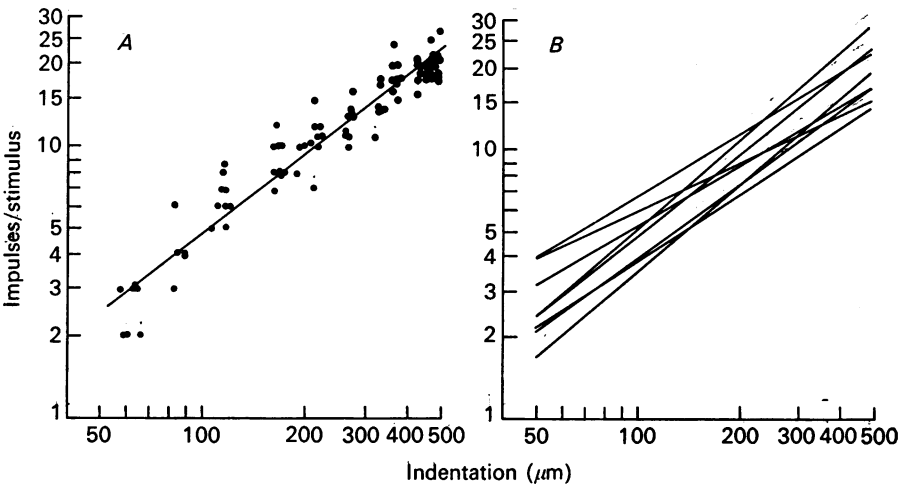

Fig. 5. Stimulus-response relation for C-mechanoreceptors. *A*, the plot on logarithmic co-ordinates of the responses of unit 16117–4 in a random-intensity trial using indentations between 50 and 500 μm. The data fit very closely the power function R (impulses/sec) $= aS^b$, where S is indentation in μm. The regression line was calculated statistically. *B*, the regression lines for this and seven other C-mechanoreceptors. The parameters are given in Table 1.

of indentation was varied. Typical responses are shown in Fig. 1 for single indentations. The results of such a trial are plotted in Fig. 5*A* for one C-mechanoreceptor (16117–4), using logarithmic co-ordinates, and the calculated regression line is drawn. The straight line has a slope of 0·9 and the equation for the power function is $R = kS^{0.99}$, where R is the number of impulses discharged, k is a constant and S is the indentation in μm. The correlation coefficient of 0·95 (Table 1) indicates a very good fit of the data points to the line, which is also borne out by inspection. The points, except at threshold, are closely grouped around the line. The slope of the line on logarithmic co-ordinates is not significantly different from one and the data are, therefore, also linearly related on linear co-ordinates.

Table 1 summarizes the results of a regression analysis for seven C-mechanoreceptors, based on random intensities trials, and one unit for non-random selection of the intensities. In each case there is a high correlation of stimulus and response on logarithmic co-ordinates for the randomized trials ($r + 0{\cdot}84$ to $+0{\cdot}99$). Regression lines were calculated with the results given in Table 1. Statistical analysis established that the regression coefficients, on the null hypothesis, were all highly significant, Standard errors of means ranged from $\pm 0{\cdot}04$ to $\pm 0{\cdot}07$, for regression coefficients of

TABLE 1. Summary of regression analysis results of the stimulus-response studies on eight C-mechanoreceptors; stimulus range 20–500 μm, plotting number of impulses R against displacement S on logarithmic co-ordinates ($\log R = a + b \log S$)

Unit	n	b	± S.E. of mean	r	a	Threshold (μm)
1197–1*	91	0·813	0·054	0·62	−1·037	30
1497–1	35	0·578	0·066	0·84	−0·387	< 70
1497–2	37	0·716	0·051	0·92	−0·710	50
1497–3	46	0·758	0·035	0·96	−0·692	25
1697–2	40	1·073	0·063	0·94	−1·450	30
2197–3*a*	27	0·911	0·073	0·93	−1·223	< 100
2197–3*b*	36	1·287	0·159	0·81	−2·143	—
9117–1	88	1·052	0·064	0·87	−1·557	70
16117–4	92	0·991	0·034	0·95	−1·301	—

n, no. of stimuli.
r, correlation coefficient.
2197–3*a*, mechanical stimulus synchronous with expiration.
3197–3*b*, mechanical stimulus not synchronized with breathing.
* Non-random intensity series, all the remainder were random intensity series.

0·58–1·07. For five of the units the regression coefficients (b) were not significantly different from 1, so that the S–R response was also linear on arithmetic co-ordinates. For the remaining units there was a highly significant difference of the regression coefficient from one. The uniformity of the stimulus response characteristics is brought out in Fig. 5*B* in which the calculated regression lines for the eight C-mechanoreceptors are plotted, again using logarithmic co-ordinates. These results were obtained from six cats and all the afferent fibres were recorded from the saphenous nerves, with receptive fields in hairy skin. When the responses during the first and second 0·5 sec of the stimulus were plotted separately, both on inspection and on statistical evaluation the response during the first half was more variable. Part of this variability was due to mechanical instabilities in the preparation, due to small movements of the skin of the leg caused by respiratory movements, and part to contact of the stimulus probe with hairs.

The increased variability of responses caused by small movements of the skin relative to the probe, due to respiratory excursions of the animal, can be seen from Table 1. Data from unit 2197–3 were used to calculate regression lines in two conditions: (*a*) using data when the mechanical stimulus was synchronized with the phase of respiration and (*b*) using this and additional data without reference to the phases of respiration. The regression coefficients differ and the correlation coefficient is smaller for condition (*b*) than for condition (*a*), and also has a larger standard deviation.

In separate trials the response of C-mechanoreceptors to movement of single guard hairs or a small cluster of down hairs was tested. All the units tested were effectively excited by stimuli delivered to the free shaft of the hairs, taking the same precautions as were used by Brown & Iggo (1967) to limit the effective movement to the hair attached to the probe.

Effect of previous stimulation of the receptors

A depressant effect on previous activity has been reported in all studies on single C-mechanoreceptors (Iggo, 1960; Bessou *et al.* 1971; Hahn, 1971; Zimmermann, 1975), and tests of mechanical sensitivity require intervals ranging from 90 sec to 3 min between stimuli to yield consistent results. The time course of the depression of excitability has been examined in more detail in the present work.

Rapidly repeated mechanical stimulation quickly depresses the responses of the afferent units. Fig. 6*A* shows the effect of indentations of 250 or 500 μm lasting 1 sec and repeated at intervals of 5 sec to 5 min. The stimulus intensities were chosen to be within the linear range of the stimulus-response curves for the two C-mechanoreceptors illustrated. At the highest repetition rates used ($<$ 5 sec intervals) the response declined very rapidly to 10 % within 50 sec. At 20 sec intervals, the initial decline stabilized at about 25 % of the control values after six to nine applications of the stimulus (2–3 min). With progressively longer intervals, stabilization occurred after *ca.* 4 min, and the responses to the standard stimulus then became uniform with small variability. When the interval between adjacent stimuli was 4 min or longer there was no statistically significant interaction between the responses, as judged by the number of impulses discharged.

The recovery of excitability, following a period of intense activity, was measured by applying a single standard test stimulus at various intervals after standard conditioning stimulation (ten repetitions of a 1 sec mechanical pulse at 5 sec intervals) that almost completely abolished any response. The results plotted on semilogarithmic co-ordinates are shown in Fig. 6*B*.

The depression of response following repetitive mechanical stimulation could be due either to a cumulative change in the axon, such as refractoriness or fatigue, or to reduced excitability of the transducer or receptor terminal processes. The two-point receptive field studies indicate that fatigue of the conducting mechanism of the non-myelinated axon is unlikely to be the cause since, after excitability of one part of the receptive field had been depressed by repeated stimulation, an adjacent place in the receptive field of the same afferent unit was still capable of initiating a normal rate of firing in the axon.

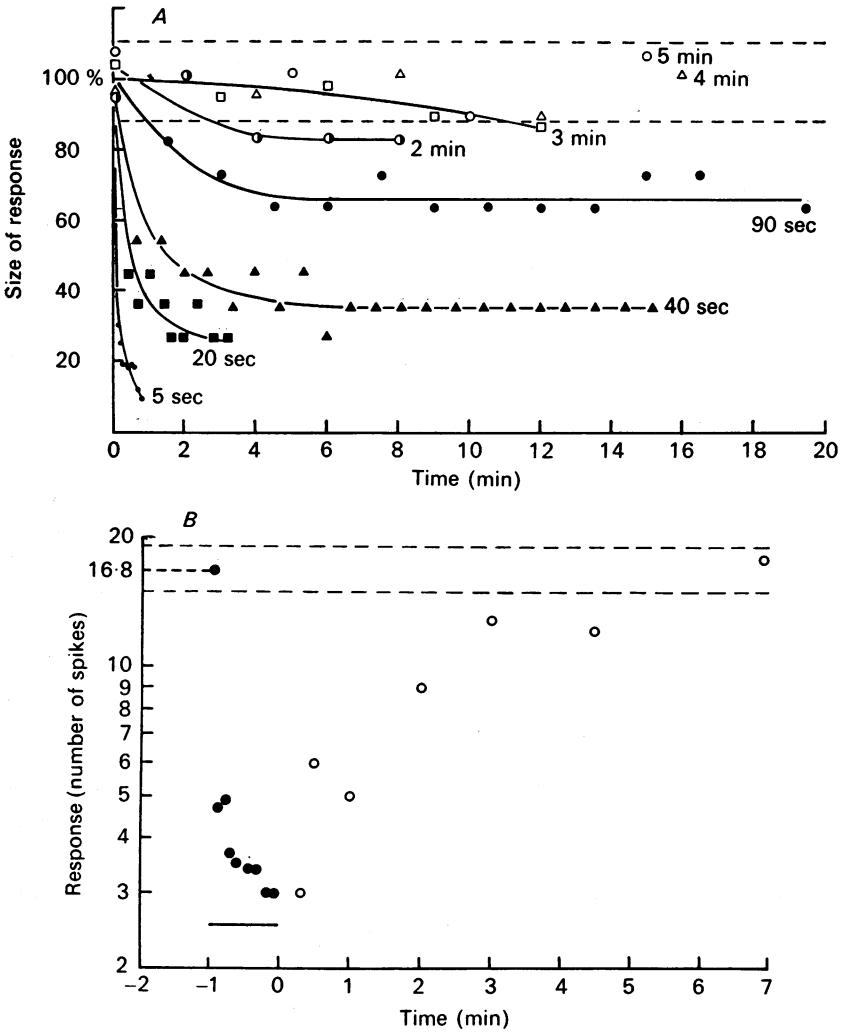

Fig. 6. For legend see facing page.

A further test used was antidromic stimulation of the afferent C-fibre to examine whether a reduced impulse-carrying capacity of the axon underlay the depressed responses. The saphenous nerve was stimulated electrically between the recording electrodes and the receptor terminals in the skin at an intensity supramaximal for the given afferent C-fibre. The number of impulses sent through the nerve ranged from 22 to 100 at 20/sec. This frequency of electrical stimulation was chosen since it was within the range of the normal discharge rate during the mechanical stimulus, and was well below the maximum rate (300/sec) at which mammalian afferent C-fibres can carry a train of impulses (Franz & Iggo, 1968). Antidromic impulses had no significant effect on the response to a standard mechanical stimulus applied 10 sec after the end of the train of antidromic volleys, in contrast to the depression that followed a series of mechanical stimuli given at 10 sec intervals. After three of the separate mechanical stimuli had generated a total of thirty orthodromic impulses, the response to further mechanical stimulation at the same place in the receptive field was less than 20 % of the normal, whereas there was no statistically significant reduction after 100 antidromic impulses.

If, as these results suggest, the depression of sensitivity occurs in the receptor terminals, then a sustained mechanical stimulus lasting several seconds and generating a train of impulses should have an effect similar to that caused by a succession of short (1 sec) mechanical pulses, particularly since the time course of recovery from the depressed excitability has a time constant of several minutes (Fig. 6*B*), thus allowing an accumulation of depression following several pulses. This hypothesis was tested by

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Fig. 6. Depression of C-mechanoreceptors by frequent iteration of skin indentation.

A, in this graph the symbols represent the responses of C-mechanoreceptors (■, ▲, ●, unit 1197–1, 500 μm; the remainder from unit 9117–1, 250 μm) to repetition of a standardized 1 sec indentations repeated at the intervals indicated. At high repetition rates there was a rapid reduction of the response, which then reached a steady value. At intervals longer than 4 min there was no interaction between successive stimuli. The dashed lines show the 95 % confidence limits for responses at intervals of 4 min and longer for unit 9117–1.

B, recovery of excitability (open circles) after a receptor had been depressed by rapid (5 sec intervals) application, during the period indicated by the filled bar, of standard 1 sec long, 250 μm indentations (filled circles). Each point during recovery was the response to a single standard indentation of 250 μm at the given time, after conditioning the receptor by iterative indentation. The control responses recorded at intervals of 9 min had a discharge of $16{\cdot}8 \pm 1{\cdot}03$ impulses and the 95 % confidence limits are indicated by the dashed lines. Unit 9117–1.

applying a mechanical stimulus that was maintained for 5 sec, during which at least thirty-five impulses were discharged. Such a stimulus was depressant, and when the excitability was tested 10 sec later with a standard mechanical stimulus, the discharge was reduced by 50%. The accumulating depression may account for the decline in response during a sustained mechanical stimulus and cause the C-mechanoreceptors to be self-limiting in their afferent discharges, since they fail to generate a sustained flow of impulses to steady mechanical stimulation, in contrast to slowly adapting mechanoreceptors with myelinated axons.

DISCUSSION

These results are in good agreement with previous published work from several laboratories. The receptive fields of the mechanoreceptors are apparently homogenous, from which it may be concluded that the afferent fibres arborize near their endings. The two- and three-point field studies establish that different parts of the terminals act independently of each other in transduction, since it was possible to modify the response to mechanical stimulation at one restricted part of the terminal arborization without altering the discharge in the afferent fibre evoked subsequently from an adjacent part of the receptive field. These effects were highly localized and, using small stimulus probes, could be limited to an area less than 500 μm in diameter. The morphology of the terminal arborization of the C-mechanoreceptors is not known in detail, although Cauna's (1969, 1973) studies of C-fibre terminals in the skin are consistent with the present results which establish that there must be extensive branching with transducer sites spread widely on the terminals. Cauna's electron-microscope studies suggest that the C-fibres end in close apposition to the basement membrane of the epidermis, within 40–60 μm of the skin surface, so that sufficiently small localized skin indentations could probably affect only a few endings to give a response that, by electrotonic spread to more proximal parts of the axon, could sum with other local responses to initiate the discharge of orthodromic impulses. Sublimal excitatory effects at different regions could, therefore, summate to cause an afferent discharge, and this mechanism accounts for the ability of the C-mechanoreceptors to respond to the slow movement of a stimulus probe across the skin surface (Bessou *et al.* 1971).

After-discharge is a characteristic feature of C-mechanoreceptors (Zotterman, 1939; Iggo, 1960), although no clear hypotheses concerning its origin have been made. The present results establish that it probably arises from visco-elastic changes in the skin that continue after removal of the applied mechanical stimulus. The present results are not consistent

with a delayed return of the transducer process itself to the resting condition, due to any intrinsically slow recovery mechanism within the receptor terminals. The results suggest, instead, that there is a re-excitation of the receptors by the restorative movement of the skin. Further support for this proposed mechanism comes from the non-directional sensitivity of the afferent units (Fig. 1); that is, the receptors can be excited both by inward and outward movement of the skin, when tested properly.

The C-mechanoreceptors can, under strictly controlled experimental conditions, accurately transform the amplitude of skin indentation to rates of afferent discharge, as the quantitative stimulus-response results establish, and thus join a growing list of mechanoreceptors which satisfy rigorous quantitative criteria. It may be doubted, however, whether the C-mechanoreceptors could actually be used for this purpose since (*a*) there is a strong temporal dependence of the stimulus-response relations on the previous history of a receptor (Fig. 6) and (*b*), as Hahn (1971) has shown, there may be a large mechanical/thermal interaction in some conditions. The sensitive C-mechanoreceptors in hairy skin of the cat are, nevertheless, a homogeneous group, and the eight units examined quantitatively in the present work had quantitatively similar *S–R* parameters (Fig. 5*B*). They correspond to the 'Group I, highly-sensitive endings' with afferent C-fibres of Iggo (1960). In some respects they resemble slow-adapting A-mechanoreceptors (SA types I and II, Chambers *et al.* 1972) since they continue to respond during sustained mechanical stimulation. However, the discharge seldom persisted for more than a few seconds (up to 5 or 10), as also reported by Bessou *et al.* (1971), in contrast to the minutes or longer for the myelinated mechanoreceptors. This relative brevity of response may depend on the morphological arrangement of the receptors and the linkage of the transducer elements to the tissues in which they lie, but the functional characteristics of the receptors also contribute.

A period of receptor activation leads to an inexcitability of the activated terminals (Figs. 3, 6), which is not due to a change in the conducting part of the axon. This diminished excitability, due possibly to the accumulation of some product or consequence of activity, is sufficient to prevent the continued discharge of impulses in the afferent fibre. One possible cause is a change in ionic composition of the slender nerve terminals which have a relatively small volume/surface ratio. The presumed permeability changes associated with transduction and the flow of generator currents would lead to relatively large alterations of internal ionic concentrations. If, for example, the terminals load up with sodium ions, this may have the effect of activating ionic pumps that clamp the membrane potential, reducing a subsequent response to mechanical stimulation until, after several minutes, the ionic conditions return to the resting state. A mech-

anism of this kind would also tend to limit the capacity of activated terminals to sustain a continued response, as during steadily maintained indentation of the skin. A further functional limitation may be imposed by the unknown characteristics of the spike-initiation sites in the terminal arborization of the C-mechanoreceptors.

The results establish that a dynamic equilibrium, between the transducer action and the restorative processes, can be reached after a short time, so long as the mechanical stimulation is not too severe. The dominant role in this response is played by the nerve terminals, since a large number of antidromic impulses invading the conducting elements of the receptor terminal arborization do not cause any appreciable change in response to a standard mechanical stimulus. This is in striking contrast to the severely depressant effect of mechanical stimulation. All the results, taken together, point to the transducer-bound events as underlying the activity-evoked depression.

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