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SENSATIONS EVOKED BY INTRANEURAL MICROSTIMULATION OF SINGLE MECHANORECEPTOR UNITS INNERVATING THE HUMAN HAND

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SUMMARY

1. Intraneural microstimulation (i.n.m.s.) was performed in awake human volunteers, using tungsten micro-electrodes inserted into median and ulnar nerve fascicles supplying the skin of the hand. The same electrodes were used alternatively to record impulse activity from single nerve fibres at the i.n.m.s. sites.

2. Monitoring occasionally, with a proximal electrode, the impulse traffic evoked by i.n.m.s. distally in the same fascicle, established that the stimulation procedure could be made selective enough to activate single myelinated fibres in isolation, while also permitting multifibre recruitment.

3. Monitoring propagated impulses also established that i.n.m.s. of a single myelinated fibre supplying a low-threshold mechanoreceptor in the hand might evoke an elementary sensation. Such sensations were fully endowed with cognitive attributes amenable to psychophysical estimation: quality, magnitude and localized projection.

4. Psychophysical tests were made during i.n.m.s. at intraneural sites where single-unit activity was recorded from classified RA, PC, SA I or SA II mechanoreceptors. Changes in excitability of the nerve fibre of an identified unit, induced by further i.n.m.s., certified that the recorded unit had been stimulated during psychophysical tests.

5. Comparing physical location of the receptive field of a recorded unit and localization of the projected field of the corresponding elementary sensation, revealed that either predicted the other accurately. This further assisted identification of the unit activated by i.n.m.s.

6. The type of a recorded unit and the quality of the elementary sensation evoked by its activation were also reciprocally predictive. RA units evoked intermittent tapping, PC units vibration or tickle and SA I units evoked pressure. SA II units evoked no sensation when activated in isolation.

7. Afferent impulse frequency determined magnitude of pressure in the SA I system, and frequency of vibration in the PC system. In the RA system, stimulation frequency determined frequency of tapping–flutter–vibration sensation at relatively low rates and subjective intensity of sensation at high rates.

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8. These findings endorse the concept that quality of sensation is coded in specific sensory systems. Further, they provide novel evidence that sensory quality, magnitude and localization can be exquisitely resolved at cognitive levels on the basis of input initiated in a single mechanoreceptor unit.

INTRODUCTION

To unravel laws that govern the ability of the human brain to decode the afferent message from primary somatosensory units, and on the assumption that the input from single units may reach cognitive levels, repeated attempts have been made to stimulate sensory units in isolation in conscious subjects. Almost a century after Blix, von Frey and others started applying controlled punctate stimuli to the skin (for a review in English, see von Frey, 1906), Hensel & Boman (1960) persevered with the advantage of simultaneous sensory unit recording from surgically exposed, cut, nerves in themselves and five medical students. Less heroically, Bishop (1943) delivered electric sparks, while Scharf, Hyvärinen, Poranen & Merzenich (1973), and P. R. Burgess too (personal communication, 1981), inserted needle electrodes near identified hair follicles or cold spots in the skin. In none of these experiments was there objective proof of type and number of units stimulated. Recently, Torebjörk & Ochoa (1980) used conventional microneurography (Vallbo & Hagbarth, 1968) for single nerve fibre recording combined with attempted intraneural microstimulation (i.n.m.s.) of classified single nerve fibres in alert man. This approach was also used by Vallbo (1981), and by Konietzny, Perl, Trevino, Light & Hensel (1981). However, the ability to record signals from a single fibre close to the electrode tip does not guarantee that that particular fibre can also be stimulated in isolation by the same electrode. Evidence that a recorded fibre had actually been activated could be produced by documenting changes in nerve fibre excitability following prolonged tetanic stimulation (Torebjörk & Ochoa, 1980). In addition, the matching of the receptive field of a recorded single unit with the field to which a 'pure' sensation was projected during stimulation (Torebjörk & Ochoa, 1980; Vallbo, 1981), together with the matching of sensory unit type with the 'specific quality' of sensation, gave confidence that such evoked sensations were the result of isolated activation of single units (Torebjörk & Ochoa, 1980).

Here we report further evidence for selective intraneural stimulation of single myelinated fibres associated with low-threshold mechanoreceptors innervating the human hand. Intraneural monitoring of afferent impulses induced by i.n.m.s. showed a one-to-one relationship in time between single-unit activation and elementary evoked sensation. This establishes that a single sensory unit can indeed be activated intraneurally with our method and validates a 'pure and specific' elementary sensation as its cognitive correlate (Torebjörk & Ochoa, 1980). We now reclaim that the brain can normally discriminate specific quality, precise localization, and even magnitude of a sensation, on the basis of the input from single primary units of certain types. Through integrating novel data about the sensory correlates of activation of individual PC, RA, SA I and SA II units, with their known receptor–response characteristics, we offer an updated interpretation of the role of specific mechanoreceptive systems in discriminative touch.

METHODS

Material. Microneurography and intraneural microstimulation were carried out in fifty-three experimental sessions on six healthy subjects, five males and one female, ranging in age from 33 to 46 years. Forty-three experiments were performed in the median nerve at upper arm, 10–15 cm proximal to the medial epicondyle. At wrist level, five experiments were performed in the median nerve and five in the ulnar nerve. A total of 108 low-threshold mechanosensitive units with receptive fields in glabrous (100 units) and hairy (eight units) skin of the hand were studied. They were classified as RA (thirty-eight), PC (fourteen), SA I (thirty-nine) and SA II (seventeen). The conduction velocities were in the range of 40–66 m/s with three exceptions: one RA (25 m/s), one SA I (22 m/s) and one PC unit (23 m/s).

General procedure. After informed consent the subject sat relaxed on a reclining chair with the arm comfortably supported. A micro-electrode was inserted manually through the skin into an underlying nerve trunk, which was localized by palpation or electrical stimulation. Awareness of electrode tip position within a cutaneous fascicle was derived either from recording afferent activity from the skin, or from evoking sensations projected to skin while stimulating electrically through the electrode. A reference electrode was inserted into subcutaneous tissues 1–2 cm outside the nerve trunk.

Electrodes and equipment. Lacquer-insulated tungsten electrodes, 200 μm in diameter, of the type designed for human microneurography (Vallbo & Hagbarth, 1968), were used both for neural recording and stimulation. After being used, the intraneural electrodes had exposed tip lengths of 30–100 μm and tip diameters of 2–20 μm. The impedance tested at 1000 Hz was 100–200 kΩ. The low-impedance reference electrode had an exposed tip length of 3–4 mm.

Nerve signals were amplified, audiomonitored, displayed on a storage oscilloscope (Tektronix 549) and stored on tape (Sangamo Sabre IV or Tandberg 115) for subsequent analysis. The wave forms and signal-to-noise ratio of single-unit potentials were studied by processing the signals through an analogue delay unit (Neurolog 740) using the full band width of the recording and display systems (300 Hz–10 kHz). A switch in the pre-amplifier permitted the electrodes to be connected to either the input of the recording system or the output from a constant voltage Grass S48 stimulator with stimulus isolation unit.

Classification of low-threshold mechanoreceptor units with myelinated fibres. For the purposes of the present study, centred on low-threshold mechanoreceptor units, mechanical stimuli (stroking, pressing, scratching and blowing) were given to the cutaneous territory of the nerve, while adjusting the position of the exploring electrode. Eventually, when the recorded potential amplitude of a single mechanosensitive unit exceeded noise level at least four times (40 μV against 10 μV noise), that unit became a candidate for various experiments, which could last up to 3 h. Having localized the unitary receptive field and classified the receptor as RA, PC, SA I or SA II, according to the criteria of Vallbo, Knibestöl and Johansson (for review see Vallbo, Hagbarth, Torebjörk & Wallin, 1979), the receptive field was mapped with calibrated von Frey hairs at 5 × threshold, and its area was outlined with ink on the skin. Needle electrodes were optionally inserted in the receptive field to stimulate the fibre electrically. Conduction velocity was then calculated from measurement of latency and conduction distance between stimulating and recording sites.

Intraneural microstimulation (i.n.m.s.). Electrical stimuli were delivered through the intrafascicular electrodes by two alternative approaches: (a) the apparatus was switched to stimulating mode after a mechanoreceptor unit had been pre-identified by recording and the tip of the electrode had been brought very close to the nerve fibre, as judged by the high potential amplitude, or after the electrode had actually impaled the myelin sheath of the fibre, as judged by the mainly positive, biphasic or complex wave form of the potential (Torebjörk, Hallin, Hongell & Hagbarth, 1970; Vallbo, 1976) or (b) the intrafascicular electrode was primarily used to deliver trains of weak electrical stimuli while gently adjusting its position, and while monitoring evoked sensations reported by the subject. Having reached an intrafascicular spot where i.n.m.s. evoked a sensation with elementary characteristics (see Results), psychophysical studies were performed. Eventually, the apparatus was switched to recording mode and the search for a unit recordable from the very spot of i.n.m.s. was started, based on the administration of natural stimuli to the cutaneous territory of the nerve.

With either approach, the subjective sensory data collected from microstimulation were matched against the electrophysiological data collected from prior or subsequent recording of classified units.

Stimulus parameters for i.n.m.s. Positive square-wave pulses of 0·25 ms duration were used. Single pulses or regular trains were given at frequencies of 1–300 Hz. Train duration was usually 2 s to allow ample time for sensory detection. Longer trains (up to several minutes) were occasionally delivered to study changes in excitability of the stimulated fibres. Intervals between trains were 30–60 s. The amplitude of the stimulating pulses was gradually raised from 0 to a level where the subject felt a first sensation. This usually occurred by 0·20–0·30 V. Higher amplitudes up to 4 V were used when studying recruitment of further sensations.

Psychophysical studies. The subjects had no cues as to when stimuli were given, or what stimulus parameters were used during i.n.m.s. sessions. They were asked to describe in their own words the qualities and temporal profiles of sensations evoked by i.n.m.s., and to map directly on a real-size picture of the hand the sites and sizes of the skin areas where sensations were projected. If they had difficulties in naming the sensations the subjects were presented with a multiple-choice questionnaire, composed from typical verbalizations collected in pilot studies. They were asked to choose alternatives from each of five categories: category I: superficial, deep; category II: stationary, migratory; category III: intermittent, sustained; category IV: painful, non-painful; category V: tapping, flutter, vibration, tickle, pressure, tension, movement, cold, warm, hot, burning, sharp pain, dull pain, itch, electrical.

The expression 'touch' was excluded since it tended to be used instinctly for tapping and pressure. In a number of experiments the subjects were also asked to assess the subjective intensity or the frequency of a sensation, relative to stimulus frequency at fixed amplitude, according to the method of magnitude estimation. The experimental procedure and the results of those studies will be described in more detail in a subsequent report.

Simultaneous i.n.m.s. and recording at two levels along a sensory fascicle. These double-electrode experiments were designed to monitor directly the ascending traffic of unitary impulses propagated during i.n.m.s. at amplitudes liminal for sensory detection. Because action potentials cannot be recorded with this technique unless the electrode tip has penetrated the perineurium and lies within the appropriate fascicle (Hagbarth, Hongell, Hallin & Torebjörk, 1970; Schady, Ochoa, Torebjörk & Chen, 1983*a*) it was necessary to insert the recording electrode into the same fascicle as the stimulating electrode. To meet this condition the distance between the two sets of electrodes needed to be fairly short because of the changing fascicular topography of human nerves (Sunderland, 1945; Schady *et al.* 1983*a*). For the median and ulnar nerves at wrist level, distances between 4 and 9 cm satisfied the anatomical requirement while preventing stimulus artifact from interfering with the neural response. Coincidence of the areas of compound projected sensation when either electrode was used for submaximal stimulation, or coincidence of the receptive territories when either electrode was used for recording, was evidence that both electrode tips lay within the same fascicle (Fig. 2).

'Marking' individual myelinated fibres stimulated by i.n.m.s. The 'marking' strategy was originally devised to label a unit which had been activated during i.n.m.s., in such a way that it could be subsequently identified during recording (Torebjörk & Ochoa, 1980). It took advantage of the possibility of modifying the excitability of a recorded myelinated fibre by i.n.m.s. at high frequency (200–300 Hz) delivered at the site of recording for 5–15 min. Subsequent recording from the fibre subjected to this challenge revealed hyperexcitability to the point of ectopic impulse generation. This could either be spontaneous or triggered by impulses initiated during natural stimulation of the corresponding receptor (Figs. 8 and 10). In either case, the fact that afferent activity initiated from the identified cutaneous receptors of classified units could trigger or interfere with such ectopic activity proved that the fibres of these particular units had been previously activated by i.n.m.s.. In this study the 'marking' technique was especially valuable in providing proof that units without sensory correlate had actually been activated by i.n.m.s.

RESULTS

Elementary sensations evoked by i.n.m.s.

Intraneural microstimulation in regular trains at liminal intensity for conscious detection evoked sensations with distinct *qualities* and *temporal profiles*. They were recognizable even for naive subjects in their first exposure. *'Tapping'* was a non-painful sensation of superficial contact on the skin, without pressure component.

Each tap was felt as a brief event, repeating intermittently during a stimulus train and described as '*flutter*' or '*vibration*' as stimulation frequency increased. '*Pressure*' was a non-painful sensation of skin compression. There was no definite sensation of contact on the skin surface. Pressure was a sustained sensation without the intermittency typical of tapping–vibration. Changing frequency of i.n.m.s. did not interconvert pressure and tapping–vibration. '*Tickling*' was a pleasant non-painful sensation compared to that evoked from the skin by down feather. It was only felt on two occasions and its temporal profile was not defined.

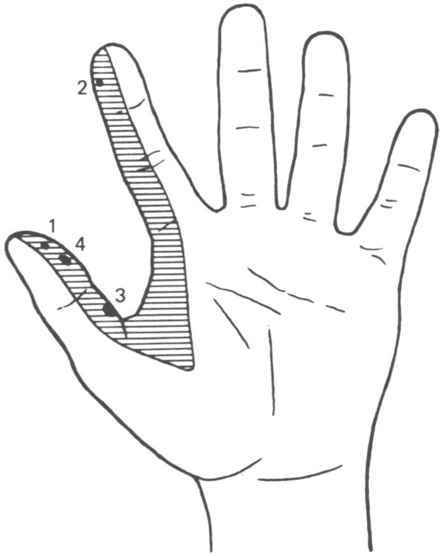

Fig. 1. Projected fields of sensations evoked by i.n.m.s. (10 Hz) given in a cutaneous fascicle of the median nerve above elbow level. Subject's on-site drawing on real-size picture of own hand. Discrete elementary sensations, projected to fields 1–4 (tapping, stinging pain, dull pain and pressure), were recruited in consistent order when raising stimulus amplitude between 0 and 0·35 V. The hatched area marks maximal projected field of confluent sensation evoked at high stimulus amplitude (above 0·70 V); it reflects a fascicular province within the median nerve cutaneous territory of innervation (Schady *et al.* 1983*a*).

Sensations of stinging or dull pain, itch and warmth were also reported. Such sensations were never associated with stimulation of low-threshold mechanoreceptor units with myelinated fibres, and are not included in this study.

The *elementary sensations* evoked by i.n.m.s. were felt as though originating in a discrete, monofocal area of skin. We call this the *projected field* as opposed to the *receptive field* from which a sensory unit can be naturally activated. The site of a projected field was always stationary as long as the stimulating electrode position remained constant; its size was not perceptibly influenced by stimulus frequency. A continuous increase in stimulus amplitude, beyond detection threshold for the first elementary sensation, failed to cause migration or continuous expansion of its projected field. Instead, there was discontinuous recruitment of new elementary sensations projected multifocally while the projected field of each sensation remained immutable (Fig. 1).

The *subjective magnitude* of an elementary sensation did not change for a given frequency when the stimulus amplitude was increased beyond detection threshold. Again, rather than a continuous crescendo magnitude, there followed sequential recruitment of new elementary sensations, each having their private quality, temporal profile and subjective magnitude.

In repeated recruitment trials at a given i.n.m.s. site, it was found that the stimulus amplitude values at threshold for each recruited elementary sensation were remarkably reproducible, and in consequence so was the order of recruitment of elementary sensations in the sequence. Thus, each new elementary sensation was recruited as an all-or-nothing phenomenon, with its fixed threshold, projected field, quality, temporal profile and magnitude. Eventually, during advanced recruitment through raising stimulus amplitude, the gaps between projected fields were progressively abridged, until an intense sensation was projected to a large confluent area corresponding to the innervation territory of one or two adjoining digital nerves (Fig. 1). At that stage the discrete sensory characteristics described for elementary sensations were no longer recognizable. Instead, there was a compound sensation with a more or less painful 'electric' quality and an admixture of intermittency over a sustained temporal background.

In a few recruitment experiments, the magnitude of a first elementary sensation grew together with its projected field upon increasing stimulus amplitude. This was observed only with i.n.m.s. at wrist level. It was taken to reflect successive recruitment of several units of a common type and projection. Such sensations, which were graded in magnitude and projected field size rather than being all-or-nothing, were not included in the present material.

Correlative recruitment of single-unit potentials and of elementary sensations. In an effort to elucidate the neurophysiological correlate of an elementary sensation at the primary sensory neurone level, the ascending traffic evoked by i.n.m.s. was monitored in several experiments with recording electrodes inserted proximally into the same nerve fascicle. One such experiment is illustrated in Fig. 2 and the results are described in detail below.

The electrode used for i.n.m.s. was inserted at wrist level into a sensory fascicle of the ulnar nerve which supplied the radial palmar digital nerve territory of the fifth finger. A second electrode was used for recording from the ulnar nerve 8·5 cm proximally in the lower forearm (Fig. 2*A*). Having established that the electrodes lay in the *same* sensory fascicle, as described in the Methods, the pulse amplitude of 10 Hz stimulation through the distal electrode was gradually raised from 0. At low stimulus amplitude no neural response was recorded by the proximal electrode (Fig. 2*B*) and no sensation was reported. At 0·20 V a triphasic, mainly negative potential was recruited in all-or-nothing fashion (Fig. 2*C*). It was clearly a single-unit potential recorded from a myelinated fibre with a conduction velocity of 43 m/s. Recruitment of this unit coincided with the subject's report of a first discrete elementary sensation of intermittent tapping projected to a small field in the pulp of the fifth finger (T in Fig. 2*A*). Mechanical stimulation at that skin area evoked afferent discharges in an RA unit with similar potential amplitude, duration and wave form as the unit recorded in response to electrical intraneural microstimulation. Further increase in the amplitude of i.n.m.s. to 0·24 V recruited a next single-unit potential (Fig. 2*D*) derived from a fibre with a conduction velocity of 56 m/s. Recruitment of this unit was strictly associated in time with subjective report of the next sequential sensation: in this case sustained pressure, projected to a small field in the middle phalanx of the fifth finger (P in Fig. 2*A*). Mechanical stimulation at that skin area evoked afferent discharges in an SA I unit with potential characteristics similar to the unit recruited in correlation with pressure sensation during i.n.m.s.

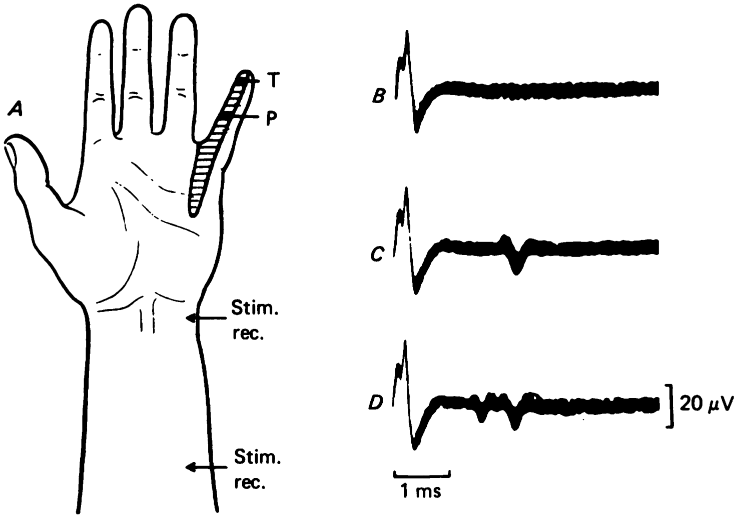

Fig. 2. Monitoring with proximal recording electrode afferent impulses evoked from a distal stimulating electrode while subject experienced elementary sensations. *A*: position of proximal and distal electrodes (arrows) within the same cutaneous fascicle of ulnar nerve assured by achieving congruous projected fields and receptive fields (hatched area) when either electrode was used for submaximal i.n.m.s. or for recording. T and P mark projected fields of tapping and pressure evoked by near-threshold i.n.m.s. (10 Hz) through distal electrode. *B*: no neural response to i.n.m.s. was recorded below threshold for sensation ($<$ 0·20 V). *C*: all-or-nothing recruitment of single unit potential at 0·20 V coincided with subjective report of tapping projected to T. *D*: recruitment of additional single unit potential at 0·24 V coincided with additional report of pressure, projected to P. Calibrations identical and ten superimposed sweeps for each record.

While maintaining the amplitude of i.n.m.s. constant at 0·24 V, the frequency of stimulation was gradually increased to 100 Hz. Tapping was felt to increase in frequency, towards vibration, without much change in the intensity of sensation, whereas the subjective intensity of sustained pressure increased progressively. The fields to which the sensations were projected remained constant in subjective size regardless of stimulus frequency. During prolonged stimulation for several minutes at 100 Hz the latencies of the units increased and a progressive degree of blocking was observed. This was paralleled by reports of a progressive decrease in subjective magnitude of pressure and by pauses in the sensation of high-frequency vibration.

Two additional experiments of this type were performed in sensory fascicles of the median nerve at wrist and lower forearm level with essentially similar results, i.e. strict reciprocal temporal correlations were found between single myelinated fibre activation and recruitment of an elementary sensation. Further, by merely observing recruitment and de-recruitment of unitary responses on the oscilloscope screen, the experimenter could predict onset, offset and numbers (up to three) of elementary sensations perceived by the subject.

Value of elementary sensations in prediction of types and receptive fields of sensory units stimulated intraneurally

When a first elementary sensation was recruited at very low i.n.m.s. amplitude (0·20–0·28 V, mean 0·25 V, $n = 32$) it was often possible to predict correctly, from the described quality and temporal profile of sensation, what type of unit to anticipate on subsequent recording. Furthermore, the projected field usually predicted within a few millimetres the actual location of the receptive field of that unit. A striking example is shown in Fig. 3. In this experiment, i.n.m.s. at 0·23 V and 20 Hz, administered in a sensory fascicle of the median nerve at elbow level, first evoked flutter sensation projected monofocally to a small field of the pulp of the thumb. Nothing else was felt. When using the electrode for recording, manual stimulation of the skin evoked high-amplitude impulses from an RA unit. Careful mapping demonstrated that the receptive field overlapped the projected field and that the sizes were similar (A in Fig. 3). This intrafascicular spot was abandoned and the electrode was gently advanced during ongoing i.n.m.s. until a new elementary sensation was volunteered at 0·25 V; sustained pressure was projected monofocally to the middle phalanx of the index finger. On recording, an SA I unit dominated the neurogram; the receptive field overlapped the projected field of pressure (B in Fig. 3). A new

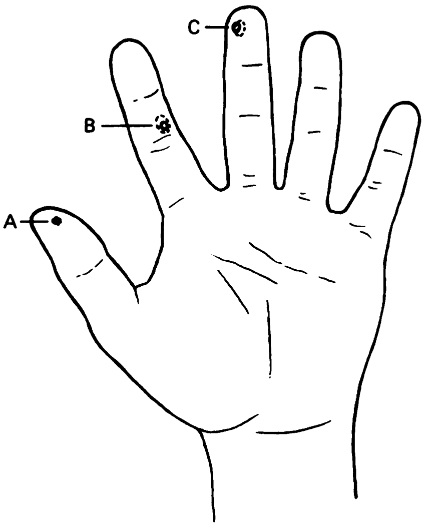

Fig. 3. Accurate prediction, based on quality and projected field of three first elementary sensations evoked during median nerve stimulation above the elbow, of the type and receptive field of three correspondingly recorded units. In A, intermittent tapping sensation predicted recording of RA unit with receptive field (filled area) close to projected field (broken lines). In B and C, representing another two intraneural sites, sustained pressure sensation predicted SA I units: their receptive fields (open circles) were localized close to the fields of projected sensations (dashed lines).

adjustment of the intraneural electrode yielded sustained pressure projected monofocally to the tip of the middle finger during i.n.m.s. at 0·23 V; again, the type and receptive field location of the predicted SA I unit were verified by recording (C in Fig. 3). In both examples the projected fields of pressure were larger than the receptive fields of the SA I units.

In instances like these, the recorded single-unit potentials were typically biphasic, with the main phase in the positive direction (Fig. 4), indicating that the electrode tip had partially impaled the myelin sheath of the fibre (Torebjörk *et al.* 1970; Vallbo, 1976).

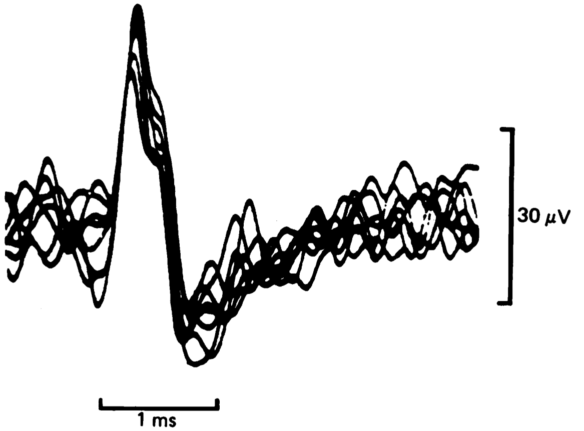

Fig. 4. Superimposed sweeps showing a mainly positive single-unit potential indicating impalement of the myelin sheath by the recording electrode.

When intensities higher than 0·28 V were required to evoke the first elementary sensation, subsequent recording often failed to identify the predicted unit. In those cases the neurogram showed multifibre activity without any particular unit in focus, reflecting that the stimulus current excited fibres which were not close enough to the electrode for individual identification by recording.

Matching type of identified sensory units, with quality of elementary sensations evoked by i.n.m.s.

(*a*) *Stimulation of RA units and sensation of tapping–flutter–vibration.* Fig. 5 shows the receptive fields of thirty-eight identified RA units clustered mainly at finger pulps. Eighteen were pre-identified by recording and twenty predicted by i.n.m.s. The sensation evoked by i.n.m.s. was invariably intermittent tapping at low (1–10 Hz) frequency and oscillatory flutter–vibration at higher frequencies ($<$ 100 Hz). When the oscillatory element progressively fused, close to the region of 100 Hz, the magnitude of the elementary sensation increased such that it was felt stronger without detectable change in frequency. Pressure or tickling were never associated with RA stimulation. The projected fields were small (under 10 mm^2) and were localized close to the receptive fields of the identified units. Single shocks were often detected as single taps from units with receptive fields in finger pulps, whereas a minimum frequency of 5 Hz or more might be required to evoke sensations from RA units with receptive fields proximally in the palm. Three of thirty-eight RA units with receptive fields in the pulp of the thumb, pulp of the index finger and in the proximal palm evoked no cognitive experience, regardless of stimulus frequency. Increasing stimulus amplitude in these three instances recruited various elementary sensations projected elsewhere, but no sensation projected to the appropriate receptive fields.

(*b*) *Stimulation of PC units and sensation of vibration or tickling.* Fig. 6 shows the receptive fields of fourteen PC units in the hand. All were pre-identified by recording. The sensation from i.n.m.s. was typically vibration. Minimum stimulation frequency requirement for conscious detection varied between 10 and 80 Hz. The frequency of perceived vibration increased with stimulation frequency up to 200–300 Hz. The projected fields were comparable in size to those of RA units, and much smaller than the broad receptive fields from which the PC units could be activated by fairly crude natural stimuli. The projected fields were localized close to the areas of maximal sensitivity of the receptive fields. Two PC-like units had receptive maxima in hairy skin of the dorsum of the proximal phalanx of the ring finger. They were particularly sensitive to stroking hairs but also the skin. Intraneural microstimulation evoked ticklish sensations projected to the receptive-field maxima in hairy skin at frequencies of 50–100 Hz. Nothing was felt at lower frequencies. Another two PC units with receptive-field maxima in the pulp of the third finger and in the palm evoked no sensation regardless of stimulus frequency.

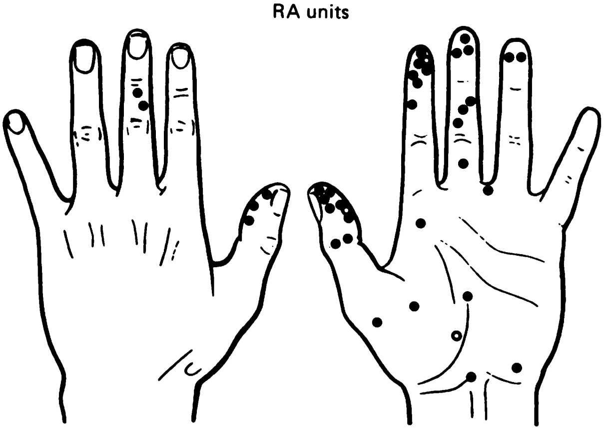

Fig. 5. Location of receptive fields of thirty-eight RA units. Note clustering in finger pulps. I.n.m.s. evoked a conscious sensation from most of the units (●); only three units had no cognitive correlate (○).

(*c*) *Stimulation of SA I units and sensation of pressure.* Fig. 7 shows the receptive fields of thirty-nine SA I units. Twenty-seven were pre-identified by recording and twelve predicted from i.n.m.s. The sensation evoked by i.n.m.s. was invariably pressure, with a *sustained* temporal profile even at low stimulation frequency. This was in striking contrast to the *intermittent* sensations evoked from RA and PC units. Single impulses were never felt. A minimum stimulus frequency of 3–10 Hz was usually required to elicit the sensation of pressure, which increased in magnitude with stimulus frequency. The projected fields were somewhat larger than for RA units and were also quite accurately localized to the corresponding receptive fields.

Eleven of thirty-nine SA I units evoked no sensation: four of these were only tested at 1–10 Hz and it is conceivable that stimulus frequency was below the critical requirement for sensation. The remaining seven units were tested up to 100 Hz and gave no sensory correlate: their receptive fields were localized both in fingers and palm, as indicated in Fig. 7. Proof that some of the single SA I units without sensory correlate had been stimulated by i.n.m.s. was obtained by 'marking' their nerve fibres, as shown in Fig. 8. Following 5–15 min of 200–300 Hz i.n.m.s., at amplitudes which did not induce any sensation, these SA I units became hyperexcitable and generated high-frequency bursts of impulses in response to natural activation of their receptors. Thus, the stimulus amplitudes used for psychophysical testing were high enough to stimulate the units and yet no sensation was perceived.

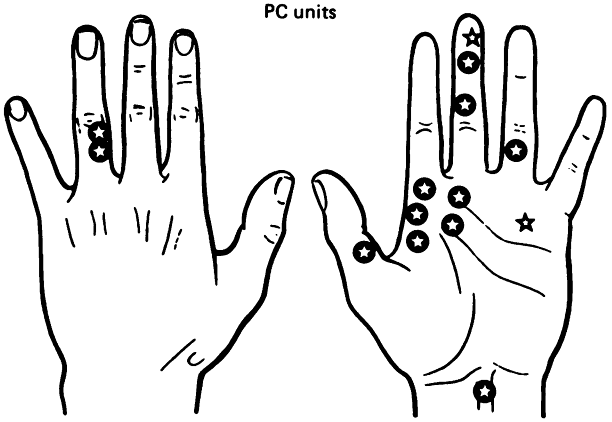

Fig. 6. Location of receptive fields of fourteen PC units. I.n.m.s. evoked sensations from twelve units (encircled stars) and no sensation from two units (stars).

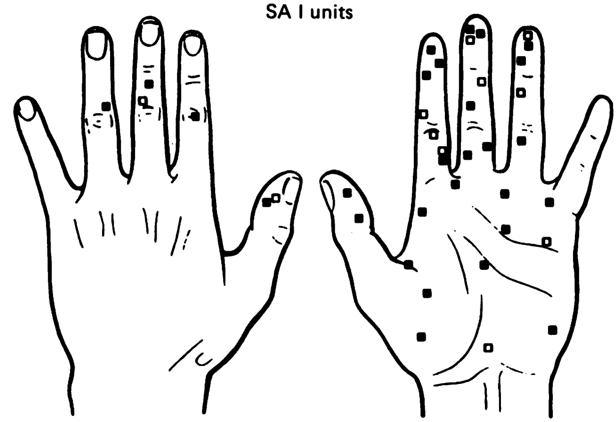

Fig. 7. Location of receptive fields of thirty-nine SA I units. I.n.m.s. evoked a sensation from twenty-eight units (■) and no sensation from eleven units (□).

(*d*) *Stimulation of SA II units without sensation.* Fig. 9 shows the receptive fields of seventeen SA II units. They were all detected by recording. The receptive fields

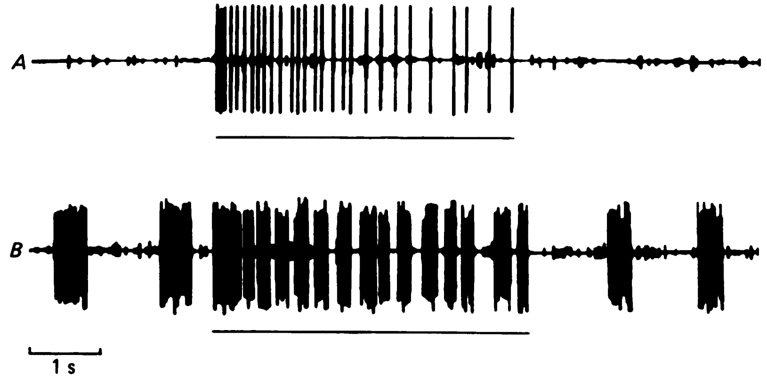

Fig. 8. Response of SA I unit to pressure (horizontal line) before (*A*) and after (*B*) i.n.m.s. at 200 Hz for 10 min. In *B*, post-tetanic spontaneous and triggered bursts of impulses provide evidence of prior activation via i.n.m.s. of this recorded unit.

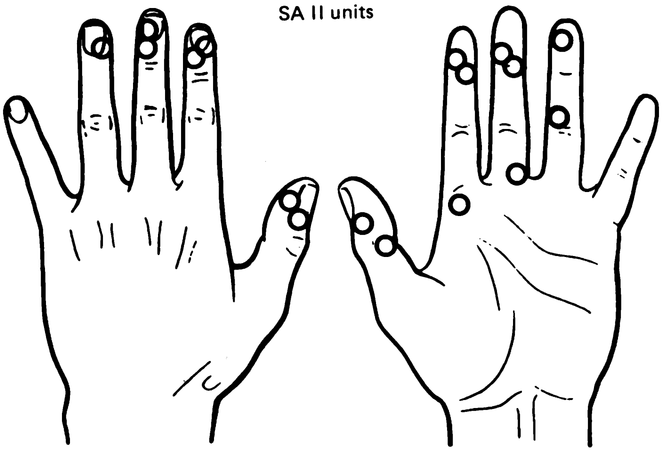

Fig. 9. Location of receptive fields of seventeen SA II units. Note clustering close to nails and joints. I.n.m.s. failed to evoke sensation from any of these units.

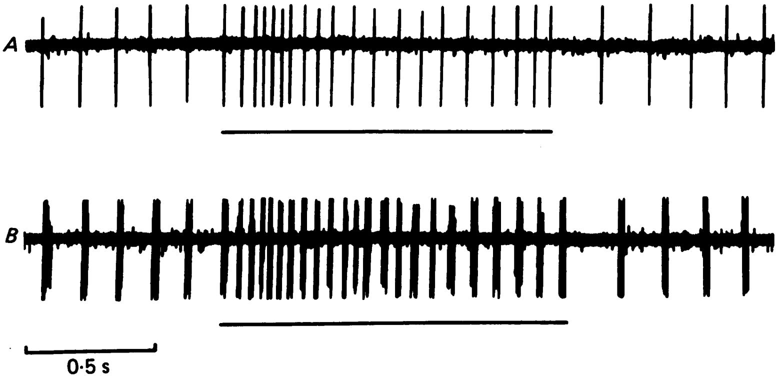

Fig. 10. Response of SA II unit to pressure (horizontal line) before (*A*) and after (*B*) 'marking' by i.n.m.s. at 300 Hz for 10 min. Note hyperexcitability in the form of bursting discharges in *B*, indicating that previous i.n.m.s. had stimulated the fibre. Yet no sensation was reported.

were fairly large and usually found near nails or finger joints. Most of the units had a resting discharge of 5–20 impulses/s and all gave very regular, slowly adapting, responses to pressure, skin stretching or joint movements. The background discharge was temporarily inhibited after such stimuli, as well as while warming the skin. Despite ongoing discharge, no particular sensation was projected to the receptive field of any individual SA II unit. Intraneural microstimulation at frequencies up to 100 Hz always failed to evoke conscious sensation even after priming the subjects for possible tactile or kinetic sensations from skin, nail or joint. Proof that the units had been stimulated by i.n.m.s. was obtained by 'marking' their fibres (Fig. 10).

DISCUSSION

The present results confirm the notion that activation of certain types of single cutaneous sensory units may evoke conscious sensation (Hensel & Boman, 1960; Vallbo & Johansson, 1976; Torebjörk & Ochoa, 1980; Vallbo, 1981). Further, they contribute insight into laws that govern cognition of quality, magnitude and localization of cutaneous sensation and into the roles of specific sensory units in discriminative touch.

The case for isolated activation of single myelinated primary sensory units through i.n.m.s.

(*1*) *Anatomical circumstances.* The subjective attributes of an elementary sensation evoked by i.n.m.s. were thought by Torebjörk & Ochoa (1980) to carry enough of a 'unitary' connotation so as to be construed as tentative criteria for single-unit activation. Indeed, subjective quality plus spatial and temporal features and electrical threshold were seemingly pure or non-divisible. However, it might be argued that any elementary sensation thus evoked results from spatial summation of the input of several units simultaneously activated by i.n.m.s. Although such an accident would not be expected to yield all-or-nothing, qualitatively pure sensations, with clean temporal profiles, it is still conceivable that this could be the case if only units of the same type and identical thresholds were being co-activated for every elementary sensation evoked. On probability grounds this is unlikely in view of the random distribution of myelinated fibre diameters within fascicles. Further, an additional unlikely condition would be required for an elementary sensation to be the result of co-activation: that the fibres co-activated intraneurally should have overlapping or closely neighbouring projected sensory fields. Since we have shown that an elementary projected sensory field predicts the receptive field of a sensory unit, this requires by implication that fibres co-activated in the nerve should have overlapping or closely neighbouring receptive fields in the skin. Although there is some evidence that in cat dorsal root there is a tendency towards microbundling of fibres with common cutaneous origin (Wall, 1960; Merrill & Wall, 1972), the indirect evidence available speaks strongly against the possibility that the same applies to peripheral nerves. Indeed, anatomical tracings of myelinated fibres focally infarcted at one site in a fascicle have documented that degenerated fibres are widely dispersed even a few centimetres away from the injury (Asbury & Johnson, 1978; Parry & Brown, 1981). Also, the psychophysical evidence illustrated in Fig. 1, where elementary sensations recruited from a particular i.n.m.s. site were of different qualities and were projected multifocally to remote skin fields, implies that myelinated fibres that are sequentially stimulated close to the tip of the electrode are of random type and do not have common peripheral origin. As anticipated, it does become less unlikely for neighbouring fibres to evoke sensations with neighbouring projected fields when stimulated at a short distance from their peripheral termination (Schady, Torebjörk & Ochoa, 1983*b*). For that reason, most of the experiments in this study were performed above the elbow, 50 or more cm away from the innervation territory in the hand.

(*2*) *Intramyelin impalement.* Another line of argument in favour of selective stimulation of single units through i.n.m.s. concerns the potential wave forms. In many experiments the positive wave form of the single unit potentials (Fig. 4) indicated that the intraneural electrode tip had actually impaled the myelin sheath of a fibre (Tasaki, 1952). This would create a low-impedance route to the axon which would favour selective recording from that axon and selective activation of the same axon by anodal pulses, otherwise too low in amplitude and of the wrong polarity to activate additional fibres by an extracellular route (Zealear & Crandall, 1982; see also Vallbo, 1981). Thus, in these instances the experimental conditions were propitious for single-unit preparations.

(*3*) *Unitary correlations.* Lastly, the results of the double-electrode experiments, which allowed the afferent traffic along myelinated units excited by i.n.m.s. to be monitored while the subject experienced evoked elementary sensations, provide the best evidence for isolated activation of a single unit as the basis of an elementary sensation. It is not likely that impulses in other axons elicited by i.n.m.s. passed without detection in these experiments, since it has been shown that a recording electrode of the type used can pick up impulses from practically all mechanoreceptive units in a median nerve fascicle (Hagbarth *et al.* 1970) and the distance between the electrodes was so short that escape of fibres to other fascicles was probably negligible. Since the potentials recorded by the proximal electrodes had a triphasic, mainly negative wave form, suggesting extracellular recording from uninjured fibres, it can be accepted that the potentials were propagated centrally and not blocked at the site of recording. The correlations in time between recruitment of each single unit and each elementary sensation, plus the parallel block of impulse conduction and elementary sensations were unambiguously revealing. Finally, the qualities and projected fields of the evoked elementary sensations accurately predicted the types and receptive fields of the units being monitored. Coincidence is but a remote possibility.

On all these grounds we conclude that the described elementary sensations evoked by i.n.m.s. are the result of activation of single myelinated sensory units.

The repertoire of specific elementary sensations evoked via low-threshold mechanoreceptor units from the hand

As defined by their quality and temporal profile, a limited range of elementary sensations can be evoked through i.n.m.s. of single sensory units connected to low-threshold mechanoreceptors in the hand. The sensation of intermittent tapping–flutter–vibration was consistently attributed to stimulation of RA units, sustained pressure to SA I units and vibration or tickle to PC units. Although the subjects experiencing elementary sensations described sensory quality using everyday terminology, the sensations evoked by i.n.m.s. were often not comparable to those evoked by natural stimulation of the skin. This is probably explained by single-unit activation as opposed to natural co-activation. Any natural mechanical stimulus to the skin elicits activity in a number of afferent units of different types, setting up a pattern of impulses in the population of units (Johansson & Vallbo, 1976), which implies that even the simple sensation of 'touch' is normally a composite of discrete elementary sensations. In the light of the present results, for example 'touch' would be expected to contain tapping from RA units, pressure from SA I units and perhaps vibratory elements from PC units. The word 'touch' therefore is an ambiguous expression not suitable to describe the elementary sensations elicited by i.n.m.s. of single sensory units.

Electrical stimulation of the post-central gyrus of awake humans often evokes complex paresthesia-like sensations, probably reflecting co-activation of somatosensory systems (Penfield, 1958; Libet, Alberts, Wright, Lewis & Feinstein, 1975; Libet, 1982). Interestingly, focal cortical stimulation at liminal intensity can evoke simple sensations, like tapping, pressure or vibration, which are comparable to elementary sensations reported here. Libet (1982) has hypothesized that such simple, specific sensations reflect activation of one type of cortical column.

Implicit in the foregoing is the concept of sensory specificity. Indeed, not only do morphologically distinct types of sensory end-organs respond fairly specifically to adequate stimuli, and physiological specificity is maintained through the neuronal chains up to the post-central somatosensory cortex (Mountcastle, 1957; Powell & Mountcastle, 1959), but after by-passing receptors (via i.n.m.s.) in a range of identified units, quality of sensation is specified for unit types (Torebjörk & Ochoa, 1980). No sensation other than pressure came out of SA I unit stimulation, and although tapping became flutter–vibration at higher frequencies of RA stimulation, interconversion between pressure and tapping–flutter–vibration never occurred. In this regard our findings conflict with Vallbo's (1981) report that sensations from RA units were not invariant but 'described as touch, pressure, vibration or tickle, and sometimes as a combination of two of these alternatives'. However, we agree in that temperature sensations were never evoked by i.n.m.s. of low-threshold mechanoreceptor units. We may add that neither pain nor itch were ever evoked by i.n.m.s. of such units, regardless of stimulus frequency.

A possible example of quality indiscrimination is given by the sensation of vibration. It was evoked both from RA and PC unit activation at high frequencies, and subjects denied any recognizable difference. Nevertheless, there was a difference in that the RA system concerned low- and intermediate-frequency events, whereas the PC system preferably concerned high-frequency events. These results are in line with Talbot, Darian-Smith, Kornhuber & Mountcastle (1968), who concluded from correlative studies in the monkey and man that PC units signal high-frequency vibration, whereas RA units signal flutter in the lower-frequency range. Another qualification with regard to specificity is concerned, again, with PC units. Occasionally a sensation of tickling rather than vibration was felt from PC-like unit stimulation. Several explanations are conceivable: (a) subjects may have used tickling and vibration as synonyms, (b) separate subtypes of primary 'PC' sensory units (with separate central end-stations) may not have been discriminated by our method of classification, and (c) separate specific end-stations in the brain might utilize a common morphophysiological instrument in the periphery. At present we cannot comment on the likelihood of any of these possibilities, but note that similar ambiguity may apply to itch *versus* dull pain, either sensation being evoked from stimulation of C polymodal nociceptors (Torebjörk & Ochoa, 1981).

Decoding subjective intensity or frequency of elementary sensations

Since Adrian & Zotterman (1926) showed that increased intensity of a natural stimulus is encoded as increased frequency of neural discharge, it is accepted that frequency of the afferent input is decoded as magnitude of sensation. However, increasing stimulus intensity also recruits adjacent units and so it has remained uncertain how much each mechanism of summation contributes to encoding the magnitude attribute.

The experiments with recruited sensations shed some light on the contribution of spatial summation to sensory magnitude. As long as the projected fields of recruited elementary sensations of the same quality were separate, magnitude of sensation did not increase with recruitment. If the projected fields of similar elementary sensations were overlapping, both magnitude and area of sensation increased with recruitment (see also Schady *et al.* 1983*b*).

That temporal summation of impulses in individual units may be decoded as sensory magnitude was transparent for the sensation of sustained pressure, the magnitude of which paralleled the stimulus frequency for an individual SA I unit. Pressure was already a sustained sensation at detection frequencies of 5–10 Hz, and subjects could not recognize frequency itself. In contrast, increasing stimulus frequency for an RA or PC unit clearly changed the frequency attribute of sensation, although eventually fusion progressively occurred. Beyond fusion, subjective intensity of sensation grew as a function of frequency, at least for RA units. Obviously, the C.N.S. treats the incoming messages differently in these systems. In the SA I pressure system, after-effects of preceding impulses summate temporally to code subjective intensity, but the brain cannot identify the temporal pattern of the code from an individual unit. In the RA and PC systems the impulse frequency is faithfully reproduced and recognized, past the synaptic chain, until submerged by fusion at high frequency. As sensation becomes relatively sustained in the RA system, like it is in the SA I system, subjective intensity increases with frequency. These observations reveal novel aspects of decoding of magnitude at the unitary level in the somatosensory system.

Cerebral localization function

The cortical representation of innervation of the skin, being somatotopically arranged, forms a basis for the cerebral function of localization of cutaneous stimuli. For fingertips, a punctuate touch can normally be localized with millimetre accuracy. To what extent is this refined function dependent upon spatial recruitment of various units? The results of i.n.m.s. reveal something remarkable: that a train of impulses initiated in a single low-threshold mechanoreceptor unit is sufficient to provide fairly good localization (Torebjörk & Ochoa, 1980; Vallbo, 1981). Indeed, when felt, just a single impulse from a single microstimulated RA unit is enough for localization. Thus it emerges that the conscious human brain resolves the body map at the unitary level. Said colloquially, the brain knows the address of cutaneous mechanoreceptors, at least in the fingers.

In view of evidence that the neuronal chains from modality-specific cutaneous receptors project to modality-specific cortical columns (Mountcastle, 1957, 1978), which are actually segregated in multiple somatotopic maps (Paul, Merzenich & Goodman, 1972; Merzenich, Kaas, Sur & Lin, 1978; Dykes, Rasmusson & Hoeltzell, 1980), it is anticipated that differences in the relative localizing accuracy of the various somatosensory modality systems may eventually be shown.

Possible roles of mechanoreceptive units in discriminative touch

The psychophysical data, obtained while stimulating single sensory units in awake subjects, may be examined for an interpretation of how the input from specific somatosensory systems contributes to tactile recognition. The exercise calls for prior consideration of intermediate knowledge gathered on (a) regional gradients of sensory acuity in the hand, (b) sensory detection thresholds *versus* receptor thresholds and (c) temporal resolution mechanisms.

(a) Neurologists have traditionally disclosed regional differences in tactile acuity of the human skin by measurement of two-point discrimination threshold. Microscopists have found anatomical correlates for these differences in the varying concentrations of cutaneous receptors in different regions of the human skin. Sensory physiologists, sampling by microneurography, have contributed a striking illustration of the increasing density of innervation from palm to fingertip (Johansson & Vallbo, 1979*a*). While sampling projected fields via i.n.m.s. also provides a measure of such density gradient in the human hand (see Fig. 5, and also Schady *et al.* 1983*b*), the technique contributes an additional piece of information: there is an extra acuity gradient that concerns detection of impulses from individual sensory units. Johansson & Vallbo (1979*b*) claimed that single impulses evoked by highly controlled natural stimulation of RA units innervating fingertips could be detected, whereas detection of stimuli from such units in the centre of the palm required a larger input. This has now been verified by i.n.m.s. Thus, there are at least two factors determining regional acuity: receptor density in the periphery and differential decoding priority of the brain. A third factor, which concerns sizes of projected fields, is presented in a separate report (Schady *et al.* 1983*b*).

(b) From studies of stimulus–response properties of mechanosensitive units in the human hand, the ranking order of receptor thresholds starting from the lowest is PC, RA, SA I and SA II (Johansson & Vallbo, 1976; Johansson, Vallbo & Westling, 1980). However, when the same types of units are ranked for minimum impulse frequency required for conscious detection of input from single units, the order is RA, SA I, and PC. Also individual SA II units did not evoke sensation during i.n.m.s.; thus, when considered alone, receptor characteristics may provide a misleading measure of the subjective correlates of activity in somatosensory systems.

(c) It is probably no coincidence that trains of impulses initiated from individual RA and PC units evoke sensations with sharply resolved intermittent temporal attributes. Why should this happen with both types of rapidly adapting systems, and only with those types? Presumably, this design provides detection of stimulus occurrence and recurrence, thus registering every physical encounter of the skin, as required in the texture recognition of objects by active touch (Gordon, 1978). This view remains compatible with our psychophysical finding that rapidly adapting systems (at least the RA), in addition to resolving temporally, resolve a magnitude attribute at cognitive levels. However, as described earlier, at the single-unit level such magnitude attribute concerns intensity, rather than velocity of the sensation, as proposed by Franzén & Lindblom (1976) from combined psychophysical and single-unit stimulus–response studies during controlled skin indentation in human subjects. Short of any velocity attribute in the elementary sensations volunteered during i.n.m.s., we share the opinion of Darian-Smith & Oke (1980) that the sensation of velocity of a mechanical stimulus is not based on information from any single unit. We tentatively submit that it is a complex elaboration based on the time interval separating sensations evoked from different units, with acknowledged localization, activated in succession by natural stimulation.

We can now integrate known data on receptor physiology with this new information on cognitive attributes of single-unit activity, and attempt to interpret the roles of various mechanosensitive units in discriminative touch.

The PC units are extremely dynamic and have very low mechanical thresholds and receptive fields with indistinct borders (Johansson & Vallbo, 1976; Johansson, 1978). Their innervation density is relatively low in the glabrous skin of the hand (Johannson & Vallbo, 1979*a*). Their temporal pattern of discharge can reflect the surface pattern of a very fine grating (Darian-Smith, Davidson & Johnson, 1980). The subjective correlates of single PC unit activation include a sensation of vibration or tickle, and a relatively high detection threshold in terms of frequency. Their projected fields are smaller than their receptive fields. The localizing capacity of the PC system coupled with its low mechanical threshold enables it to announce displacement of very light objects causing vibrations while passing over skin irregularities. In everyday tasks of the exploring hand the PC system seems suited to provide an over-all idea of very fine textures without providing a more exact spatio-temporal detail that the RA system probably gives.

RA units are dynamic, have low mechanical thresholds, small receptive fields and high innervation density, particularly in fingertips (Johansson & Vallbo, 1976; Johansson, 1978; Johansson & Vallbo, 1979*a*). Their temporal pattern of discharge reflects the spatial pattern of slightly coarser gratings than do PC units (Darian-Smith *et al.* 1980). Their subjective correlates include a sensation of skin contact at low detection threshold, small and accurately localized projected fields, and faithful reflection of a temporal pattern. They seem ideally suited as instruments to recreate a spatio-temporal image of a textured surface (sandpaper, cloth, etc.) being scanned by the exploring hand. The recognition of texture by active touch involves spatial displacements of skin relative to object along time, an act where the physical details touched are reflected as a spatio-temporal pattern of impulses. Unless the elements of that pattern are decoded as separate cognitive events, interpretation of the physical characteristics of the object would be indiscriminative. The RA system combines excellent requirements for texture recognition, high sensitivity throughout the system, good temporal resolution and precise localization capacity.

SA I units have relatively static receptor responses and higher mechanical thresholds than RA units, in addition to small receptive fields and high innervation density, particularly in fingertips (Johansson & Vallbo, 1976, 1979; Johansson, 1978). They respond to compressive strain in the skin (Phillips & Johnson, 1981*b*), and because of the skin mechanics they are most effectively activated by edges indenting the receptive field (Phillips & Johnson, 1981*a*; Johansson, Landström & Lundström, 1982). Their temporal pattern of discharge can reflect the spatial pattern of fairly coarse gratings (Darian-Smith *et al.* 1980) such as the Braille dot patterns (Johnson & Lamb, 1981). Their cognitive correlates include a sensation of pressure, a detection threshold higher than for RA units, and projected fields which are larger than for RA units but also accurately localized. The SA I system decodes intensity rather than temporal pattern. Regarding the cognitive role of the SA I system in tactile recognition, we necessarily take issue with the view of Harrington & Merzenich (1970), who suggested that SA I input evokes no conscious pressure sensation. Also, there are no grounds in our results for the belief that SA I units have a function in vibration sensation (Järvilehto, Hämäläinen & Laurinen, 1976) although it may be speculated that, through synchronized spatial summation, the SA I system might evoke undulating pressure sensation. Coupling the receptor and the cognitive attributes of the SA I system suggests that it is well suited to create a spatio-intensity image of the size, contour and force exerted by objects indenting the skin. However, for recognition of fine texture through active touch the SA I system would lack the sensitivity of the RA system. The mechanical thresholds of SA I units are higher and they contribute a conscious input which, being temporally summated into a more or less sustained sensation, blurs the ability of sensing each afferent signal as a new cognitive event. Therefore, the SA I system seems less suited than the RA system to recognize the finest details in a changing texture pattern during active touch, an act where space must be translated into a sharp time pattern to recreate faithfully the space image upon decoding. Only a dynamic system can punctually register every physical encounter and thus reflect rapid spatial change.

SA II units are often spontaneously active. They have static receptor responses at high mechanical thresholds (Johansson & Vallbo, 1976). Their receptive fields are fairly large and their receptors respond to remote, directional shearing forces in the skin (Johansson, 1978). Their innervation density is relatively low, with some clustering around nails and finger joints (Johansson & Vallbo, 1979*a*). SA II units evoke no sensation when stimulated in isolation. If they contribute any conscious sensation at all, against the prediction of Harrington & Merzenich (1970), it must be through spatial summation. It is tempting to support the hypothesis that SA II units might contribute proprioceptive feed-back to the motor control of the hand (Knibestöl & Vallbo, 1980; Knibestöl, 1975), for instance in adjustments of grip forces (Johansson & Vallbo, 1983). Whatever sensory role the SA II system might have, it is clearly inappropriate to include it in psychophysical studies in a common parcel with the SA I system. Not only are their primary sensory units different morphologically and physiologically, but from our results it is clear that their central processing is different too.

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