Receptive Field Properties of Unmyelinated Tactile Afferents in the Human Skin

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[1]*Department of Physiology, Göteborg University, SE-40530 Göteborg; and* [2]*Department of Clinical Neurophysiology, Sahlgrenska University Hospital, SE-41345 Göteborg, Sweden*

Wessberg, Johan, Håkan Olausson, Katarina Wiklund Fernström, and Åke B. Vallbo. Receptive field properties of unmyelinated tactile afferents in the human skin. *J Neurophysiol* 89: 1567–1575, 2003; 10.1152/jn.00256.2002. We recorded, with the microneurography technique, single-unit impulses from nine cutaneous mechanoreceptive afferents with conduction velocities in the C range and receptive fields in the hairy skin of the forearm. The units responded with high impulse rates to light touch and had low monofilament thresholds. The geography of receptive fields was explored with a scanning method: a lightweight probe with a small and rounded tip was made to scan the field area in a series of closely adjacent tracks while single-unit activity was recorded. The fields of the nine units varied considerably in size as well as complexity. The individual field consisted of one to nine small responsive spots distributed over an area of 1–35 mm^2 when explored with a moving indentation of 5 mN. The fields were roughly round or oval in shape with no preferred orientation. The size of the response differed between individual sensitive spots in a field, suggesting a highly nonuniform terminal organization. The properties of the fields seem consistent with a role of tactile C afferents to provide information about pleasant touch and skin-to-skin contacts to central structures controlling emotions and affiliative behavior.

INTRODUCTION

It has been known for several decades that cutaneous innervation in various mammals comprises not only fast-conducting myelinated afferents that respond to light touch but, in addition, a system of unmyelinated afferents with a similar high sensitivity to skin deformation (Bessou and Perl 1969; Burgess and Perl 1973; Bessou et al. 1971; Douglas and Ritchie 1957; Iggo 1960; Iggo and Kornhuber 1977; Kumazawa and Perl 1977a; Lynn and Carpenter 1982; Shea and Perl 1985; Zotterman 1939). However, for a long time it seemed that such a slow system of sensitive mechanoreceptive afferents was lacking altogether in man. Two sets of findings supported this view. First, unmyelinated afferents responding to light touch had not been found in man although several other types of C afferents had been identified using the microneurography technique (Schmidt et al. 1995; Torebjörk 1974; Torebjörk and Hallin 1974). Second, psychophysical studies suggested that the sensation of touch is lacking altogether in patients suffering from large fiber neuropathy as well as in normal subjects when the myelinated afferents are blocked experimentally (Cole et al.

1995; Forget and Lamarre 1987; Hallin and Torebjörk 1976; Mackenzie et al. 1975; Sinclair and Hinshaw 1950; Torebjörk and Hallin 1973).

Sensitive C mechanoreceptors in the human skin were first described in the face area by Nordin (1990), although Johansson et al. (1988) reported in passing one single unit a few years before. As such units had not been found in other skin areas, it was tacitly assumed that the facial skin had a unique innervation pattern differing from the rest of the human body. However, it has now been shown that tactile C afferents are present in the hairy skin of the arm and leg as well (Edin 2001; Vallbo et al. 1993, 1996, 1999), suggesting a more general distribution.

In this light, it seems pertinent to explore, in more detail, the functional properties of the low-threshold C-mechanoreceptive afferents. Their basic response characteristics have been described in previous papers demonstrating that they differ considerably from the myelinated tactile units and from nociceptors (Nordin 1990; Vallbo et al. 1999). The present study is focused on the receptive field characteristics, an aspect schematically described in previous studies in man as well as in other species. It was found that receptive fields of human tactile C afferents vary considerably in extent and complexity being composed of one or several small sensitive spots. Findings of the present study have been reported in abstract form (Wiklund Fernström et al. 1999).

METHODS

Material

Data were collected from nine cutaneous afferents that responded to light touch and conducted impulses in C range, i.e., about 1 m/s. The units were recorded in nine experiments from nine subjects, four females and five males, age 20–31 yr. The subjects were students from the local medical or dentistry faculties. Informed and written consent was obtained from all subjects and the experiments were performed according to the Declaration of Helsinki. The ethical committee of the Faculty of Medicine, Göteborg University, approved the study.

The receptive field area of an individual unit was scanned with a light probe to assess the field geography. Altogether 22 scans of the nine receptive field areas were pursued using three different indentation forces as summarized in Table 1. The units of the present report are a sub-set of the sample presented in a previous paper where

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general response properties of human tactile C afferents were described (Vallbo et al. 1999).

Nerve recording and search procedure

Details regarding the microneurography approach and exploratory tests to assess basic properties of the individual units may be found in a previous paper (Vallbo et al. 1999). Briefly, nerve impulses were recorded from single afferents in the lateral antebrachial cutaneous nerve. The nerve, which is a small branch of the musculo-cutaneous nerve, was explored either 1–3 cm proximal or 1–3 cm distal to the cubital fold. When the tip of the microneurography recording electrode had attained an intrafascicular position, the experimenter searched for single units by lightly stroking his fingertips over the skin on the radial surface of the forearm. When we encountered a well-isolated unit that readily responded to these stimuli, it was further studied.

The nerve signal was recorded using a passive band-pass filter set to 0.2–4.0 kHz. Data were sampled to a PC computer and further analyzed using the ZOOM/SC system developed at the Department of Physiology, Umeå University, Sweden. Sampling rates were 12.8 kHz for the nerve signal, 400 Hz for a strain gauge signal, and 25.6 kHz for timing signals that were used to indicate the onset and stop of probe movement (see following text). Each recorded nerve impulse was inspected off-line on an expanded time scale, and impulse trains were accepted for subsequent analysis only if they could be properly validated as originating from a single afferent.

Exploratory tests

Thresholds to mechanical stimuli were assessed with von Frey monofilament bristles made of nylon wires and calibrated with a high precision electronic balance to give desired forces. The force of the weakest hair in the series that made the unit produce clear responses in repeated tests was taken to the protocol as the threshold of the unit.

Conduction velocity was estimated from the stimulus response latency to mechanical tap stimuli using a hand-held strain gauge device. The device consisted of a handle carrying a metal bar ending with a Perspex probe with a rounded tip. Strain gauges on the two surfaces of the metal bar were connected to a bridge amplifier providing a signal of the indentation force. The device was calibrated prior to the experiment using small weights. Distinct taps were delivered toward a highly sensitive spot within the receptive field and the minimal latency observed was used to estimate conduction velocity of the unit (Vallbo et al. 1999).

Assessment of receptive fields geography

SCANNING PROCEDURE.   A scanning method was used to explore the geography of the individual receptive field. Details have been described in a previous paper (Vallbo et al. 1995). In short, a small and light probe was moved by an *x-y* plotter over the skin surface in a series of closely adjacent tracks covering the receptive field of the unit. The tip of the probe was a hemisphere with a diameter of 1 mm. The probe was fixed to a light aluminum tube held vertically by low-friction plastic bushings allowing the tube to slide freely up and down so that the probe would neatly follow any curvature of the skin surface. The tube was loaded with weights to provide vertical indentation forces of 2.2, 5, or 20 mN as assessed with a high-precision electronic balance. On the other hand, the actual indentation force was not recorded during the experiment. Hence, a certain variation around the nominal indentation force cannot be excluded.

Probe speed over the skin surface was 2 mm/s. The individual scan regularly started in the distal-lateral corner of the rectangular skin area to be explored. The probe was first moved the full distance of the track in the proximal direction and then back along the same track in the distal direction before it shifted 0.23 mm to the next track. With one unit (Table 1, unit 5) the inter-track distance was 0.36 mm instead of 0.23 mm.

Because a step motor is driving the probe in the modified *x-y* plotter, there is a possibility that vibrations of the moving probe can activate a mechanosensitive afferent. We previously investigated this possibility experimentally with myelinated tactile afferents by attaching a sensitive accelerometer to the probe. It was found that such vibrations were well dampened and very weak, and no coupling between probe acceleration and unit activity could be detected (Olausson et al. 2000). In the present study, the lower probe movement speeds required a lower step motor frequency of 60 Hz. However, no signs of activation of C units at fixed inter-spike intervals indicative of driving of a unit by vibration at this rate, or a subharmonic thereof, were ever observed.

CONSTRUCTION OF RECEPTIVE FIELD MAPS AND DENSITY PLOTS. The data obtained in the scanning procedure allowed the calculation of instantaneous position of the probe at the very moment when the individual spike appeared. On the basis of these data spatial event plots were constructed (Figs. 3 and 4). Color coded two- and three-dimensional density plots of receptive fields were derived from the spatial event plots with the approach described by Vallbo et al. (1995). In short, spike density in the spatial event plot was computed by overlaying a grid with nodes separated by 0.5 mm. The spike density at each node was computed as a weighted sum of all spikes within 1 mm of each node. The weighting function was $\cos^2(\text{distance}*\pi/2)$.

TABLE 1.   *Field properties of individual units and database*

Unit Code	No. of Sensitive Spots	Size of Receptive Field, mm²		Indentation Threshold, mN	Number of Scans		
		2.2 mN	5 mN		2.2 mN	5 mN	20 mN
1	1	0.3	1.0	1.3	2	1	
2	2	0.9	1.5	0.6	1	1	
3	3	6.9	11.3	0.3	2	3	2
4	3	—	9.1	2.5		2	
5	4	8.9	18.7	2.5	1	1	
6	4	—	16.9	—		1	
7	4	19.4	19.9	0.6	1	1	
8	4	—	19.1	—		1	
9	9	—	35.0	2.5		2	
Mean	3.8 ± 2.2	7.3 ± 7.7	14.7 ± 10.5	1.5 ± 1.0			

Entries give the number of sensitive spots of the individual field, field size as assessed with 2 different indentation forces, and von Frey thresholds as well as the number of scans pursued with the individual afferent using 3 different indentation force levels. von Frey thresholds were taken at the most sensitive spots in the receptive fields. The entries on field properties are based on selected sets of data from each unit rather than on averages. They are derived from the one unidirectional spatial event plot that carried the largest number of impulses from the unit. Unit code numbers refer to fields presented in Fig. 5 in order from *top left* to *bottom right*.

The data on field properties collected with a given indentation force, as presented in text, table, and figures, are based on one unidirectional event plot, i.e., the one that carried the largest number of impulses from the unit. Similarly, the density plots are based on the data from probe movements in one direction only.

In one unit (8 in Table 1), a few stray impulses appeared at low discharge rate, scattered over most of the scanned area (15×15 mm). These impulses were removed from the spatial event and density plots for this unit, based on the fact that the stray impulses were located in completely different locations in the spatial event plots for the two different probe movement directions, whereas the shape and location of the main clusters were consistent. It seems plausible that these discharges are due to a simultaneously recorded thermoreceptor or sympathetic efferent, the activity of which was not affected by the moving probe.

ASSESSMENT OF FIELD SIZE. To assess the size of the receptive fields, the extent of the field was defined as the area enclosed by the convex hull, i.e., by a series of straight lines of minimal total length that encircled all the spike symbols of the spatial event plot. An example is shown in Fig. 3B. All calculations were made using software written in Matlab (Mathworks, Natick, MA).

RESULTS

Identification of C afferents

Figure 1 demonstrates two key features for discrimination between unmyelinated and myelinated mechanoreceptive afferents. Figure 1A indicates schematically the target point for a skin indentation as well as the site of microneurography recording electrodes a few centimeters above to the cubital fold. Figure 1B shows the neural response to a distinct tap at the target point delivered manually with a blunt probe; *bottom*
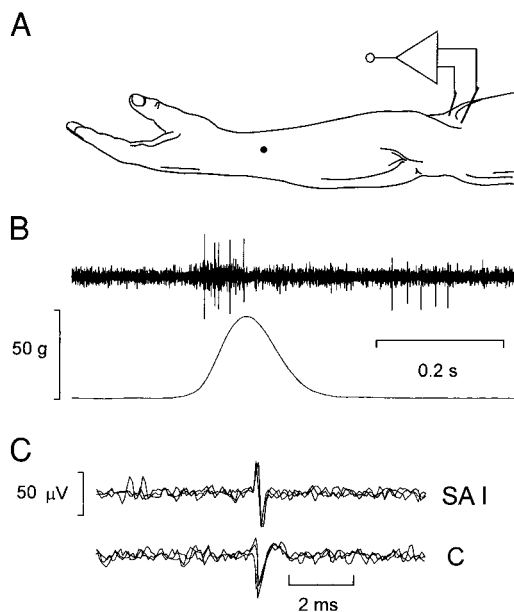

FIG. 1. Estimation of conduction velocity. *A*: microneurography recording site in upper arm and target point in the forearm for a mechanical tap stimulus illustrated in *B*. *B, top*: responses of 2 separate afferents to an innocuous tap stimulus. The units had overlapping receptive fields at the target point. *Bottom*: the time course of the skin indentation force. *C*: nerve impulses from the record in *A* displayed on expanded time scale to highlight difference in shape. The fast afferent was a Merkel unit (SA I), whereas the slow one was a low-threshold or tactile C mechanoreceptive afferent with a von Frey threshold of 1.3 mN. Unit code number 1 (Table 1). Distance between target point and recording electrode was 247 mm.

shows the time course of indentation force, whereas *top* demonstrates that the tap stimulus elicited two trains of impulses. Initially, a series of five biphasic impulses appeared during the raising phase of the indentation. About 250 ms later, well after the stimulus was over, another series of five impulses appeared that clearly differed in shape compared with the first five impulses. In Fig. 1C, the difference in spike shape is highlighted on an expanded time scale showing that the early impulses were biphasic, whereas the late impulses were triphasic with a dominant negative phase. On the basis of the difference in spike shape as well as stimulus response latency, it was concluded that two separate mechanoreceptive units were excited. Estimates of conduction velocity from stimulus response latencies indicated that the biphasic impulses propagated at a speed of at least 30 m/s, whereas the negative spikes propagated at a speed of about 0.8 m/s. Thus one of the afferents was myelinated, whereas the other was unmyelinated. Other observations, not to be reported, indicated that the fast conducting afferent was a Merkel (SA I) unit whose receptive field was partly overlapping with that of a C-mechanoreceptive afferent.

It deserves attention that the mechanical tap stimulus was not adequate to assess very accurately the conduction velocity, particularly not for the fast-conducting afferent. First, it is not possible to define the exact time of stimulus onset. Second, the target point on the skin was not optimal for this unit, implying that the sense organ was probably not excited until indentation force had reached a relatively high level. With the slow unit, on the other hand, the error in conduction velocity due to the indistinct takeoff of the stimulus record would be much smaller considering the relative long latency.

The impulse shapes as shown in Fig. 1C are characteristic of myelinated and unmyelinated nerve fibers as seen in other microneurography recordings, i.e., unmyelinated fibers regularly provide triphasic impulses with the most prominent phase in the negative direction. Myelinated afferents, on the other hand, usually provide biphasic impulses with the initial—and often the more prominent—phase in the positive direction. Recordings from myelinated afferents only rarely give triphasic impulses (Inglis et al. 1996; Vallbo 1976). The impulse rates of the two afferents were in the same order of magnitude, about 50 imp/s, indicating that both were very responsive to innocuous skin deformation.

Unit sample and data base

We explored nine mechanosensitive C afferents with receptive fields in the hairy skin of the forearm (Table 1). Their conduction velocities were estimated to 0.8–1.2 m/s ($n = 9$) on the basis of response latencies to distinct tap stimuli. The distance between receptive field and recording electrode ranged from 11 to 31 cm. The median duration of recording was 61 min (range, 14–96 min).

The afferents were classified as tactile mechanoreceptors because of their high sensitivity to innocuous skin deformation. Thus they responded strongly to light strokings with a finger tip over the skin, impulse trains reaching peak rates of 45–84 imp/s ($n = 9$). Moreover, their thresholds to stimuli with monofilament bristles were low (0.3–2.5 mN, $n = 7$, Table 1).

Exploration of receptive fields

As described in METHODS, receptive fields were explored with a scanning technique using a small probe that lightly indented the skin while it was slowly moved in a series of closely adjacent tracks over the skin surface. Altogether 22 scans were performed using three different indentation forces (Table 1). Figure 2 illustrates raw data from a small segment of a scanning session with a single mechanoreceptive C afferent. Figure 2A shows nerve impulse responses from two adjacent tracks. As described in METHODS, the probe regularly traversed the individual track twice, first in the direction from distal to proximal along the forearm, then in the opposite direction. Figure 2B shows a sequential record of the same four scanning movements as displayed in A, on a more compressed time scale, with instantaneous impulse rates at the top and time marker signals of probe movements below.

Basic structure of receptive fields

On the basis of the kind of data displayed in Fig. 2, *spatial event plots* were constructed representing maps of the receptive fields. Examples are shown in Fig. 3. The positions of the arrowheads represent the instantaneous positions of the probe at the very moments when nerve impulses reached the recording electrode. Because the exploring probe traversed the individual track on the skin surface twice, two sets of data were
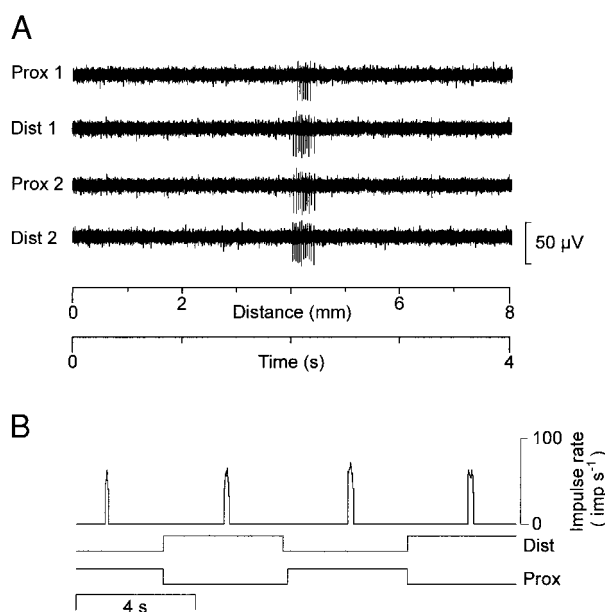

FIG. 3. Receptive field maps of 2 tactile C afferents. *A* and *B*: spatial event plots of 2 different units. *A, top,* show total response to the scanning movements, i.e., all impulses associated with probe movements in proximal as well as distal direction along the arm. Other panels refer to response to probe movement in 1 direction alone. Individual events, i.e., nerve impulses, are indicated by arrowheads pointing in the direction of probe movement, blue for movements in the proximal direction and red for movements in the distal direction. The lower left corner of the individual box corresponds to the distal-lateral corner of the skin area explored, i.e., the starting point of probe movement, while the *x* axis represents the proximo-distal dimension. *B, bottom*: broken lines illustrate the approach to assess receptive field size. Total number of impulses in the 4 unidirectional plots is, in order from *A* middle to *B* bottom, 91, 101, 295, 406. Indentation force in scanning procedure 5 mN. Unit code numbers, *A,* unit 3, and *B,* unit 9 (Table 1).

FIG. 2. Extract of raw data for receptive field analysis. *A* shows responses of a tactile C afferent to probe movements along 2 adjacent tracks, 0.23 mm apart and 8 mm in length. Prox 1 and Dist 1, records associated with proximal and distal movements along the same track; Prox 2 and Dist 2, responses from the other track. The individual record corresponds to the full probe movement and the responsive spot was located right in the middle. Note that the starting points for Prox and Dist movements, i.e., 0 on the distance scale, are located at different ends of the track. *B*: a sequential record on a compressed time scale of the events in *A* displaying instantaneous impulse rates along with marker signals indicating phases of movement. High level of the records labeled Prox or Dist indicates that the probe was moving in the proximal and distal directions, respectively. In the short interval when both marker records are low, the probe was shifted sideways 0.23 mm from track 1 to track 2. Indentation force 2.2 mN. First and last movement phase are slightly truncated in *B*. Unit code number 1 (Table 1).
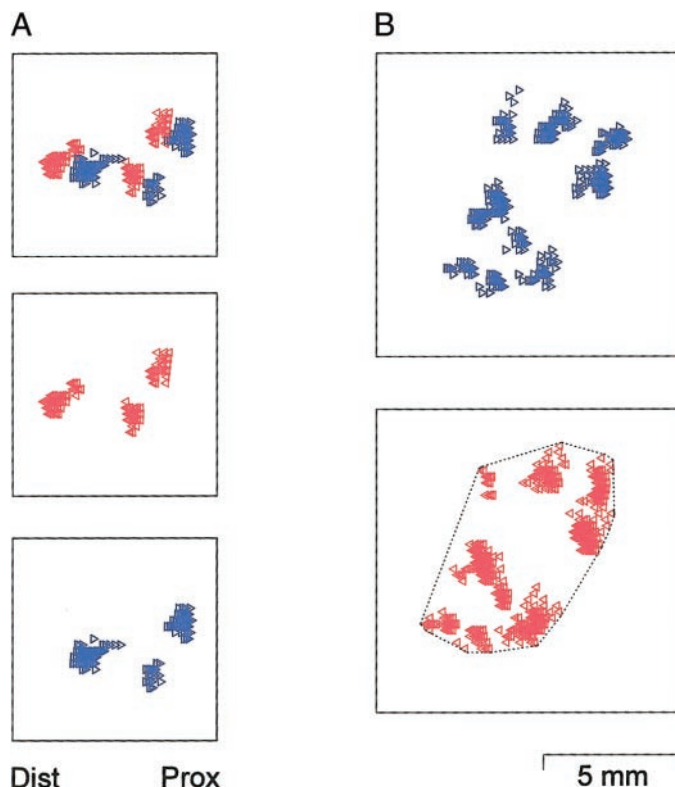
collected. One derived from probe movements in the proximal direction along the subject's forearm and the other from movements in the distal direction (cf. Fig. 2). Fig. 3A, *top,* shows data for both movement directions as described in legend. *Middle* and *bottom* show the same data as two separate twin plots, each one based on data from one direction of probe movement. Figure 3B shows similar twin plots for another unit. It may be appreciated that most impulses appeared in clusters separated by silent areas, indicating that the receptive fields are composed of a limited number of small spots of high sensitivity. The geography of the nine fields will be described in more detail in the following text.

Directional dependence of field geography

Figure 3 illustrates the general finding that twin maps derived from proximal and distal probe movements of a scanning are similar, albeit not identical. Nonetheless, Fig. 3A reveals that there was a systematic shift in the locations of the two sets of symbols. Symbols derived from proximal movements are located more proximally along the subject's arm than symbols from distal movements. Such a systematic shift was regularly

seen although the size of the shift varied between units. It seems most likely that the shift is accounted for by the slow impulse conduction in the afferent nerve fibers. Because the arrival of impulses at the recording electrode is delayed (cf. Fig. 1), the stimulating probe had progressed a short distance when the nerve impulse was recorded. In the total sample, the predicted amount of spatial shift based on the response latency to tap stimuli of the individual units (0.11–0.35 s, Fig. 1) would be 0.4–1.4 mm. This range matched the range actually observed in the spatial event plots. For example, with the unit of Fig. 3A, the shift between the two spatial event plots was about 1 mm, whereas the latency to tap stimuli (0.2 s) would predict a shift of 0.8 mm. The observation of a systematic shift in the maps corroborates the notion that our afferents conducted impulses in the C range. In previous studies, when fast-conducting myelinated afferents were explored with the same stimulation technique, shifts of similar magnitude were never observed (Olausson et al. 2000; Vallbo et al. 1995).

In a few cases, the *size* of response was larger with probe movement in one direction, and the number of impulses as well as the peak impulse rate differed. An example is shown in Fig. 3B where it may be appreciated that more impulses were evoked at several sensitive spots by probe movements in the distal direction (*bottom*) compared with movements in the proximal direction, as detailed in the legend. Such directional differences were not consistently observed but appeared to depend on the indentation force. It was seen in both of the two scans pursued with the highest indentation force (20 mN), but in only 2 of 20 scans with the lower forces (2.2 and 5 mN).

Consistency of field geography

To explore the consistency of unit response, the receptive fields of four units were scanned twice or three times using an identical force (Table 1). Up to as many as seven scans were pursued with one unit. Figure 4 shows representative examples of repeated scans with two different units. It may be seen that the basic structures of the maps were uniform although some minor differences appeared. In general, differences were not

FIG. 4. Consistency of unit response. *A* and *B*: spatial event plots with 2 different units. *Top* and *bottom*: derived from 2 separate scans. *A*: unit 1, indentation force: 2.2 mN. *B*: unit 4, indentation force: 5 mN.

larger than those between two unidirectional maps derived from a single scan (cf. Figs. 3 and 4). A substantial difference was only found between the two scans with high indentation force (20 mN, unit 3).

To summarize, the scanning method yielded consistent data because maps derived from interlaced probe movements in the two directions were very similar (twin field maps, 9 units) as were maps based on repeated scans (4 units). However, the *size* of response was found to differ in some pairs using identical stimulus settings. A source of variation might be the indentation force, which we did not monitor. A variation in true indentation force could be due to friction between the bushings and the tube that carried the stimulating probe (cf. Edin et al. 1995). This interpretation seems to be consistent with our finding that differences in response size with identical indentation force were mainly seen with larger loads providing 20-mN indentation force or more (unpublished observations). The lateral pressure on the probe shaft would increase with indentation force due to larger dimpling of the skin and higher resistance to lateral movement. However, it seemed justified to conclude that the present approach yielded consistent data to describe the receptive field geography, when our standard indentation loads were employed (2.2 and 5 mN).

Properties of fields

The characteristics of the nine fields as explored with an indentation force of 5 mN are presented as color-coded density plots in Fig. 5 and in Table 1. It deserves attention that the procedure to produce the color coded plots involves a certain smoothing of contrasts as well as suppression of low impulse rates as may be appreciated by comparing Fig. 5 with Figs. 3 (unit 3 and 9) and 4 (unit 1 and 4). On the other hand, the color coded density plots highlights the variation in response intensity within the field. It is obvious that the fields varied considerably in shape, size, and complexity between units. The smallest field, illustrated in Fig. 4 *A,* consisted of one single sensitive spot covering a skin area of 1 mm^2. On the other hand, the largest and most complex field of the sample, consisted of at least nine spots, scattered over an area of 35 mm^2. Means and SD for field size were 14.7 and 10.5 mm^2 using 5 mN indentation force (Table 1).

The highly sensitive spots of the individual field were irregularly distributed over an area that was roughly oval. As may be seen in Fig. 5, there was no preferred orientation of the fields. Although the sensitive spots were usually well separated by silent areas, this was not always the case. Therefore it was not always obvious how to define a single spot and, in a few cases, the number of spots attributed to an individual field might be slightly arbitrary. Anyway, the data of Table 1 yielded a highly significant correlation between number of spots and field size ($r = 0.96$, indentation force 5 mN). A regression analysis indicated that field size increased by 4–5 mm^2 per sensitive spot.

It is obvious from Figs. 3 to 5 that the sensitive spots of an individual field may vary considerably with regard to size as well as peak impulse rate. Analyses of correlations between field size, on the one hand, and monofilament threshold and relative distance from elbow, on the other, failed to disclose dependence between field size and sensitivity as well as between field size and location.
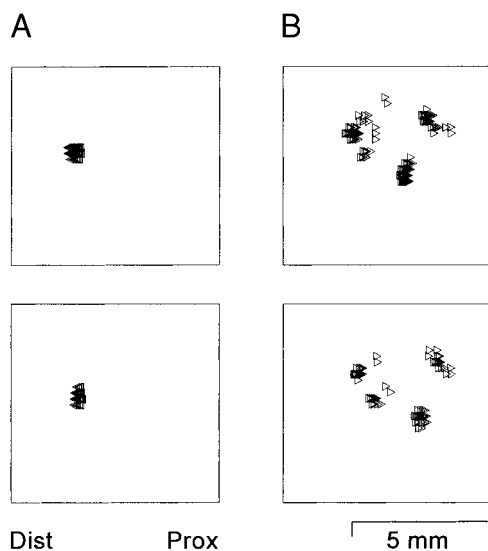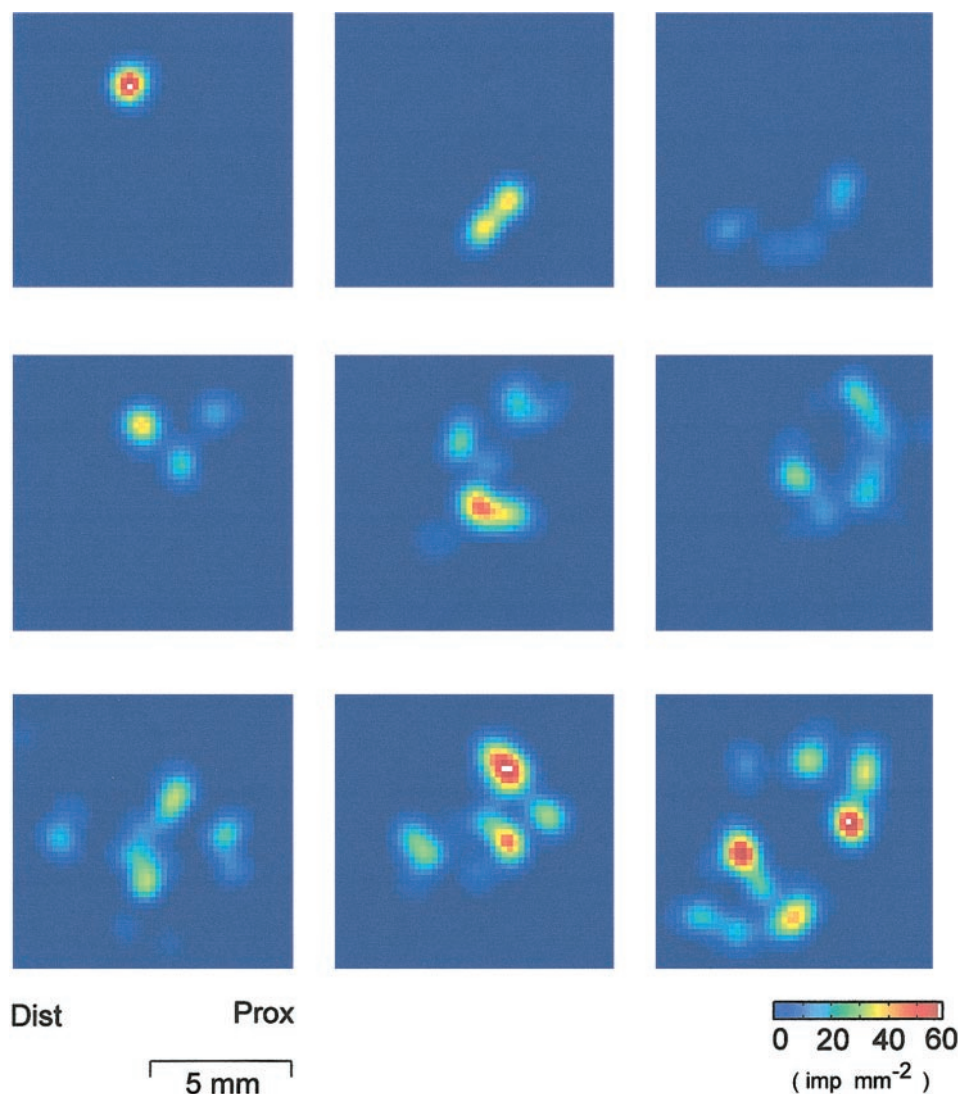
FIG. 5. Field geography of 9 tactile C afferents. Color coded 2-dimensional density plots of receptive fields of the 9 units studied. Same order as in Table 1 from *top left* to *bottom right*. Plots are oriented as in Figs. 3 and 4. Indentation force of 5 mN.

Dependence of field geography on indentation force

From myelinated afferents it is well known that the amount of response as well as the size of a mechanoreceptive field may be highly dependent on stimulus properties, particularly indentation force (Johansson 1978; Olausson et al. 2000). To study this aspect, five units were explored with two or three different forces (Table 1). Figure 6 shows three-dimensional plots of one unit scanned with three different forces. It is obvious that the basic field structure, consisting of three high-sensitive spots, was well preserved over this range of indentation forces, although the relative peak activity at the individual spots appeared to be slightly different with different forces. It was a general finding that the number of spots and their relative locations were identical with different indentation forces. In Table 1, it may also be seen that the field size increased substantially when indentation force was raised from 2.2 to 5 mN. In three of the units, field size increased by almost 100%.

When the smallest field was explored with low stimulus intensity (2.2 mN), impulses appeared over a distance of only 0.5 mm or less along three or four tracks, 0.23 mm apart (Fig. 4*A*). Measurements of the field size of this unit from four separate unidirectional maps yielded values from 0.16 to 0.30 mm², using 2.2 mN indentation force.

DISCUSSION

The present study substantiates the conclusion advanced in previous reports (Vallbo et al. 1993, 1999) that the hairy skin of the human forearm is supplied with very sensitive mechanoreceptors connected to unmyelinated afferents, suggesting that a slow tactile system has a general distribution rather than being limited to the facial skin (Nordin 1990). This is further supported by a recent study that suggests that similar types of units are present in the thigh (Edin 2001). The afferents' high sensitivity to skin deformation is evident not only from their low thresholds but even more from the high impulse rates in response to indentation forces as low as 2.2–5 mN, corresponding to 0.22–0.5 g weight, as used in the present study to explore their receptive field.

Scanning method to define field geography

Low-threshold mechanoreceptive C afferents in the skin were originally identified by Douglas and Ritchie (1957) in the
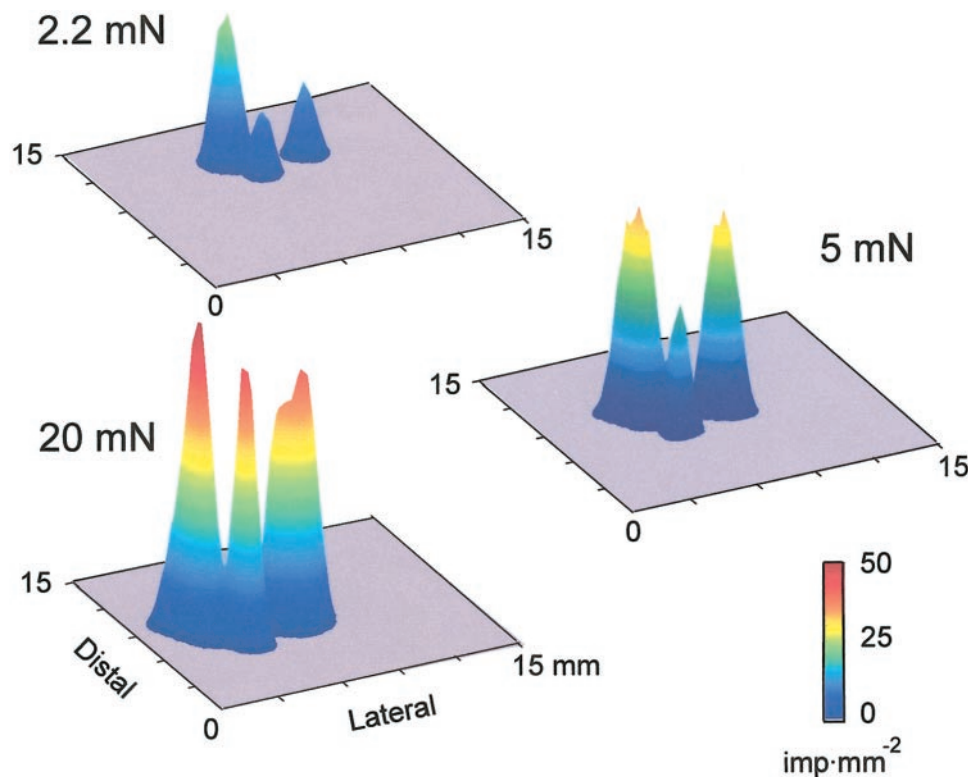
FIG. 6. Field dependence on indentation force. Color coded 3-dimensional density plots of a single receptive field explored with 3 different indentation forces. The rhomboids represent skin areas of 15 × 15 mm. Peak impulse rate in *bottom left* is 41 imp/s. Unit 3.

cat, and the functional properties of the units have since been described in various mammals. Available data indicate that the C-mechanoreceptive afferents in man have similar properties as in other species. However, the receptive fields have not been described in detail. In most studies, it is stated that the sensitivity is uniform (Bessou et al. 1971; Iggo 1960; Iggo and Kornhuber 1977; Shea and Perl 1985), whereas, in two papers alone, it is reported in passing that some spatial variation of sensitivity was observed within the individual field (Kumazawa and Perl 1977a; Nordin 1990). In the present study, it was demonstrated that the fields of the human tactile C afferents are composed of one or several very small spots with high sensitivity separated by less-sensitive regions. The method of stimulation was essential to disclose the detailed structure of the fields. The scanning approach yields solid documentation of instantaneous target point and unit response as a basis for the construction of field maps. Moreover, the method provides high spatial resolution. Similar data are difficult to collect using hand-held instruments as in previous studies.

While the present study is the first to systematically explore unmyelinated afferents in man with a scanning method, this approach has been used in several studies of myelinated mechanoreceptive afferents (e.g., Johnson and Lamb 1981; Looft 1986; Olausson et al. 2000; Vallbo et al. 1995). The particular design employed in the present investigation is a slight modification of the method previously used to explore myelinated afferents from the same skin area (Olausson et al. 2000; Vallbo et al. 1995). The difference is that the speed of the scanning probe was reduced to meet a unique property of the tactile C afferents, i.e., their limited dynamic range that results in the saturation of unit response already at moderate speed of mov-

ing stimuli (Bessou et al. 1971; Shea and Perl 1985; Vallbo et al. 1999).

Human tactile C afferents can exhibit pronounced fatigue after activation, that is, the firing rates with repeated activation is lower than the first (Vallbo et al. 1999). While fatigue was previously elicited by relatively strong activation over a larger area, it is conceivable that the repeated activation of a C afferent by a probe moving along a single track could induce a certain degree of fatigue. From the present data, it is difficult to directly assess the resulting degree of suppression of firing as well as the relative effects of fatigue on the most sensitive spots and on neighboring areas in the receptive field. If the effect of fatigue is a general lowering of the firing rates, the end result would be a spatial sharpening, so that the most sensitive spots stand out slightly more than would have been the case if fatigue was not present.

Structure and size of receptive fields

Our analysis indicated that the stem fiber of the tactile C afferent commonly branches to terminate with a number of sensitive nerve endings distributed within a relatively small area rather than providing a continuous mesh of responsive terminals as suggested by most previous studies (see preceding text). A relatively large variation was found within a single field between individual spots with regard to size as well as amount of response in terms of impulse rate. This finding suggests that the terminal organization consists of a limited number (1–9) of mechanosensitive endings, or densely packed clusters of endings, that may vary widely in size and sensitivity.

The size of the field varied considerably between units, ranging from 1 to 35 mm^2 (Table 1). A number of studies in

other species have reported figures within this range (Bessou et al. 1971; Iggo 1960; Iggo and Kornhuber 1977; Kumazawa and Perl 1977a; Shea and Perl 1985), whereas Nordin (1990) found substantially larger fields in the human face (mean 85 mm^2). However, it should be stressed that detailed comparisons between field size data collected with different techniques of stimulation might be misleading because field size may be highly dependent on stimulus parameters. Particularly, indentation force is an important variable as previously shown for myelinated afferents (Johansson 1978; Olausson et al. 2000) and confirmed for tactile C afferents in the present study. As Nordin (1990) used about 10 times stronger stimuli than we to assess field size, this may partly account for the difference in field size between his sample from the face area and our sample from the forearm.

One type of mechanoreceptive C-afferent, classified as nociceptors (CM units), was identified long ago in the human skin (Torebjörk 1974). The most obvious difference between the nociceptive and tactile units is obviously the sensitivity. Available data suggest little overlap between the two groups in this respect (Vallbo et al. 1999). In a sample of CM units ($n = 77$) from the foot and the leg, Schmidt et al. (1997) found only a few units (3%) with thresholds close to the highest in our sample. In addition to the difference in sensitivity, the present study might have identified another difference, i.e., that the tactile units have smaller receptive fields. Schmidt et al. (1997) reported fields that are an order of magnitude larger (10–363 mm^2) than those of the present sample (0.3–35 mm^2). On the other hand, it cannot be excluded that fields of both types differ in size between arm and leg because the field sizes of tactile C afferents in the leg have not been measured (Edin 2001).

The fact that the most sensitive spot of a tactile afferent may be very small might have a general bearing on threshold assessment and classification of mechanoreceptive C afferents as either tactile or nociceptive. If an experimenter assumes a uniform sensitivity but neglects the delicate punctate structure of the field, there is a risk that the most sensitive spot might be missed in threshold assessment using von Frey bristles. As a result, a too high threshold value would be taken to the protocol, and the unit might be classified as a nociceptor rather than a tactile unit. It deserves attention that an individual sensitive spot, and even an individual field of a tactile C afferent may be very small when explored with low forces. In our sample, we found a field that did not exceed 0.3 mm^2 when scanned with a low force (2.2 mN).

Functional role of tactile C afferents

In contrast to the fast conducting tactile afferents in the human skin, the functional role of the low-threshold mechanoreceptors with unmyelinated afferents has received much less attention. On the basis of their response properties, as described in previous reports (Nordin 1990; Vallbo et al. 1993, 1999), they have been denoted tactile afferents although little is known about their central connections or their effects within spinal cord and brain (Kumazawa and Perl 1977b). However, a recent psychophysical study of a human subject with large sensory fiber neuropathy suggests that such afferents may account for detection of light touch (Morin et al. 2000). This finding lends additional justification for the term *tactile* C afferents.

The present study demonstrates that a proportion of these afferents have small, punctate, receptive fields. This finding might, at first sight, suggest that this system has a role in spatial discrimination of mechanical stimuli, complementary to the myelinated afferents. However, it seems unlikely that this is their primary function. Virtually all mechanical stimuli applied to the skin will activate one or more of the different types of low-threshold receptors with myelinated afferents, and due to the low conduction velocity of C-afferents, time in the order of 1–2 s might be necessary to integrate the two sources of spatial information within the CNS. The problem is further compounded by the unique receptor response properties observed in C afferents, for example, the pronounced receptor fatigue and delayed acceleration of the response with prolonged stimulation in some units (Vallbo et al. 1999). Moreover, the receptive fields were highly nonuniform; this appears to make them less suitable for fine spatial resolution.

The alternative interpretation is that tactile C afferents have a unique and different primary function compared with the myelinated afferents. We have previously reported that while the tactile C units are sensitive to dynamic events, they normally only respond within a narrow low-frequency range of skin deformation and that they are also prominently activated by slow movements over the skin. It seemed reasonable to hypothesize that an essential role of the tactile C afferents is to convey information to limbic structures of light skin deformation that might promote a pleasant feeling of touch as a counterpart to the unpleasant feelings associated with painful stimuli (Vallbo et al. 1993, 1999).

This speculated function would fit with a global hypothesis advanced by Craig (1996) on the role of the small-diameter primary afferents, which innervate all parts of the body. He proposed that the small-diameter afferents, which include noci- and thermoreceptive afferents from skin as well as afferents from deep structures and viscera, have the unique role to monitor "the physiological status or well-being of the tissues and organs of the body."

The importance of emotional aspects of skin contact is highlighted by the Harlow's classical work in which it was found that baby monkeys could show affection for a surrogate mother if it provided tactile comfort (Harlow 1958).

Further support for the interpretation that the afferents may subserve limbic and emotional functions is provided by a recent fMRI study of the above-mentioned patient with large sensory fiber neuropathy (Morin et al. 2000). It was found that a light touch stimulus, which was slowly moving over the hairy skin of the forearm, produced a strong activation of the insular cortex. It seems likely that the activation of the insula region was a result of tactile C-afferent input as the patient was lacking myelinated afferents from the stimulated area. This is in agreement with previous reports of the existence of cells that respond to innocuous, slowly moving brush stimuli in the superficial dorsal horn in rats (Light and Willcockson 1999), and that lamina I spinothalamo-cortical projections terminate in the insular cortex in primates (Craig et al. 2000). The same cortical region has also been found to be activated in humans during pain (Brooks et al. 2002), temperature (Craig et al. 2000), and itch (Drzezga et al. 2001) sensations. Finally, it has been demonstrated in another fMRI study that pleasant touch gives rise to a different activation pattern in the human brain than neutral touch, notably activation of an area in the orbito-

frontal cortex close to areas responding to pleasant taste and smell (Francis et al. 1999). It appears likely that units with low conduction velocity and small, nonuniform receptive fields, as reported in the present study, would be suited to code the essential features of stimuli produced by affiliative or friendly skin-to-skin contact.

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