Quantitative Analyses of Dynamic Strain Sensitivity in Human Skin Mechanoreceptors

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Edin, Benoni B. Quantitative analyses of dynamic strain sensitivity in human skin mechanoreceptors. J Neurophysiol 92: 3233–3243, 2004; doi:10.1152/jn.00628.2004. Microneurographical recordings from 24 slowly adapting (SA) and 16 fast adapting (FA) cutaneous mechanoreceptor afferents were obtained in the human radial nerve. Most of the afferents innervated the hairy skin on the back of the hand. The afferents’ receptive fields were subjected to controlled strains in a ramp-and-hold fashion with strain velocities from 1 to 64% s⁻¹, i.e., strain velocities within most of the physiological range. For all unit types, the mean variation in response onset approached 1 ms for strain velocities >8% s⁻¹. Except at the highest strain velocities, the first spike in a typical SAIII unit was evoked at strains <0.5% and a typical SAII unit began to discharge at <1% skin strain. Skin strain velocity had a profound effect on the discharge rates of all classes of afferents. The “typical” peak discharge rate at the highest strain velocity studied was 50–95 imp/s depending on unit type. Excellent fits were obtained for both SA and FA units when their responses to ramp stretches were modeled by simple power functions (r² > 0.9 for 95% of the units). SAIII units grouped with SAII with respect to onset latency and onset variation but with SA1 units with respect to dynamic strain sensitivity. Because both SA and FA skin afferents respond strongly, quickly, and accurately to skin strain changes, they all seem to be able to provide useful information about movement-related skin strain changes and therefore contribute to proprioception and kinesthesia.

INTRODUCTION

It has become increasingly apparent that mechanoreceptors in the hairy skin may play an important role in proprioception and motor control. Movements at nearby joints activate a majority of the fast-conducting afferents originating from skin mechanoreceptors on the back of the human hand (Edin and Abbs 1991). Moreover, the ways these afferents respond suggest that they provide high-fidelity information of both the static and dynamic aspects of joint movements. The static strain sensitivity of slowly adapting skin afferents from the back of the hand endow them with a static joint-position sensitivity at least on par with that reported for human muscle spindle afferents in the wrist and long finger extensor muscles (Cordo et al. 2002; Edin 1992). Grill and Hallet (1995) have reported also that the dynamic sensitivity of slowly adapting skin mechanoreceptors are comparable if not superior to those of muscle spindle primary and secondary afferents. Moreover, skin afferents from wide areas of the human thigh appear to provide high-fidelity information about knee-joint movements (Edin 2001). Skin mechanoreceptors thus seem suitable for providing proprioceptive information. Indeed, not only does electrical stimulation of the back of the hand induce movement illusions in a fair proportion of subjects but so do various spatial patterns of skin stretch applied to the dorsal aspect of individual metacarpophalangeal joints (Collins and Prochazka 1996). Finally, there is evidence that at least under some experimental conditions, sensory inputs from skin mechanoreceptors have precedence over inputs from muscle receptors: when a conflict is artificially created between the input pattern from skin mechanoreceptors and that of muscle spindle afferents, humans seem to primarily judge finger-joint movements and postures on the basis of sensory cues from the skin (Edin and Johansson 1995).

Taken together the above-cited evidence suggests that skin receptors play a significant role in proprioception: they are capable of conveying relevant information of high quality; when activated, they can induce movement illusions; and their inputs seem in some circumstances be more important to the CNS than the inputs from muscular receptors. Our knowledge about this putative proprioceptive system is, however, still quite limited. Yet the capacity of cutaneous mechanoreceptors to convey proprioceptive information must depend on both their static and dynamic strain sensitivity and the consistency of their responses. Because it is not yet possible to record simultaneously from multiple identified afferents, population properties pertaining to skin mechanoreceptors must be inferred from recordings in single units. The aim of this study was to extend previous findings regarding strain sensitivity of slowly adapting mechanoreceptors in humans (Edin 1992) by a quantitative investigation of the dynamic sensitivity of both slowly and fast adapting skin mechanoreceptors to controlled skin strains within the physiological range of strain amplitudes and velocities. The results give further support to the notion that skin mechanoreceptors are able to provide information of high quality about skin-strain patterns and thereby about joint configurations.

METHODS

Subjects

Data were obtained from 22 healthy female subjects who gave their informed consent to participate in accordance with the Declaration of Helsinki. During the experiment, the subjects were seated in a dentist’s chair with their left arm supported by a vacuum pillow. The left hand was supported on a lump of clay that was shaped to fit the palm of the hand such that the metacarpophalangeal (MCP) joints were

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slightly flexed (15–25°), and the wrist joint was midway between full extension and flexion.

**Neurophysiological technique**

Single-unit recordings originating from skin mechanoreceptive afferents were obtained by microneurography (Vallbo and Hagbarth 1968). Briefly summarized, the radial nerve was impaled 5–10 cm proximal to the elbow joint with a tungsten electrode (200 μm shaft diameter) coated with a 25–30 μm layer of lacquer except for the distal 10–40 μm. The distal 1 mm of the electrode was tapered to a 5–15 μm tip. The electrical impedance measured in situ at 1 kHz was 100–700 kΩ. The recorded neural signal was amplified near the recording site (10,000 times; bandwidth: 0.47–5.7 kHz). Once in an intraneural location, the electrode was manipulated in minute steps until single-unit activity was evident in the recording. When such unitary activity was evident, the corresponding receptor was located. Receptive fields (RFs) were characterized using von Frey hairs (0.06, 0.125, 0.25, 0.5, 1, 2, 4, 8, 16, and 32 mN). The threshold was defined as the smallest force that evoked an afferent response to ≥50% of the taps at the most sensitive spot. The skin area within which the afferent responded to stimuli of four times the threshold force was defined as the RF (Fig. 1A). Classification was carried out in three steps. First, only afferents with RFs that followed with the skin when it was translated laterally were considered cutaneous; other afferents were ignored. Second, cutaneous afferents that responded to a steady indenting force of 32 mN with a sustained discharge were classified as slowly adapting (SA), whereas afferents that responded only with on or on-and-off responses to indentation were classified as fast adapting (FA). Third, SA units were subdivided according to their discharge pattern during sustained indentation: afferents that showed irregular interspike intervals were classified as SA1 (Chambers et al. 1972; Edin 1992; Iggo and Muir 1969). The remaining SA units were subdivided into SAII and SAIII on the basis of their RFs and strain sensitivity: SAII units were those with ill-defined RF borders and strain sensitivity exclusively or predominantly in one direction, whereas SAIII units were characterized by sharp RF borders and largely omnidirectional strain sensitivity (Edin 2001). FA units that responded to remote taps were classified as FAI (Pacinian corpuscles), and the ones that did not were classified as FAII (putatively Meissner corpuscles).

**Stretch application**

The stretch device consisted of two parallel arms with strain gauges (Fig. 1B). The device was suspended, via a vertical beam, to a pole that was attached to the ceiling and the floor to provide mechanical stability. One arm of the device was fixed and the other was positioned by a computer controlled servo (DC-100 Hz, r.m.s. noise: <0.5 μ). The arms of the stretcher were positioned on the skin such that the RF was located midway between the arms. When the servo-controlled arm was moved away from the stationary arm, strain was applied to the skin chord fixed between the two arms. The friction between the subject’s skin and the arms of the actuator was practically always sufficient to stretch the skin, but if slips occurred, they were revealed by sudden changes in the forces measured at the two arms. The initial distance between the two arms of the stretching device was always 20 mm. Because the aim of the study was to characterize the afferents’ dynamic strain responses in general terms, the amount of strain applied was expressed as a percentage of the original distance between the bars, e.g., a 2-mm movement of the servo-controlled arm corresponded to 10% strain. Stretch stimuli were delivered in a ramp-and-hold fashion. During velocity runs, the skin was stretched to 8% at a velocity of 1, 2, 4, 8, 16, 32, or 64% s⁻¹ in a randomized order (Fig. 2). The duration of the ramp phase thus ranged from 0.125 to 8 s in the velocity runs. The hold phase lasted for 2.5 s, and then the stretcher returned at a velocity of 16% s⁻¹ to the resting position where it remained for 3 s. Each velocity was repeated twice and accordingly a complete velocity run consisted of 14 ramp-and-hold stretches. Amplitude runs were similar to velocity runs, but the stretch velocity during the ramp phase was always 32% s⁻¹ and the stretch amplitude during the hold phase was 1, 2, 4, 8, 16, and 20% (a total of 12 runs). The interval between runs was variable but never <10 s.

Stretch stimuli were applied along a proximal-distal axis except with a few receptors located at sites that required other stimuli orientations. When several runs were available from a single receptor, the run selected for analysis showed the best neural signal-to-noise ratio and lacked signs of movement artifacts (such as unintentional movements by the subject or sliding between the stretcher and subject’s skin). A minute prestretch was sometimes induced when the stretcher was positioned on the skin surface, and this evoked a continuous discharge in some afferents. After the first ramp-and-hold trial, all of these afferents ceased to discharge during the inter-trial periods and were otherwise in all respects similar to other afferents.

The stretcher was confirmed to operate as specified, but the actual stimulus delivered to the skin, and in particular to the RF under study, had to be assessed empirically. To visualize the relative motion of different skin areas subjected to stretch, small reflectors were attached to the skin surface and recorded with an infrared CCD camera (40-Hz frame rate) (Sandstro ¨m et al. 1996). Because the stretcher in its normal configuration would cover the skin area of interest, a special pair of beams was attached to stretch the skin to make visualization possible (Fig. 1C). Taking the stiffness of the bars into account, the analysis showed that the actual amplitude delivered by the bars was ~6% less than the nominal values, i.e., if the nominal stretch was, for instance, 16%, the actual stretch midway between the bars was ~15%. These kinds of measurements could not be carried out during the neurophysiological experiments, but the difference between the nominal and...
actual stretches was considered small and therefore not taken into account when the results were compiled and reported.

To identify a suitable range of skin strain velocities, maximum skin-strain velocities at the dorsal part of the hand during very fast voluntary wrist or finger flexion were measured using the CCD camera (100-Hz frame rate). The maximum strain velocity for any of the digit II-IV was 85% s⁻¹ (range: 55–85), for conjoint four-finger flexion 151% s⁻¹, and for wrist flexion 323% s⁻¹. The selected range of skin strain velocities thus encompassed most of the physiological range.

\[ \text{Data sampling and processing} \]

The nerve signal was digitally sampled at 12.8 kHz, and the force and position signals were sampled at 800 Hz. Individual nerve spikes were retrieved from the nerve signal recordings under visual inspection using a previously described algorithm (Edin et al. 1988). Statistical tests were performed with mixed repeated-measure ANOVA unless otherwise stated using Statistica 6.0 (StatSoft). When deemed necessary the variables were logarithmically transformed. Statistically
significant outcomes were defined as those with $P$ values < 0.05. Nonlinear power regressions were calculated using the `nlinfit` function of Matlab (The MathWorks).

RESULTS

Recordings were obtained from 40 low-threshold skin mechanoreceptive afferents in the human radial nerve, originating in the dorsal part of the hand and the lower arm (Fig. 1A). The afferents were unequivocally subdivided into 24 SA and 16 FA units. The SA units were further subdivided into 7 SAI, 7 SAII, and 10 SAIII and the FAI units into 13 FAI and 3 FAII. FAII afferents were excluded from many analyses because of their low number.

Although a few receptors showed irregular RFs, most had an elliptical form. The median RF size was 2.4, 15.7, 0.8, and 3.1 mm$^2$ for SAI, SAII, SAIII, and FAI, respectively (ranges were 0.8–4.9, 3.1–50, 0.8–3.1, and 0.8–50 mm$^2$, respectively).

Skin-strain velocity had a profound effect on the discharge rate of all classes of afferents. Representative examples of responses in SAI, SAII, and FAI afferents are shown in Fig. 2 (the ramp-and-hold sequences were applied in random order but were arranged according to ramp velocity in this illustration). The apparent consistency in responses to repeated stimulations was a feature common to all afferents.

SA units responded to all ramp velocities with a clear dynamic response, i.e., during the ramp phase, they showed a discharge rate above that explained by the stretch amplitude per se and continued to discharge throughout the entire hold phase while adapting to the static strain level. All SA units ceased to discharge early during the return phase, i.e., none showed an off response. This was also true for spontaneously active SA units that did not resume their activity until shortly after the strain level had returned to the baseline.

FA units, as expected, discharged only while the skin strain changed. Indeed, in addition to responding to phases of increased skin strain, practically all FA units also displayed an off response during the return phase (Fig. 2C). All FA units readily responded to ramp velocities $\geq 8$–16% · s$^{-1}$ but typically showed no or feeble responses at lower velocities. The RF of the particular FAI afferent in Fig. 2C was located just proximal to the proximal interphalangeal (PIP) joint of the index finger. The spikes evoked in this afferent during static hold phases were synchronous with the subject’s heart rate and did not represent a nonadapting response to skin stretch. The tautening of the skin evidently enabled the arterial pulsations to activate the dynamically sensitive receptor (cf. Macefield et al. 1992).

Static strain sensitivity

Amplitude runs were applied to a subpopulation of SA afferents (3 SAI, 4 SAII, and 5 SAIII) and analyzed in the same manner as in a previous study (Edin 1992). In short, the mean discharge rates during the last 1,500 ms of the plateau and the early 500 ms of the plateau were plotted against the stretch amplitude. A linear regression was then carried out to estimate the impact of the strain amplitude on the mean discharge; the resulting slope was interpreted as a measure of static strain sensitivity. The median strain sensitivity during the early hold phase was 1.6, 2.7, and 2.3 imp · s$^{-1}$ · %$^{-1}$ and during the late hold phase was 0.2, 1.6 and 1.2 imp · s$^{-1}$ · %$^{-1}$ for SAI, SAII, and SAIII, respectively. These results were similar to those previously reported on static strain sensitivity (1.6 and 1.0 for SAI and 2.2 and 1.8 imp · s$^{-1}$ · %$^{-1}$ for SAII for the early and late hold phase, respectively) (Edin 1992).

Response latency and consistency

If the strain-sensitive cutaneous afferents subserve proprioception and kinesthesia, one would expect them to respond both promptly and consistently to skin-strain changes. These response features were assessed by measuring the latency from the ramp onset to the first strain-evoked spike: the mean latency was taken as a measure of the promptness of the response and the SD of the latency as a measure of the response consistency. The mean values of these measures were plotted against the velocity for each unit type in Fig. 3A (note the logarithmic scales). As expected, the onset latency decreased markedly with increased strain velocity and so did the latency variation. There were, however, significant differences with respect to the onset latency [$F(3,22) = 7.0, P < 0.002$] and onset latency variation [$F(3,15) = 4.3, P < 0.025$] among the unit types. Specifically, type I units (● and ○ in Fig. 3A) showed longer latencies and a larger onset variation than SAI and SAII (□ and ■ in Fig. 3A). This was particularly evident at strain velocities $\leq 8$% · s$^{-1}$, whereas type I units approached the group of SAI–III units at higher strain velocities. Indeed, for all unit types, the mean variation in response onset ap-
proached 1 ms for strain velocities $>$8\%/s. These latencies and latency variations correspond to strain amplitudes as illustrated in Fig. 3B. Except at the highest strain velocities, the first spike in a typical SAIII unit was evoked at strains $<$0.5\%, and a typical SAII unit began to discharge at $<$1\% skin strain. Moreover, the onset variability was not only fairly stable for SAII and SAIII units within the tested strain velocity range but more importantly, it was small. Indeed, the first spike in a SAII or a SAIII unit typically occurred within a strain range of $<$0.2\% irrespective of strain velocity (Fig. 3B, right). In contrast, type I units started to discharge relatively late during the ramp and with a comparatively large variability at strain velocities $<$16\%/s. At strain velocities $>$8\%/s, however, all afferent groups responded in a similar fashion.

Dynamic strain sensitivity

Because of the nonlinear responses of skin mechanoreceptive afferents, there is no simple and straightforward way to characterize the dynamic components of their discharge. For this reason, several related features of the afferents’ responses during the ramp phase were investigated in parallel.

Peak discharge rate. The peak discharge rate provides an extreme estimate of the response by only taking into account a single interspike interval. This measure, i.e., the inverse of the shortest interspike interval, displayed a fairly linear relationship to the ramp velocity for many units. At the lower velocities only SA units, however, consistently showed an increased discharge rate that could be attributed to the strain velocity. In contrast, as many as 5/13 of the FAI afferents failed to discharge more than one spike during the ramp phase for strain velocities $<$4\%/s. Nevertheless, a linear function was fitted to relate the strain velocity to the peak discharge rate. The mean calculated slope was 0.87, 1.34, 0.81, and 1.47 imp \cdot s$^{-1}$/\% \cdot s$^{-1}$ for SAI, SAII, SAIII, and FAI units (Fig. 4A). This slope indicates that the typical peak discharge rate at the highest strain velocity studied was $\approx$50–95 imp/s depending on unit type. A single-factor ANOVA analysis revealed that the slope differed among unit types [$F(3,33) = 3.37, P = 0.03$]. Interestingly, whereas the SAIII units grouped with SAI with respect to onset latency and onset variation (Fig. 3), they grouped with SAI units with respect to sensitivity to strain velocity.

Mean discharge rate. The extreme opposite to the peak discharge rate as a measure of “dynamic responses” is the mean discharge rate during the ramp, i.e., the number of spikes during each ramp divided by the duration of the ramp. Although the mean discharge rate ignores any irregularities in the discharge rate during the ramp phase, the relationship between the mean discharge rate and the strain velocity was for all units similar to the one observed for the peak discharge rate. The estimated slope relating the strain velocity to the mean discharge rate was of course smaller than for the peak discharge rate but also more similar among unit types (Fig. 4B): 0.69, 0.65, 0.59, and 0.58 imp \cdot s$^{-1}$/\% \cdot s$^{-1}$ for SAI, SAII, SAIII, and FAI, respectively.

Instantaneous discharge versus strain amplitude. The instantaneous discharge at any moment evidently represented not only the amplitude of the strain but also the strain velocity. To further characterize the dynamic sensitivity of the recorded units, an elegant method introduced by Lennerstrand (1968) and used by Grill and Hallet (1995) was adopted. Figure 5A illustrates the response in a single SAIII unit with abscissa representing the strain amplitude. In Fig. 5B is shown the instantaneous discharge rate plotted against the strain amplitude at the middle of the interspike intervals that appeared during the ramp phase of a certain velocity. Apparently, the discharge increased roughly linearly with the strain amplitude for each ramp velocity, but the magnitude of the increase was profoundly influenced by the ramp velocity (Fig. 5B). Indeed an increased slope with increasing strain velocity was observed for the majority of the units (22/27 analyzed units; afferents that did not show an increasing slope leveled off already at 4–8\%/s). Finally, to extract the dynamic contribution to the discharge rate, a second linear regression was applied but this time relating the calculated static slopes to the corresponding ramp velocity (Fig. 5C). Evidently this slope (imp \cdot s$^{-1}$/\% \cdot s$^{-1}$) is yet another representation of dynamic sensitivity. Because this measure normalizes the sensitivity to 1% stretch at a velocity of 1\%/s, the numerical value of this slope is small: mean values for SAI, SAII and SAIII were 0.056, 0.061, and 0.073, respectively. Unfortunately, too many of the FAI units did not display more than a few interspike intervals during the ramp (at low ramp velocities because of their feeble responses, at high ramp velocities because of the short duration of the ramp) and were therefore exempt from this analysis.

Power regression analysis

Straight lines described adequately the relationship between the dynamic response and the strain velocity for many units,
whereas for other units the discharge rates clearly leveled off at higher strain velocities. Moreover, none of the explored measures of dynamic sensitivity provided a convincing representation of the dynamic sensitivity of FA units. For reasons like these, the discharge rate was modeled as a power function of the type

\[ F_q = \frac{a}{v^b+1} \]

where \( F_q \) represents the discharge rate (peak or mean discharge rate as defined above) and \( v \) the ramp velocity (similar power functions have repeatedly been applied to analyze skin mechanoreceptive afferents; see Essick and Edin 1995; Knibestål 1973, 1975). The parameters \( a–c \) were determined for each unit by nonlinear regression. The \( c \) parameter represents the spontaneous discharge rate; \( b \) corresponds to the curvature of the relationship and determines the velocity range in which the receptor show the highest differential sensitivity (units with \( b < 1 \) responded poorly at low velocities, whereas the discharge rate of units with \( b > 1 \) leveled off at higher strain velocities); finally, the parameter \( a \) defines the gain of the response.

With few exceptions, the regression produced excellent fits among all afferent types whether the mean or the peak discharge rate was used as the measure of discharge rate during the ramp (Fig. 6, A and B). Using the mean discharge rate, the regression failed with two units only (1 SAII and 1 SAIII), and the median \( r^2 \) was 0.97 for predicting the mean discharge rate; \( r^2 \) was >0.9 for all 38 analyzed units and >0.95 for 29/38 units (76%) using the mean discharge rate. The regressions yielded parameter \( b \) in Eq. 1 less than unity for all SA units and for the majority of the FAI units (12/16 units). Accordingly, for the large majority of the units, the discharge rate increase declined with increasing strain velocity as is shown in Fig. 6, A and B. Parameters \( a \) and \( b \) was inversely related (Fig. 6C), i.e., small values for parameter \( a \) were associated with large values for the parameter \( b \) and vice versa.

The obtained \( r^2 \) as well as the parameters \( a–c \) differed among unit types (Fig. 6D; all tests performed with Kruskal Wallis test considering multiple comparisons \( P \) values). FAI units showed the smallest \( a \) parameter and largest \( b \) parameter. The parameter \( c \) that corresponds to the spontaneous discharge rate was typically positive for SA units type II and III, whereas it was negative for all FA and SAI units. The fit \( (r^2) \) was excellent for all unit types but SAI units showed slightly lower values primarily because of their intrinsically higher discharge variability.

The dynamic sensitivity, i.e., the change in discharge frequency given a change in strain velocity, corresponds to the slope of the power function. Specifically, the dynamic strain sensitivity can be calculated by derivation of Eq. 1 with respect to velocity (\( v \))

\[ \text{FIG. 5. Assessing dynamic strain sensitivity. A: single neural recordings plotted against the strain (rather than time) during 8\% ramp stretches in a velocity series. B: superimposed instantaneous discharge rates for the unit in A as a function of stretch amplitude and the corresponding least-square regression lines that describes the discharge rate as a function stretch amplitude and has a slope that correspond to the increase in discharge rate per unit stretch, i.e., imp · s\(^{-1}\)% per % amplitude. C: the slopes calculated in B as a function of strain velocity (note log-log axes). After Lennerstrand (1968) and Grill and Hallet (1995).} \]
FIG. 6. Power regression analyses. A and B: mean discharge rates as a function of strain velocity for FA units (A) and SA units (B). —, best fit; ⊥, the ±99% confidence interval; •, average discharge rate at each strain velocity. C: parameters $a$ and $b$ in the power function were inversely related; —, logarithmic least-square fit. D: parameters $a$–$c$ (cf. C), the product $a \cdot b$ that represents the dynamic sensitivity at 1% strain velocity, and the $r^2$ value of the power regressions. —, the median value for the indicated units types; and the lower and the upper end of the rectangles depict 25 and 75 percentiles. E: —, median dynamic strain sensitivity as a function of strain velocity (☉, the 25 and 75 percentiles).
\[
\frac{dF}{dv} = a \cdot b \cdot v^{b-1}
\]  

The product \(a \cdot b\) thus equals the dynamic stretch sensitivity when the strain velocity \(v\) equals 1\%\cdot s\-1. Figure 6E depicts the median dynamic strain sensitivity as a function of strain velocity (calculated from Eq. 2) across all unit types. Among all units, SAI showed the highest dynamic strain sensitivity across all strain velocities, but all unit types except FAII typically showed their highest dynamic strain sensitivity at the lowest strain velocities.

Regressions with the peak discharge rate rather than the mean discharge rate during the ramp stretch were successful in fewer units (28/40) but among the successful units, the median \(r^2\) was 0.97.

**FA I subgroups**

Most FAI units (8/13) showed a discharge pattern during the ramp that was similar to SA units: the discharge rate increased with increasing strain velocity and increasing strain amplitude (Fig. 7A, units 6-1 and 39-4). The other group of FAI afferents instead showed an early peak during the ramp followed by a steady decline as if they rapidly adapted to the stimulus despite the continuous increase in strain (Fig. 7A, units 23-3 and 26-2). This difference in discharge patterns was obvious when the stretch amplitude at which the peak discharge occurred was plotted against the ramp velocity (Fig. 7B). The FAI units thus seem to fall into two main groups: one group that consistently showed their peak discharge late during the ramp and another group that with increasing ramp velocity peaked earlier and earlier. For the 64\%\cdot s\-1 ramp velocity ramps, the group that responded “early” showed their peak discharge 39 ms from the start of the ramp (range: 28–64 ms; the mean corresponds to 2.5% stretch). The late responding group, on the other hand, showed their peak discharge rate 116 ms from the start of the ramp (range: 78–127 ms; the mean corresponds to 7.4% stretch). Similar results were obtained for ramps with velocities 16 and 32\%\cdot s\-1 (\(P < 0.0016\)), whereas no obvious differences were evident at velocities <4\%\cdot s\-1. Notably, the two groups of FAI afferents showed no differences in indentation threshold, RF area, or location.

**DISCUSSION**

It is obvious from a simple visual inspection of the back of the hand that various finger and wrist movements are associated with distinct skin-strain patterns. Moreover, these strain patterns are dependent on the position and movements at multiple joints (Edin and Abbs 1991). The magnitude of the local strain depends not only on the distance from the joints but also on the joint sizes. Thus skin areas close to a joint are influenced more than distant skin areas, and larger strain changes will, for instance, be caused midway between the MCP joints and the wrist joint by flexion of the wrist than by flexion of the MCP joint. In short, the relationship between joint movements and skin-strain patterns is rather complex. Because the crucial stimulus to cutaneous mechanoreceptors is skin deformation, the strategy chosen to analyze the potential role of skin mechanoreceptors in providing proprioceptive information was to determine how individual mechanoreceptors respond to strain changes rather than to joint movements per se (Edin 1992). Such information combined with appropriate measurements of skin-strain changes during actual movements should make it possible to quantitatively assess the capacity of skin receptors to encode specific joint configurations and movements.

The accuracy of the strain pattern representation and consequently of the proprioceptive information depends on both the strain sensitivity and the response variability of individual receptors. It has previously been shown that low-threshold fast-conducting afferents from the human skin are endowed with a significant static strain sensitivity (Edin 1992). This study extends these findings by demonstrating that skin afferents also show a profound dynamic sensitivity and, moreover, show highly consistent responses.

**Applied and appropriate stimuli**

Although the strains applied to the skin were controlled very accurately (r.m.s. noise: <0.005\% strain), the strains applied to the individual cutaneous receptors were not really as well
defined. When the arms of the stretcher were placed on the skin, there was inescapably a local indentation of the skin that often evoked transient afferent responses. This indentation elongated to an unknown extent the skin patch fixed between the arms of the stretcher. The force required to effectuate the skin stretch was not analyzed in detail but did vary between subjects due to diverse skin properties and between locations due to differences in the mechanical properties of various skin areas and the coupling between the dermis and subjacent tissues. Overt slips between the actuator and the skin were evident in the force records but minor slips might have been overlooked. In addition, the strain that affected the receptor organs was not necessarily on par with the strain applied at the surface. How strain at the skin surface is transferred to deeper layers of the skin is largely unknown, but it seems unlikely that strain in the dermis could have been larger or even on par with the strain measured at the surface of the epidermis. This should mainly effect the sensitivity estimates for FAII (Pacini) and SAII (Ruffini) because their receptor organs are situated in the dermis and not adjacent to the epidermis while those of type I units are situated in or close to the epidermis as are presumable the receptor organs of SAIII afferents. Finally, due to the finite stiffness of the actuator arms in contact with the skin, the strain actually applied to the skin was somewhat smaller than those nominally applied (described in more detail in METHODS). Consequently, there are a number of factors complicating the application of strain stimuli yet they invariably work in the same direction, that is, they result in local strains at the level of the skin receptors that are lower than the strains nominally applied. In addition, irrespective of the afferents’ optimal stimulus direction (cf. Edin 1992), strain stimuli were applied in a proximal-distal orientation unless precluded by the location of the receptors. It therefore seems safe to claim that the dynamic sensitivity of human skin mechanoreceptors presented in this paper is at least as high as stated.

The use of strain stimuli could, however, be questioned given that there is good evidence that tensile stress rather than strain is the appropriate stimulus of both FA and SA afferents. In a series of elegant studies, Grigg and collaborators have characterized stretch responses in both RA and SAII from the depilated hairy skin of rats and mice (Del Prete and Grigg 1998; Del Prete et al. 2003; Grigg and Del Prete 2002; Robichaud et al. 2003). Not all RA afferents in these studies, however, correspond to FAI afferents in the present study. Moreover, as clearly pointed out by the authors, the RA afferents in the rats and mice have very different properties from the FAI units in humans. For instance, uniaxial strains of ~40% were required to effectively activate the RA afferents (Del Prete and Grigg 1998), i.e., magnitudes larger than those evidently required to reliably activate human FAI afferents. Nevertheless, Grigg et al. were able to dissociate stress and strain by applying pseudorandom Gaussian noise and taking advantage of the viscoelastic properties of the skin. They concluded that the neuronal responses in not only RA but also SAII units (and C mechanoreceptive afferents) are related to tensile stress (and its derivatives) rather than strain. Similarly, Phillips and Johnson (1981) claimed that the responses of SAI afferents in the glabrous skin of monkeys were explained most effectively by the profiles of maximum compressive strain. Although the force required to effectuate the actuator arms was measured in the present study, these measurements did not allow reliable estimates of even uniaxial skin stress because the recorded force were influenced by, for instance, the exact angle of the actuator arms in relation to the skin and the properties of the subjacent tissues. Within the physiological range of strains and strain velocities of the present study, however, skin viscosity did not seem to play any major role in shaping the afferents’ response (see force records in Fig. 2), and, accordingly, it seems justified to use strain rather than stress to characterize the response properties of the afferents.

Characteristics of SAI, SAII, and FAI units

The recorded units were beyond reasonable doubt correctly subdivided into SA and FA units. Furthermore, SA units were unequivocally divided into two groups, viz., those that showed regular (SAII and SAIII) and irregular (SAI) interspike intervals to steady indentations (Chambers et al. 1972; Edin 1992; Iggo and Muir 1969). The subdivision of FA units into type I and II was, however, less secure. While FAII units regularly but FAI units practically never respond to “distant” stimuli (Knibestöl and Vallbo 1970), it is difficult to differentiate FAI units with relatively large RFs and well demarcated borders from FAII units with relatively small RFs but obscure boundaries without a detailed mapping of the RFs (Johansson 1978) and analyses of vibration responses (e.g., Johansson et al. 1982). A low proportion of FAII units (3/40) is, however, expected from previous studies using various recording techniques and classification methods (Edin 2001; Edin and Abbs 1991; Edin et al. 1995; Hallin 1990). Moreover, the reported results would not be affected if in fact one or a few of the FA units were incorrectly classified.

It has recently been proposed that SA afferents in human nonglabrous skin can be subdivided into three groups (Edin 2001). In addition to SAI and SAII there seems to be a distinct group, SAIII, that shares properties of both SAI and SAII units. Like SAI units, SAIII units have small, sharply delineated RFs (often <1 mm²) and show omnidirectional stretch sensitivity, but like SAII units, they have a single highly sensitive spot and show a regular discharge whether it is spontaneous or evoked. Although the morphological structures that corresponds to SAIII afferents are unknown, some of the properties of these structures can be predicted from the afferents’ functional properties: the receptors are expected to be located superficially (to explain the small RFs) and be symmetrical in any plane normal to the surface (to explain the omnidirectional strain sensitivity). Interestingly, while the SAIII afferents grouped with SAI units in terms of their sensitivity to strain velocity (Fig. 4), they grouped with the SAI units with respect to onset latency and onset variability (Fig. 3).

It was possible to model the mean discharge rate of all types of afferents as a power function of strain velocity ($F_q = a \cdot v^b + c$; Fig. 6). The parameters $a-c$ were not the same across all units but the differences were small (Fig. 6D). Because $b$ on the average was <1 for all unit types, the dynamic strain sensitivity was highest at the lowest strain velocities (Fig. 6E), and this was particularly evident for the FA units. SA units as a group thus showed higher dynamic sensitivities than FA units at low strain velocities (<16% \cdot s⁻¹), and vice versa at high strain velocities (≥16% \cdot s⁻¹). But equally important in a functional sense are the pronounced differences between unit classes with respect to response consistency and variability.
The analyses demonstrate that SAII units and to some extent SAIII units are the only unit types that respond both quickly and consistently to lower strain velocities; at higher velocities, both SAI and FAI are “recruited” with a consistency similar to SAII units but still with a somewhat longer latency (Fig. 3). The different velocity sensitivities regarding high or low velocities imply that the SA receptors may have the role of transmitting information about the slow skin strains, like when a joint is flexed or extended with a low angular velocity. On the other hand, FA units are more sensitive to high-velocity skin strain and may provide additional information about faster movements and movement transients.

Knibestøl (1973) reported that RA afferents (i.e., FAI units) from the glabrous skin showed a wide range of responses to indenting stimuli from low-velocity threshold, sensitivity, and maximal discharge rates to high-velocity threshold, sensitivities, and maximal discharge rates. Similarly, Edin and Essick (1995) reported that a population of FA afferents (consisting almost exclusively of FAI afferents) recorded from both glabrous and hairy skin also defined a continuum based on their responses to moving tactile stimuli. FAI afferents thus appeared to display a wide dynamic range. The apparent subdivision in Fig. 7 of the FAI units in two groups of which one adapts extremely fast may therefore be an artifact due to the limited sample size in the present study.

Relationship between strain changes, movements and the dynamic sensitivity

Although the estimates of dynamic sensitivity may appear to be numerically small, it should be noted that as a result of the static as well as dynamic sensitivity practically all units were forced to discharge at high rates during phases of increased skin strain (cf. Fig. 3). The only published account that quantitatively describes skin strain in areas near a moving joint is a 20° flexion movement at the MCP joint of the index finger (Edin 1992). If we translate this into 0.008–0.032 imp/s, increased 0.4%, i.e., before a flexion movement would have occurred on average within 30 ms from the onset of the ramp (i.e., before the flexion had reached 6–7°). Moreover, the onset variability in terms of angular position would have been <0.33–0.66° for the SAII units irrespective of the flexion velocity. Also, not only was the response onset typically consistent in all classes of skin mechanoreceptors, but so was the overall discharge pattern (as illustrated in Figs. 2 and 7).

Skin mechanoreceptors thus respond strongly, quickly, and accurately to skin-strain changes, and it seems reasonable to believe that qualitatively the same statements can be made for actual position changes at nearby joints. Indeed, a very tight coupling between movements at nearby joints and changes in instantaneous discharge rates have been observed in skin afferents record from the human thigh during knee-joint movements (Edin 2001). These conclusions are at variance with those of Grill et al. (1997). They imposed passive flexion movements at the metacarpophalangeal (MCP) joint of the index finger while recording the responses in muscle spindle and skin afferents in the radial nerve. Their results indicate that spindle afferents on average commenced their discharge ~50 ms earlier than skin afferents, and they therefore proposed that cutaneous mechanoreceptors compared with muscle spindles play a limited role in providing signals for on-line coordination of movements. While the claim of Grill et al. (1997) may hold true, it should be noted that their conclusion was based on population estimates from a sample of 15 spindle and 13 cutaneous afferents, not responses in individual afferents. More disturbingly, the exact locations of the RFs of the skin afferents were not reported (except that they were found “proximal to the MCP joints”) although the RF location profoundly influences responses of skin afferents to movements at specific joints. For instance, according to Edin and Abbs (1991), as many as 96/107 afferents recorded in the radial nerve responded to passive movements at one or more joints, but only 41 (43%) of these responded at all to movements at the MCP joint of the index finger.

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