Chapter 1
Sensual Touch: A Slow Touch System Revealed with Microneurography

Åke Vallbo, Line Löken, and Johan Wessberg

Abstract Unmyelinated afferents responding to light touch were first described in furry animals in 1939. In humans, a similar type of afferents was identified about 50 years later (CT, C tactile) using the microneurography technique. CT afferents are present in hairy but not in the glabrous skin. Receptive fields are small (maximal 35 mm^2) and patchy.

Thresholds of CT and Aβ tactile afferents fall in the same range, whereas response properties differ in most other respects. CT afferents exhibit a pronounced and long-lasting fatigue. Maximal impulse rate is about ten times higher in Aβ as CT rate does not exceed 100 impulses s^{-1}.

CT afferents exhibit intermediate adaptation.

A key difference emerges when the dynamic range is explored using light touch stimuli moving over the skin surface. In Aβ afferents, the impulse rate increases monotonously with speed of movement, whereas in CT afferents maximal rate occurs at a fairly low speed (about 1–3 cm s^{-1}) which corresponds fairly well to human caressing movements. The CT response to a moving touch stimulus is dependent on the temperature of the moving object with the optimal response at a neutral temperature. A similar effect is not present in Aβ afferents.

Psychoneural analyses indicate that subjects' estimate of pleasantness during slowly moving skin touch matches the impulse rate of CT when the speed of movement or temperature of the moving object is varied. Aβ afferents do not exhibit a similar correspondence.

Functional properties of CT afferents as well as psychoneural correlations are consistent with the interpretation that the CT system has a key role in physical contact with an amiable conspecific, that is, your parents, lover, kin, or friends. It seems

Å. Vallbo, M.D. • J. Wessberg, M.D., Ph.D. (✉)
Institute of Neuroscience and Physiology, The Sahlgrenska Academy,
University of Gothenburg, Medicinaregatan 11, Box 432, Göteborg SE 405 30, Sweden
e-mail: ake.vallbo@gu.se; johan.wessberg@gu.se

L. Löken, Ph.D.
Department of Anatomy, University of California San Francisco, 1550 Fourth Street, San Francisco, CA 94158, USA
e-mail: linesofie.loken@ucsf.edu

that the social touch hypothesis is a reasonable interpretation of the survival value of a seemingly superfluous tactile system. On the other hand, the exact role of the CT system remains to be clarified.

It is now well established that the human touch system is not as uniform as earlier thought. Innocuous mechanical events are mediated not only by fast-conducting myelinated afferents (Aβ) but, in addition, by slowly conducting unmyelinated afferents (C). Thus, the human tactile system is dual at the level of primary afferents, consisting of a fast and a slow system, differing in conduction velocity by a factor of about 50. Similar dual systems are also present in furry animals. However, different terms and acronyms are currently used for the slowly conducting tactile afferents, that is, CT (C tactile) in human studies and CLTMR (C low threshold mechanosensitive receptors) in studies of furry animals. Still other terms and acronyms may be found in earlier papers. In the present chapter, the term "tactile afferents" is preferred rather than "mechanoreceptive" or "mechanosensitive" afferents as these terms would include units with lower sensitivity which are commonly assumed to have nociceptive functions. To complete the list, it may be noticed that there is yet another set of tactile afferents in furry animals in addition to the fast-conducting Aβ and the unmyelinated CLTMR, that is, thin myelinated afferents (Aδ) which innervate certain kinds of hair follicles (Brown and Iggo 1967; Li et al. 2011). So far, Aδ tactile afferents have not been identified in man, whereas mechanoreceptive Aδ afferents of presumed nociceptive function have been described on the basis of microneurography recordings (Adriensen et al. 1983).

The interest in the unmyelinated tactile system has expanded markedly in recent decades once the idea was launched that the functional role of CT is not in the sensation of tickle as earlier assumed but rather in more fundamental limbic functions, notably in relation to affective touch (Vallbo et al. 1993, 1999). A large number of studies on CT and CLTMR systems have appeared in recent decades using a variety of methods ranging from molecular biology, genetic labeling, and pharmocogenetic activation in rodents, to microneurography, psychophysical investigations, and functional brain imaging in humans (Morrison et al. 2010; Olausson et al. 2010; Vrontou et al. 2013; McGlone et al. 2014). The various experimental approaches have been mutually fertilizing in expanding our knowledge, allowing a deeper understanding of the slow tactile system.

The primary purpose of the present chapter is to give a survey of properties of human CT primary afferents, particularly in relation to current ideas on their functional significance, notably the hypothesis of their role in affective and social touch. The chapter includes due references to data from studies of nonhuman species. This seems appropriate because human CT and CLTMR in furry animals appear to be homologs. On the other hand, studies in rodents indicate that the population of

CLTMR in animals is not homogenous but may include several subgroups, an issue that has not been explored in man.

History

As an introduction, the present chapter starts with a short tracing of the scientific history of the slow tactile system starting with furry animals and proceeding to man.

CLTMR in Furry Animals

Evidence for the existence of a slow tactile system (CLTMR) in animals was first presented almost 75 years ago. In 1939, the Swedish physiologist Zotterman proposed that light touch activates not only large afferents but also small unmyelinated afferents (Zotterman 1939) (Fig. 1.1a). Recording from thin strands of the cat saphenous nerve he noticed that touching the skin on the lower leg produced impulses of three different sizes, designated A beta (β), A delta (δ), and C in accordance with the Erlanger–Gasser scheme (Erlanger and Gasser 1924). He concluded that the C-spikes represent impulses in unmyelinated afferents, although his experimental approach did not allow him to prove this proposal by assessing their conduction velocities. Zotterman emphasized a unique and striking response feature of the low threshold C mechanoreceptive afferents, that is, a prominent and long-lasting after-discharge which was not seen in large diameter tactile afferents. On the basis of this finding, he suggested that unmyelinated tactile afferents might account for the sensation of tickle: "The itching after-sensation to light touch is most probably due to fibers conducting at C rates" (Zotterman 1939). The tickle hypothesis then remained unchallenged for almost five decades.

An important step was taken about 20 years later when Douglas and Ritchie (1957) demonstrated a number of fundamental properties of the slow tactile system using an elegant spike collision technique (Fig. 1.1b). Using a cat saphenous nerve preparation with intact connection to the skin Douglas and Ritchie (1957, 1962) monitored the compound C fiber volley produced by repetitive electrical stimuli. When light tactile stimuli were simultaneously delivered to the innervation zone of the nerve they found a dramatic decrease of one major component of the compound C fiber volley. Their conclusion was that the extinction observed was due to collision of impulses traveling in opposite directions in the same fibers, that is, impulses initiated in sensory terminals by the touch stimuli and impulses elicited by the electric stimuli delivered to the nerve trunk. Thus, they showed beyond doubt that the slow tactile afferents conducted impulses at a speed of about 1 m s^{-1} indicating nonmyelinated axons. In addition, their study demonstrated that these nerve fibers are abundant in nerves innervating hairy skin of the cat.
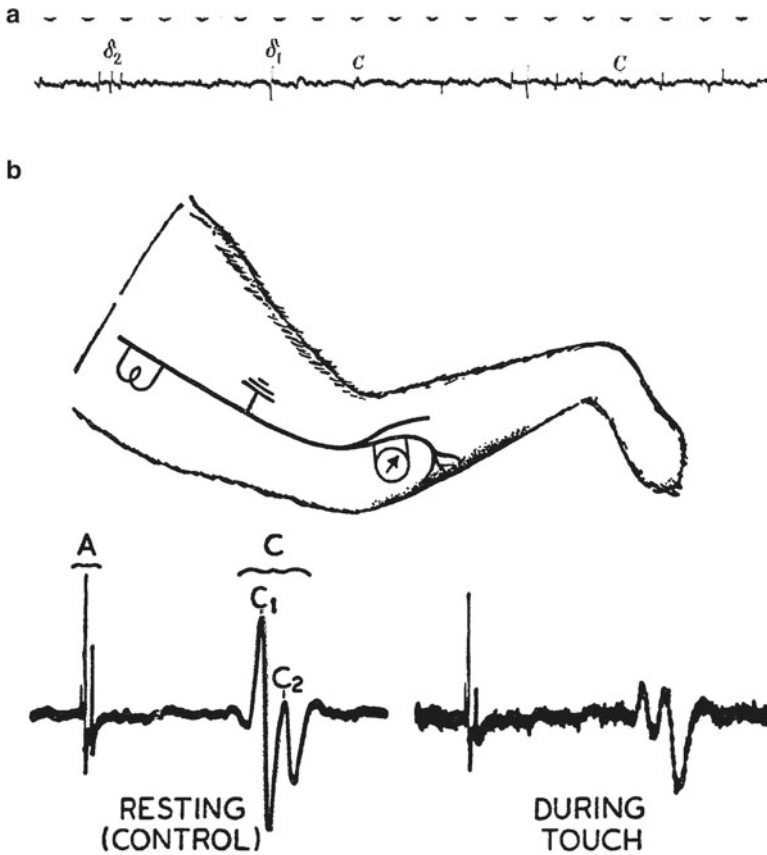
Fig. 1.1 Primary recordings of CLTMR. (**a**) A record from Zotterman's paper 1939 showing Aδ, and C impulses in cat saphenous nerve responding to skin deformation. This publication represents the first recordings ever of single unit impulses in mammalian C fibers. Time 1/50 s. (**b**) Douglas and Ritchie's collision experiment. The cat saphenous nerve was electrically stimulated above the knee to produce a compound action potential which was recorded distally at the level of the knee. The peripheral end of the nerve was kept intact and connected to the skin. Records show the compound action potential consisting of two A components (Aβ and Aδ) and two C components, C1 and C2 as seen in the resting (control) situation (left-hand record). The long latency proves that the C volleys were conducted at a speed of about 1 m s^{-1}. Right-hand record was collected while the innervation zone of the nerve on the lower leg was stimulated continuously with light touch. It may be appreciated that the C1 component markedly decreased in size proving that its constituent fibers responded to innocuous touch. In contrast, the C2 component remained invariant indicating non-tactile functions

Douglas and Ritchie (1957, 1962) were the first to observe another key feature of tactile C axons of interest in relation to recent studies in man. They noticed that the propagation velocity of one component of the compound C fiber volley markedly decreased as a result of preceding activity. Remarkably, the slowing was prominent in nontactile C axons (component C2 in Fig. 1.1b), whereas it was not seen in tactile

axons (component C1 in Fig. 1.1b). (Note that the slowing is not illustrated in Fig. 1.1b.) They concluded that postactivation slowing of impulse propagation is a prominent feature of several kinds of C fibers, whereas it is largely lacking in tactile C afferents. The relevance of this difference for microneurography studies in man will be further discussed in a later section.

Single unit analysis of CLTMR was pioneered by Iggo and coworkers who presented detailed descriptions of response properties to innocuous touch, for example, high sensitivity to skin deformation, large response to hair movements, intermediate adaptation, and pronounced postactivation fatigue effect of the sense organ, which may last up to 30 min (Iggo 1960; Iggo and Kornhuber 1977). In 1971, an important publication from Perl's group (Bessou et al. 1971) emphasized a distinct difference between CLTMR and Aβ tactile afferents with regard to their dynamic response properties. They wrote that as the velocity of a glass rod "stroked across the receptive field … is progressively decreased, the frequency (of the discharge) … first increases and then declines". In myelinated tactile afferents, on the other hand, impulse rate increases monotonously with velocity of touch movement. In spite of the detailed information on functional properties of tactile C afferents extracted in these studies, Zotterman's tickle hypothesis was continuously accepted as it seemed supported by consonant demonstrations of long-lasting after-discharge (Bessou et al. 1971; Nordin 1990). A singular deviation from the tickle idea was advanced already by Douglas and Ritchie in their 1957 paper where they speculated in passing, without advancing any arguments that central effects of tactile C afferents might be at subconscious levels rather than in contributing to conscious percepts.

Identification of CT in Man

For some time low threshold C mechanoreceptors were thought to be lacking altogether in man. Twenty years of microneurography investigations failed to demonstrate them in human nerves, in spite of many studies focused on unmyelinated afferents. Hence, it was generally assumed that the tactile C-system had vanished altogether in the evolutionary progression to man, an idea supported by the finding that CLTMR afferents are less numerous in monkey than in cat nerves (Kumazawa and Perl 1977). The interpretation that human skin is not innervated by tactile C afferents was supported by studies of two different kinds. Psychophysical tests in normal subjects indicated that touch sensibility disappears when large afferents are blocked by pressure (Torebjörk and Hallin 1973; Mackenzie et al. 1975). Similarly, it was reported that the neuronopathy patients have "a total loss of the senses of touch, vibration, pressure and kinaesthesia" (Fourneret et al. 2002; Forget and Lamarre 1990). Neuronopathy is a rare condition when the cell bodies of the large myelinated afferents in dorsal root ganglions have been destroyed bilaterally over many spinal segments either as a complication to a virus disease or from repetitive attacks of polyneuropathy. As a result, only small diameter afferents remain from skin, muscles, and other deep structures. These studies all seemed to support the

prevailing view that tactile information is carried exclusively in large myelinated Aβ afferents. The problems that these patients are facing have been well described in a book written by a physician who carefully studied one of the neuronopathy patients (Cole 1995).

The first description of low threshold C-mechanoreceptive afferents in man was based on recordings from the face area. Nordin (1990) presented a decent sample, although one single unit had been described already 2 years earlier (Johansson et al. 1988). The interpretation that human tactile C afferents (CT) seemed to be present in the face area alone invited speculation that they might have a role in the pathological condition of trigeminal neuralgia (Nordin 1990). However, soon afterwards it was demonstrated that CT afferents are, in fact, quite numerous in hairy skin of upper and lower extremities, suggesting a wide distribution over the human body (Vallbo et al. 1993, 1999; Edin 2001).

It may be asked why microneurography failed to identify CT units during 20 years of intense studies of mechanoreceptive afferents starting in the late 1960s. It seems that two experimental selections were particularly relevant for this odd neglect. First, a major number of microneurography studies on tactile mechanisms were focused on the glabrous skin of the hand where CT afferents were never seen (Johansson and Vallbo 1983). Successively it has become more and more evident that CT are, in fact, lacking altogether in glabrous skin as they have not been reported from any microneurography laboratory. On the other hand, psychophysical findings in studies of mechanisms behind allodynia have suggested that there are afferents that share some properties with CT afferents (Nagi and Mahns 2013). Second, a large number of detailed studies of C afferents were pursued using a particular modification of the microneurography method, that is, the marking technique, described in more detail below (Hallin and Torebjörk 1974; Schmidt et al. 1995). The marking technique has a disadvantage in this context in that it largely fails to catch CT afferents, whereas it is well suited for analysis of nociceptive afferents. This strange effect is due to a unique axonal property of CT afferents as mentioned above, that is, their resistance to postactivation slowing of impulse propagation after repetitive firing. In addition, CT afferents seem to be scarce in the distal parts of the lower leg, which for many years was the region used in studies of nociceptive C afferents.

Microneurography Technique

Our present day knowledge of CT afferents' properties in man is largely based on recordings of impulse trains in single afferent using the microneurography technique developed by Hagbarth and Vallbo in the 1960s (Hagbarth and Vallbo 1968; Vallbo and Hagbarth 1968). A tungsten needle electrode, insulated to the tip, is inserted though the intact skin (Fig. 1.2a). Its position is manually adjusted until the tip attains an intrafascicular position and finally until the electrode discriminates impulses in a single nerve fiber of the kind you intend to study. Examples of single unit recordings from C afferents are shown in several illustrations, for example,
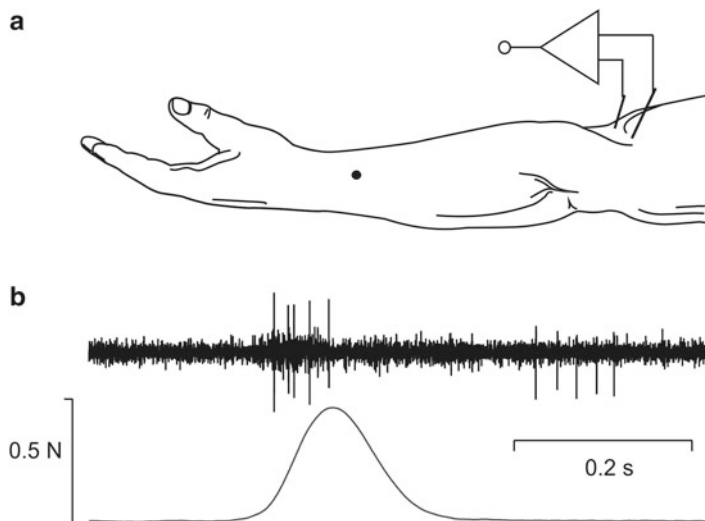
Fig. 1.2 Microneurography recording of tactile afferents. (**a**) Schematic illustration indicating location of touch stimulation on the forearm and recording device with the tungsten needle electrode in a cutaneous branch of the musculocutaneous nerve (lateral cutaneous antebrachial nerve). (**b**) Responses of an Aβ and a CT afferent to a tap stimulus. The two units had overlapping receptive fields located 274 mm from the recording site as schematically indicated in (**a**). The long latency of the CT response indicates a conduction velocity of about 1 m s^{-1}

Figs. 1.4, 1.8, 1.9, and 1.10. The electrode is freely floating in the soft tissue of the target region and it is only manipulated by hand. No micromanipulators or anesthetics are used. It might seem tempting to take advantage of the precision offered by micromanipulators to adjust electrode position, but they have not been found helpful. This is largely due to continuous movements of the target region with cardiac and respiratory cycles. If the electrode was fixed to an external micromanipulator, the tip would continually move within the nerve fascicle making impossible a stable recording of impulses from a single nerve fiber. Figure 1.2b shows a recording, which is unique because the electrode tip has appropriate contact with two tactile afferents having overlapping receptive fields. One is a myelinated Aβ afferent, whereas the other is an unmyelinated CT afferent. The difference in delay from the tap stimulus to impulse arrival at the recording site is striking. The difference in delay from skin deformation to impulse arrival in the brain suggests fundamental functional differences between the fast and the slow tactile system.

Although the microneurography technique is theoretically straightforward, it is in practice demanding, particularly in recordings of impulse trains from identified single nerve fibers. To attain an intrafascicular electrode position and, specifically, to discriminate impulses in a single nerve fiber of the kind you are interested to study may involve hours of manipulation under high mental concentration. Needle adjustments must be repeated in minute steps, guided by high-gain display of signals in the microvolt scale displayed on the computer screen. Important guidance is further

offered through a high-quality audio output from the amplifier where the faint sound of distant impulse trains in contrast to the continuous background of electronic noise and multiunit activity can be discerned. The experimenter is facing a particularly demanding task when exploring afferents from the hairy skin because most of the suitable nerves are very thin and therefore difficult to find and penetrate.

Impulse Shape Distinguishes Unmyelinated Fibers

An interesting and important feature of the microneurography recordings is that impulse shapes of myelinated and unmyelinated afferents are distinctly different. The predominant phase of C fiber impulses is always negative, whereas it is mostly positive in A fiber impulses (Fig. 1.3). C fiber impulses are triphasic suggesting a true extracellular recording. A similar triphasic shape is occasionally seen with myelinated afferents, presumably when the electrode tip is close to the regenerative membrane of a node of Ranvier. However, in the vast majority of single unit recordings from A fibers, impulses are diphasic with the initial and predominant phase in the positive direction. As impulses in multiunit recordings of A fiber activity seem to have similar diphasic shapes, the most reasonable interpretation is that the electrode sees, from an extracellular position, the current flowing through the myelin of the internode.

It should be noted that the electrical equivalent of the microneurography electrode in body tissues is a small capacitor rather than a resistance, in contrast to what one might intuitively presume (Westling 1972). Hence, we have, very likely, a capacitive coupling through the myelin. When impulses of a single A afferent stand out from the background activity by size (Fig. 1.2), the high amplitude is probably a consequence of reduced myelin thickness due to pressure from the electrode.
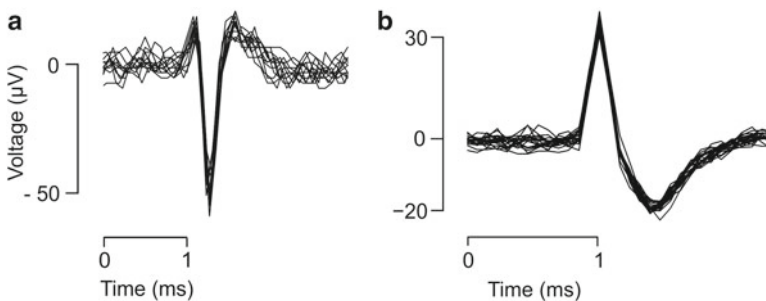

Fig. 1.3 Shapes of C and Aβ impulses in microneurography recording. Typical contours of nerve impulses in unmyelinated (**a**) and myelinated (**b**) nerve fibers. The former are always triphasic with a dominant negative phase, whereas A spikes are nearly always diphasic with the dominant phase in positive direction

More complex shapes are occasionally seen. In long-lasting recordings, the predominant phase of A fiber impulses may develop two peaks, due to a local conduction delay. The phenomenon is consistent with the interpretation that the electrode causes a thinning of the myelin to the extent that a fair amount of the depolarizing current is lost to the outside at the electrode site (Vallbo 1976; Inglis et al. 1996). Similar phenomena are never seen with C fibers.

Marking Technique

An important modification of the original microneurography technique was introduced by Hallin and Torebjörk (1974). The modification has been denoted the marking technique. It is based on a unique feature present in most kinds of unmyelinated axons; a pronounced decrease of conduction velocity in the wake of preceding impulses. Separate classes of unmyelinated nerve fibers exhibit different degrees of postactivation axonal slowing allowing clear identification.

The marking technique is highly rewarding in analyses of C afferents as it allows the identification of several units in a single recording. On the other hand, its potential is limited compared to impulse train recordings in analysis of stimulus response relations, dynamic characteristics of sense organs, and psychoneural correlation studies.

Moreover, as pointed out above the marking technique is ineffective with CT afferents because they exhibit very little axonal slowing and therefore cannot readily be identified.

Subject Care in Microneurography Experiment

In microneurography experiments, it is important to pay proper attention to the subject's emotional state and reactions. Although pain is seldom intense, there is still a risk of vagal reactions with unpleasant dizziness, or occasionally even fainting, probably more related to subject's worry in combination with exotic sensations rather than sheer pain. It is important that the experimenter strives to establish a confident relationship and prepare the subject in detail for the sensations to come when the needle electrode goes through the skin, the subcutaneous tissue, and through the nerve sheath. Ideally, the experimenter should have the experience of being a subject herself/himself to be able to give a well-informed introduction. Although pain is not prominent, the demand on the subject is considerable because she/he must keep an almost identical position for hours. Small and relatively slow movements of limbs are acceptable, whereas electrode position is jeopardized by many moderate limb movements.

Psychoneural Potential

An essential advantage of the microneurography technique is that anesthetics are not involved. Hence, sense organs and afferents are unaffected and, as subjects are fully awake, they may report in detail their sensations and cooperate in psycho-physical and psychomotor tests while impulses in a single afferent are monitored. An illustrating example concerns the tickle hypothesis. Subjects' reports of their cutaneous sensations during microneurography recordings have amply demon-strated that there is no correlation between CT-firing and tickle sensation (Wiklund-Fernström 2004). This provides a direct argument against the tickle hypothesis which had been cherished for decades in the literature.

An additional tool for psychoneural correlation analyses is offered by the combi-nation of microneurography recording, microstimulation, and psychophysical tests. Microstimulation of an identified afferent allows the assessment of effects of an individual afferent in the alert human brain, perceptive as well as neurophysiologi-cal (Trulsson et al. 2001; Ochoa and Torebjork 1983; Vallbo et al. 1984). This approach has been successful with large myelinated nerve fibers, whereas micro-stimulation of single unmyelinated afferents has not been accomplished. This is very likely related to the well-known fact that the threshold for excitation with elec-trical pulses is inversely related to fiber diameter. The high intensity required to excite an unmyelinated nerve fiber will inevitably excite a number of adjacent myelinated fibers as well.

Distribution, Terminal Organization, and Axonal Properties

The presence of the slow tactile system has been verified in the skin of face, fore-arm, and leg. More specifically, afferent impulses in unmyelinated CT fibers have been recorded in the small supra- and infraorbital nerves innervating facial skin, in lateral and dorsal ante-brachial cutaneous nerves innervating the hairy skin of the forearm and hand dorsum, and in the lateral cutaneous femoral and peroneal nerves innervating the thigh, lower leg, and the foot (Johansson et al. 1988; Nordin 1990; Vallbo et al. 1993, 1999; Edin 2001; Wessberg et al. 2003; Löken et al. 2007, 2009). On the other hand, nerves innervating the skin of the trunk have not been exploited so far. Although these findings strongly suggest that CT innervation of human skin is ubiquitous, a distinct exception is indicated by the fact that CT has never been encountered in recordings from the glabrous skin of the hand in spite of extensive analyses of tactile afferents in this skin area. Further, there is no indication that the lack of CT recordings from the glabrous skin can be ascribed to experimental fac-tors because an identical approach and recording technique was used in explora-tions of hairy and glabrous skin. Moreover, the difference between hairy and glabrous skin in man is consistent with findings in cats, rodents, and nonhuman primates where the slow tactile system, that is, CLTMR afferents have never been found in nerves supplying foot pads or monkey glabrous skin. As in humans,

CLTMRs are abundant in hairy skin of these species (Bessou et al. 1971; Kumazawa and Perl 1977; Georgopoulos 1976; Liu et al. 2007). However, interspecies correlations must not be stretched too far in these respects considering that animal CLTMR include several functional groups of different properties and recent psychophysical studies argue that CT functional homologues might be present in human glabrous skin (Nagi and Mahns 2013).

Why No CT in Glabrous Skin?

It seems tempting to search the explanation in evolution for the difference between glabrous and hairy skin regarding CT innervation in man.

The pad skin of furry animals which is the homologue of human glabrous skin was primarily designed to take the wear and tear of walking and running. It was equipped with fast-conducting mechanosensitive afferents with the prime role to provide information required for the control of muscle actions, whereas it is not used in affective touch in most species as far as we know. Hence, CT innervation would be superfluous in pad skin of many nonprimate mammals. The human hand, on the other hand, has achieved a number of additional and more complex tasks, one being caressing gestures in affective conspecific touch. It seems that the primary mechanoreceptive innervation of the pad skin consisting of fast-conducting Aβ afferents alone has been preserved during evolution in spite of the potential role of human glabrous skin in affection. However, the quality of pleasant sensation that humans experience when being touched on glabrous and hairy skin differs to some extent as demonstrated in psychophysical tests and neuroimaging studies (Löken et al. 2009; McGlone et al. 2012; Ackerley et al. 2014a, b; Guest et al. 2014).

Density of CT Afferents

Although microneurography is not suited for the assessment of proportion of separate types of mechanoreceptive afferents in a nerve, a qualitative statement seems warranted on the basis of the common experience that CT afferents are encountered roughly as often as Aβ units in forearm skin nerves (Vallbo et al. 1999; Löken et al. 2009). This finding suggests that the density of CTs is at least as high as the density of Aβ units. This conclusion seems particularly justified since the microneurography technique should favor large nerve fibers. A monkey study indicates a proximodistal gradient with fewer CLTMR in the distal parts of the extremities (Kumazawa and Perl 1977). A similar gradient is suggested in a human study focused on distal hairy skin (Löken et al. 2007). Only a few CT afferents were found on hand dorsum and in lower leg in recordings from the radial and peroneal nerves. For instance, in the peroneal nerve only 3 CT were identified in 14 experiments. As considered in a previous section, the shortage of CTs in the distal parts of the lower extremities might be one factor why CTs failed to be recognized in man for so long.

To summarize, present data suggest that CTs are abundant in the hairy skin of the human body, scarcer in the distal parts of the extremities and seem to be lacking altogether in the glabrous skin.

The human findings on this point fit with recent studies in rodents using genetic labeling and visualization of axonal endings in skin and spinal cord. Cell counts revealed that CLTMR cells constitute a very large proportion in dorsal root ganglions (DRG), by far outnumbering low-threshold Aβ mechanoreceptive afferents (Li et al. 2011). Higher densities of CLTMR cells were found in DRG innervating proximal limb areas and trunk than in segments innervating distal limb areas. Interestingly, CLTMR cells are particularly numerous in sacral segments which innervate the genital region although CLTMR afferents seem to be lacking in the nonhairy skin of rodent genitalia (Li et al. 2011, suppl. material). Moreover, it was shown that CLTMR terminals are absent altogether in rodent pad skin, as considered above.

Receptive Field Characteristics

The receptive field of a cutaneous mechanoreceptive afferent is usually defined as the skin area where adequate stimuli are effective to produce afferent impulses. It should be noted that this definition is not very distinct because the extent of the effective skin area is dependent on stimulus characteristics. For instance, in the study to be described below, a doubling of indentation force increased measured field size, on the average, by a factor of 2. Receptive fields have often been assessed using von Frey bristles (Iggo 1960; Bessou et al. 1971; Iggo and Kornhuber 1977; Kumazawa and Perl 1977; Shea and Perl 1985; Nordin 1990). A widely accepted convention is to define the field as the area where a four to five times threshold stimulus is effective (Johansson and Vallbo 1980). The von Frey approach is informative, but it is not optimal for a more detailed analysis of field topography. The findings presented below and in Fig. 1.5 are based on a more sophisticated technique. A light probe was made to move in closely adjacent tracks over the relevant skin area of the subject's forearm while single unit impulses were continuously captured for offline analysis (Fig. 1.4) (Wessberg et al. 2003). Using this approach it was found that human CT fields ($n=9$) vary considerably in size and complexity (Fig. 1.5). It may be a single spot, about 0.25 mm^2 in size or it may include up to

Fig. 1.5 Topography of sample receptive fields in human hairy skin. Field maps are based on data collected with the scanning method illustrated in Fig. 1.4. The two left-hand panels show the smallest and the largest CT field encountered. The other panels show typical fields of four kinds of Aβ tactile afferents identified in human hairy skin, that is, SAI (Merkel), SAII (Ruffini), hair, and field units. Note scale differences demonstrating larger receptive fields of hair and field units. One kind of mechanoreceptive afferent is lacking, that is, Pacinian type which is encountered only occasionally in hairy skin nerves. The procedure to produce the color-coded plots involves a certain degree of smoothing of contrasts. Hence, the true fields are more ragged than shown in the illustration
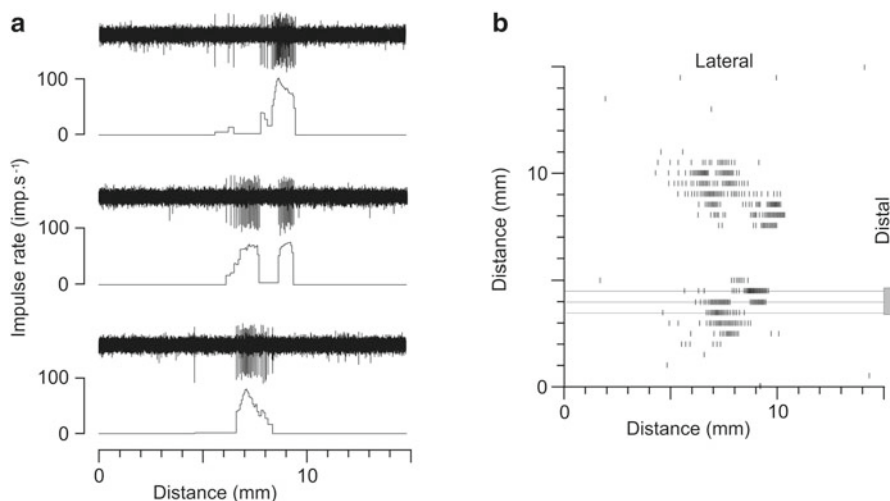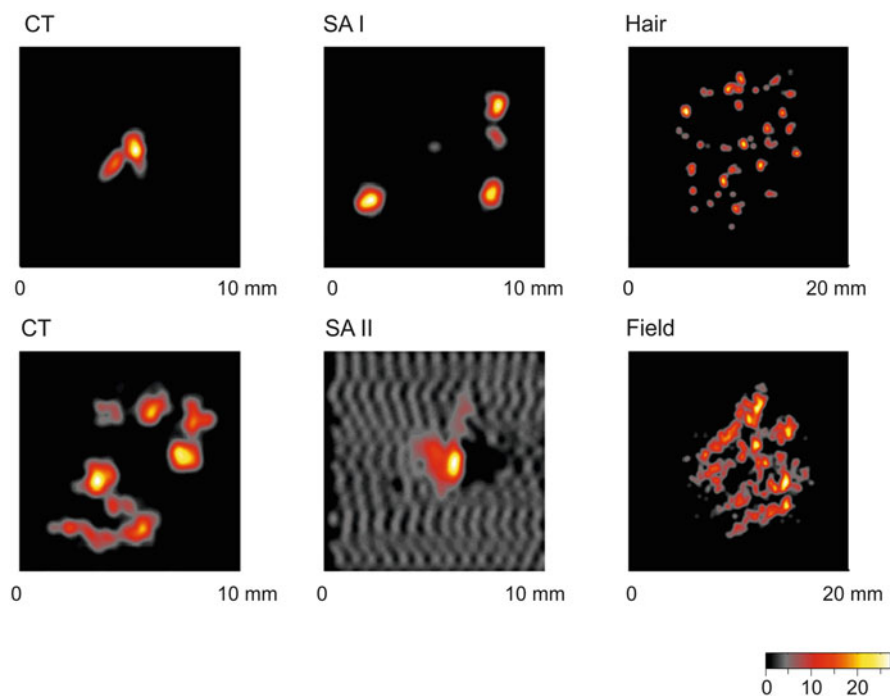
Fig. 1.4 Scanning procedure to explore receptive field topography. (**a**) Responses of a CT afferent to a scanning probe moving over the skin surface in three adjacent tracks, 0.23 mm apart. Indentation force was 2.2 mN. (**b**) XY plot of total scanned area of a CT field. Impulses are indicated by *vertical lines*. The three traces shown in (**a**) are indicated with *thin lines* in (**b**)

nine hotspots distributed over an area of 35 mm^2; mean field size was 7 mm^2 (s.d. 8 mm^2). The separate hot-spots within an individual field varied to some extent in sensitivity, as well as in size as illustrated in Fig. 1.5. Fields are roughly oval in shape with no preferred orientation. No dependence on location along the forearm emerged. This field analysis indicates that the stem fiber of a CT afferent commonly branches to terminate with a varying number of clusters of sensory terminals irregularly distributed within a relatively small area, rather than providing a continuous mesh of responsive terminals as suggested by many previous studies based on handheld field exploration. Fields of similar structure and size have been described for presumed CLTMR afferents in the mouse hairy skin on the basis of histochemical methods (Liu et al. 2007). On the other hand, studies in rodents indicate that the population of CLTMR in animals is not homogenous but may include several subgroups, an issue that has not been explored in man. Hence, it is not valid to stretch interspecies uniformities too far.

Conduction Velocity

The slow impulse propagation in CTs is readily demonstrated in microneurography recordings using tap stimuli where the long latency from stimulus to impulse response is easily perceived through headphones or loudspeakers. Particularly striking is the contrast between CT and myelinated responses where the latter are perceived to occur right at the onset of stimulus, whereas CT impulses occur much later due to a 30–50 times difference in propagation velocity (Fig. 1.2). Conduction velocity of CT afferents is about 1 m s^{-1} (0.6–1.2 m s^{-1}) as assessed from the unit's response to mechanical stimuli. Activation of the afferent by electrical pulses which bypasses several peripheral processes gives a slightly shorter latency and hence a higher conduction velocity (about 10 %). Data from the two modes of stimulation correlate well ($r = 0.8$), indicating that distinct tap stimuli are adequate to demonstrate conduction velocity in the C fiber range. Neither significant correlation has been found between conduction velocity of individual afferents and location of receptive field along the extremity, nor with other functional properties of CT units.

Conventional Test Stimuli Demonstrate Functional Differences Between Aβ and CT Systems

A traditional approach to assess physiological properties of cutaneous mechanoreceptors is to explore responses to perpendicular skin indentations. A number of fundamental features are usually assessed with this technique, for example, threshold, sensitivity, response characteristics to static and dynamic skin deformations, adaptation, and dependence on previous history. This approach is adequate to investigate basic properties and define distinctive characteristics suited for comparison

with other kinds of mechanosensitive units, that is, nociceptive and Aβ afferents. However, analyses of CT response to perpendicular indentations fail to capture essential features of the CT system which are significant for the current hypothesis on its role in affective and social touch. Accordingly, we consider separately conventional analyses using local skin indentations, on the one hand, and analyses which are largely driven by the social touch hypothesis, on the other.

Sensitivity

One aspect of mechanoreceptor sensitivity is the absolute threshold, that is, the minimal stimulus required to evoke a response. This is most easily explored using handheld von Frey bristles providing threshold values in terms of indentation force. A sample of C mechanoreceptive afferents is illustrated in Fig. 1.6 (Vallbo et al. 1999). The primary inclusion criteria were conduction velocity in the C range and response to innocuous finger stroking over the skin surface. The fact that the histogram of Fig. 1.6 is bimodal suggests that innocuous touch activates two types of C afferents. As will be further considered below, several findings indicate that the left-hand group represents CT afferents, whereas the right-hand group represents non-CT afferents. Thresholds of the CT sample are 0.3–3 mN with a median of 1.3 mN ($n=24$). Values
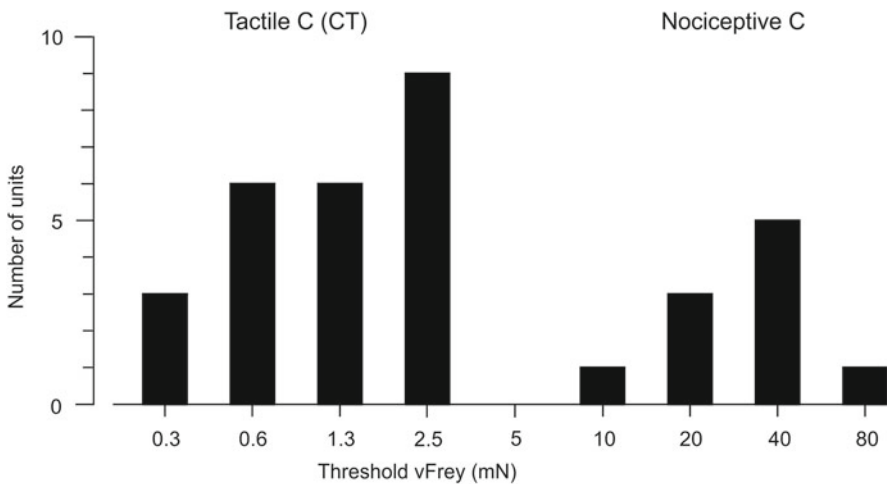

Fig. 1.6 Absolute thresholds of C mechanoreceptive afferents. Thresholds of 34 unmyelinated afferents as assessed with von Frey bristles. Inclusion criteria were any impulse response to innocuous touch beside conduction velocity in the C range. Left-hand group represent CT afferents. Their thresholds ranged from 0.3 to 2.5 mN with a median of 1.3 mN ($n=24$). The right-hand group represents non-CT afferents usually denoted nociceptive mechanoreceptive afferents

above 5 mN suggest non-CT afferents which are commonly classified as nociceptive units. They do respond to innocuous touch but just weakly, producing one or a few impulses to finger stroking.

Although the von Frey bristle approach to assess force threshold is simple in principle, the procedure requires due experience as well as attention to the possible fine grain topography of the receptive field. Obviously, if the bristle fails to hit the most sensitive spot within the receptive field, a higher value than the minimal is collected. Therefore, it might be misleading to emphasize moderate discrepancies between threshold data collected in different laboratories (Nordin 1990; Vallbo et al. 1999).

It is of interest to compare sensitivities of CT and Aβ afferents. Unfortunately, strictly comparable observations are scant but available data suggest average force thresholds of CTs are roughly twice that of Merkel and presumed Meissner's in the hairy skin (SAI and RA/FAI). More specifically, Meissner and Merkel thresholds of 0.5 mN have been reported in studies of facial and forearm skin respectively (Meissner, facial skin, $n = 6$, median; Merkel, forearm skin, $n = 10$, mean) (Johansson et al. 1988; Vallbo et al. 1995).

It should be evident from the threshold data presented above that light touch will excite both myelinated and unmyelinated afferents. Hence, stimuli targeted for CTs must be based on other response properties than sensitivity to local indentation.

Impulse Rates

Although the sensitivity is similar in the slow and the fast tactile systems in terms of threshold to von Frey bristles, the response properties differ between CT and Aβ afferents in many other respects as will be exposed in the following sections. A striking difference refers to the range of impulse frequencies. Maximal rate is much lower in CT than in Aβ afferents which may produce 800–1500 impulses s^{-1} as shown in animal experiments (Burgess et al. 1968; Iggo and Muir 1969). Figure 1.7 illustrates that stroking with a soft brush across CT receptive fields evokes peak impulse rates between 50 and 100 s^{-1} in a majority of the afferents. Although these rates are not very impressive compared to firing of Aβ afferents, they are, in fact, relatively speaking very high considering that maximal rate of C mechanoreceptive afferents as found in animal experiments is 100 impulses s^{-1} (Iggo 1960). Incidentally, the bottleneck is probably not the axon because it has been found that cat CLTMR afferents may carry about three times higher impulse rates when stimulated with electrical pulses (Franz and Iggo 1968).

As might be expected from interunit variation in force threshold of CT afferents, response to suprathreshold stimuli varies between individual CT afferents as well. Figure 1.7 shows that maximal firing rate to the semistandardized stimulus (brush stroking) is higher the lower the threshold of the unit as assessed with von Frey bristles. Thus, it seems that these two measures essentially capture the same property of the individual afferent. The histogram of Fig. 1.6 shows that threshold difference between borderline CT and borderline nociceptive afferents is not large. Moreover, the scatter plot of Fig. 1.7 might suggest a continuum between the two
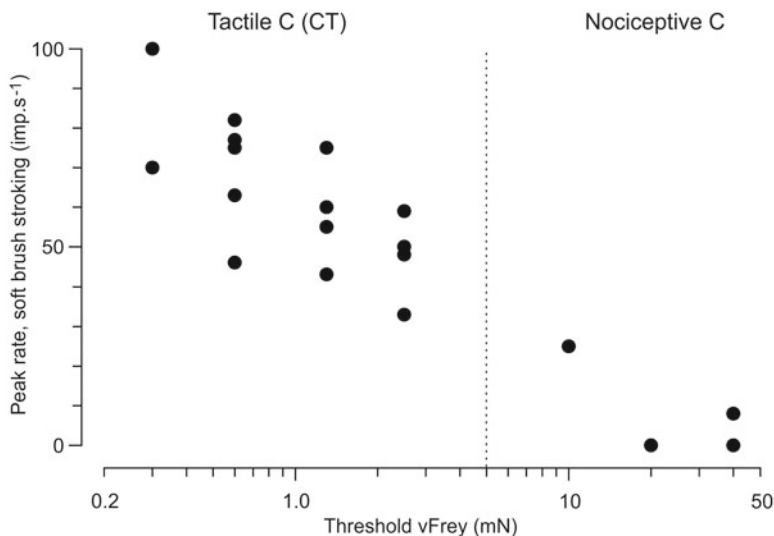
Fig. 1.7 Impulse rate to light touch stimulus versus afferents' thresholds. Peak rates to soft brush stroking over the receptive field versus von Frey thresholds. Units with thresholds above 5 mN are classified as nociceptive afferents. Subsample of the material shown in Fig. 1.6

kinds. However, a distinct difference emerges when responses to noxious and innocuous stimuli are compared (Nordin 1990; Vallbo et al. 1999). The left-hand traces in Fig. 1.8 illustrate that CT responses are similar with the two kinds of stimuli in spite of the marked difference in sensation produced by the pointed and rounded probe employed. In contrast, responses of the nociceptive afferent differ substantially because the response to the noxious stimulus is prominent, whereas the innocuous stimulus gives no response in this test (Fig. 1.8, right-hand traces). The examples of Fig. 1.8 are representative. Moreover, the difference is supported by statistical analyses, although the sample is small (Wilcoxon $P < 0.01$, $n = 5$). A further analysis with focus on borderline afferents would be of interest to test the suggestion that CTs regularly fail to distinguish between noxious and innocuous stimuli, whereas another set of C afferents (nociceptive) readily do.

Fatigue and Recovery

A distinguishing response feature of CT-units versus myelinated tactile units is that sensory endings of CTs exhibit a pronounced postactive depression. This fatigue effect is illustrated in Fig. 1.9a, showing a marked decrease of the response after a single stimulus. When a series of successive indentations are delivered, the response usually decreases with the first 2–4 stimuli to settle around a submaximal level which is dependent on interstimulus interval, as illustrated in Fig. 1.9b. Incidentally,
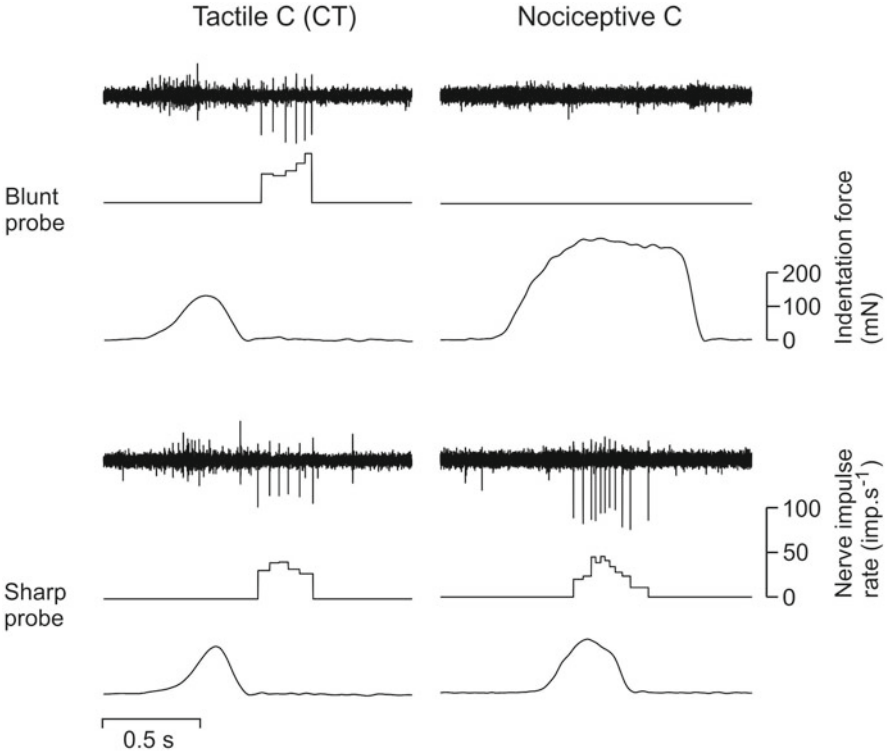
Fig. 1.8 Difference between CT and nociceptive C response to mechanical stimuli. Stimuli were local skin indentations delivered with a blunt probe (*above*) and a pointed probe (*below*), both connected to a handheld strain gauge device
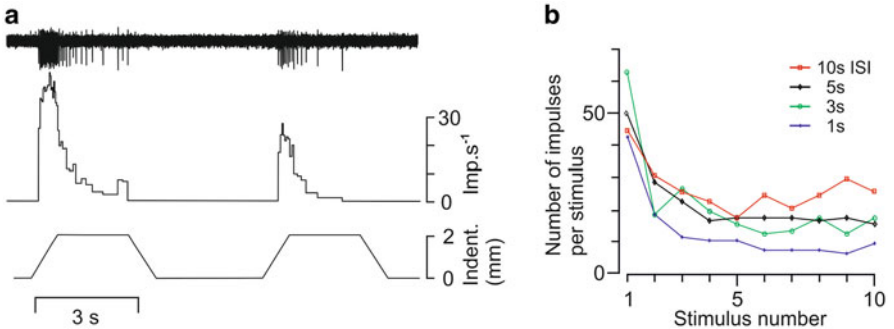

Fig. 1.9 Fatigue in a CT afferent. (**a**) Record shows the marked difference between the response to the initial stimulus and the second one delivered shortly (3 s) later. A resting period of about 60 s preceded the first stimulus. (**b**) Fatigue curves of a CT afferent repeatedly stimulated as in Fig. 1.9a at varying intervals. *Blue*, *green*, *black*, and *red curves* represent data with pauses of 1, 3, 5, and 10 s between stimuli, respectively
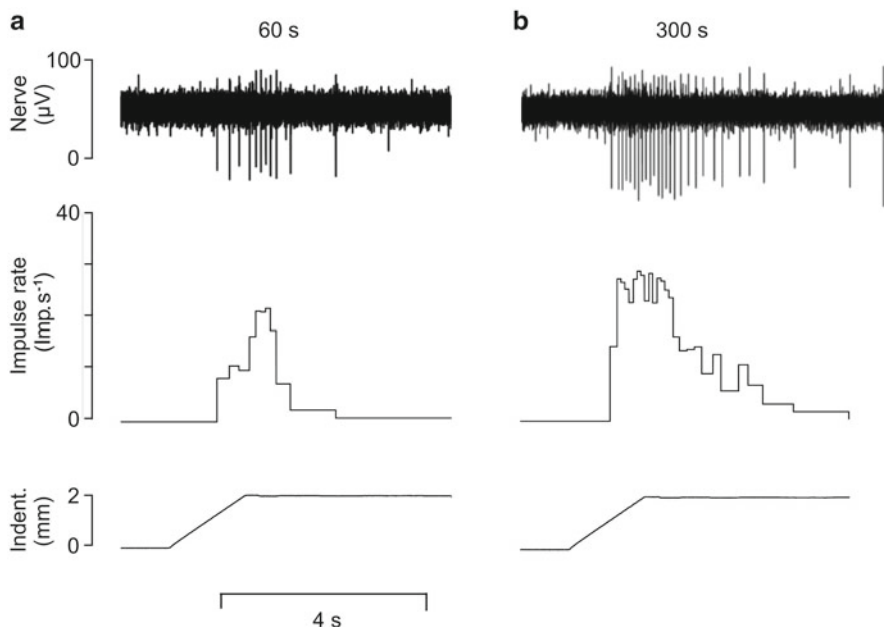
Fig. 1.10 Long-term postactivation recovery. Records show responses of a CT afferent to identical stimuli delivered after resting periods 60 and 300 s length

the curves in Fig. 1.9b illustrate a phenomenon consistently encountered in studies of CT afferents in man, that is, that the response to identical stimuli varies substantially from one test stimulus to the other for reasons which remain to be explored.

Another unique property of CT afferents is that the postactivation fatigue may be very long lasting. This is illustrated in Fig. 1.10 by the difference in response to identical stimuli which are delivered after a recovery period of 60 s versus 300 s. It may be appreciated that the response after the longer resting period is substantially larger in terms of impulse rate, number of impulses, as well as duration of discharge. There are indications that full recovery may take several minutes. However, systematic analyses regarding development of fatigue and time course of recovery remain to be pursued in man. In studies of cat CLTMRs, it has been pointed out that restoration may take several (4–30) minutes (Iggo 1960; Iggo and Kornhuber 1977). Mechanisms accounting for the depressant effect of preceding mechanical stimulation have not been explored in man. However, an analysis of cat CLTMRs suggests that important factors are transducer-bound events rather than events in conducting elements of the terminal arborization (Iggo and Kornhuber 1977). The slow recovery process implies that CT afferents are substantially more responsive to an initial touch stimulus than to succeeding stimuli. It may be speculated that the system is designed to make us more inclined to appreciate a friendly touch when first perceived. It remains to be explored if larger hedonic effects can be documented in psychophysical tests and in fMRI explorations when a skin area has remained untouched

long enough to have the CT population fully recovered. In addition, the pronounced and long-lasting fatigue in CT afferents may have significant implications of relevance for interpretation of certain microneurography findings. It seems likely that most, if not all, published CT data have, in fact, been collected from fatigued units considering that the search procedure in the experiments involves continual stroking of the test area. As a result, it must be assumed that CT units are depressed from maximal responsiveness already in the initial part of the experiment. Hence, the probability is low of encountering an unfatigued CT afferent. Occasional observations seem to support this interpretation. In a small minority of experiments, we have encountered a dramatically deviant activity, that is, a uniquely strong response to a light touch followed by an intense and long-lasting after-discharge. This kind of response has been rarely seen and only in the very beginning of an experimental session. Unfortunately it has not been possible to document this impressive response.

Adaptation

Another clear difference between the slow and fast tactile afferents concerns the response to sustained skin deformations. Aβ afferents fall in two distinct groups in this respect. Fast adapting units respond to dynamic events alone, but not to steady-state deformation, that is, they lack all static sensitivity. This is true with Pacini, Meissner, hair follicle, and field units. Slowly adapting Aβ afferents (Merkel and Ruffini), on the other hand, provide a continuous discharge during sustained skin deformation for minutes or more, albeit at a decreasing impulse rate over time. CT afferents, on the other hand, differ from both types, because they have intermediate adaptation properties in the sense that they respond initially with a burst of high impulse rate which successively decreases to zero after a few seconds of sustained indentation as illustrated in Figs. 1.9, 1.10, and 1.11a. Occasionally, an even more deviant response of CT afferents has been seen, that is, a late resumption of firing while a steady indentation is maintained. Figure 1.11b shows a representative example of delayed acceleration. It may be appreciated that the activity decreased to nearly null for a few seconds after the initial response to skin deformation. Then firing reassumed and continued for about a minute. The impulse rate was first highly irregular followed by a period of more regular discharge. Impulse rate increased to a peak of about 50 impulses s^{-1} and then fell to zero within 40 s after the peak. Among the CT afferents that exhibit delayed acceleration, the time course varies between tests and units. The example in Fig. 1.11 is an extreme whereas the duration is shorter in most cases. As the response to long-lasting steady indentation has not been systematically tested, the proportion of units exhibiting delayed acceleration is not clear, but it seems to be present in only a minority of units.

The mechanisms and the functional significance of delayed acceleration remain to be explored. On the other hand, the finding is of some interest from psychoneural point of view because the subjects consistently reported no change of the sensation when the intense firing of the CT afferent occurred. Thus, it seems that activity in a single CT afferent fails to influence the sensation of sustained skin deformation.
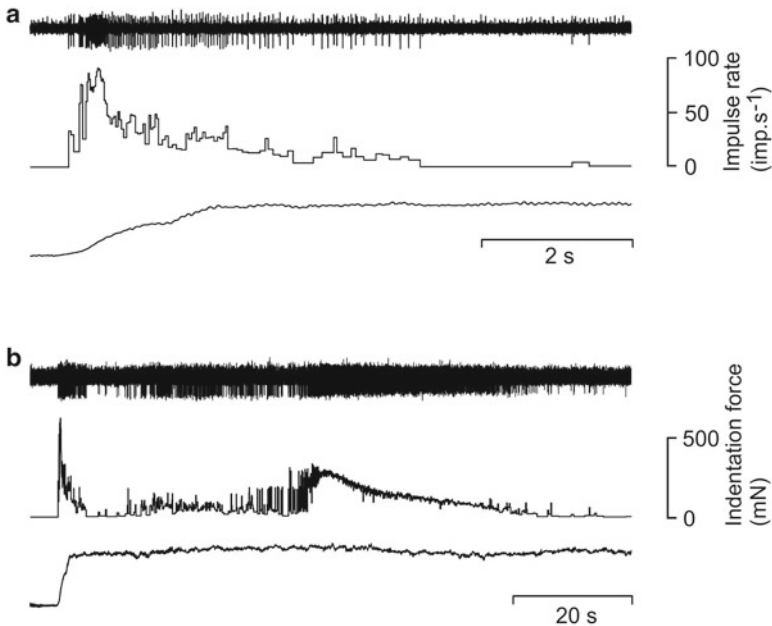
Fig. 1.11 CT response to sustained indentation. (**a**) Sample record to illustrate intermediate adaptation typical for CT. (**b**) Delayed acceleration of impulse discharge started after about 10 s. (**a**, **b**) Originate from the same recording displayed on different time scales

After-Discharge and Tickle Hypothesis

Long-lasting after-discharge in thin mechanoreceptive afferents was originally described by Zotterman (1939) in the cat and led him to formulate the tickle hypothesis, that is, that an essential role of unmyelinated tactile afferents is to account for the ticklish sensation associated with light touch. Microneurography studies confirm that there is a marked difference between the fast and the slow tactile systems in man with regard to after-discharge. In Aβ afferents, there is usually no activity after stimulus removal, whereas a prominent and sometimes long-lasting after-discharge is seen in CTs as illustrated in Fig. 1.12. On the other hand, after-discharge in CT afferents is highly dependent on temperature, as it is more frequent and more prominent at lower than neutral temperatures. In a sample of 15 CT units, after-discharge was seen in 80 % at 15 °C, but in only 13 % at higher temperatures (32 and 42 °C) (Wiklund-Fernström 2004).

Qualitative observations on psychoneural correlations, including delayed acceleration considered above, suggest that there is no correlation between tickle sensation and discharge in CT afferents. Moreover, it has been repeatedly observed that neuronopathy patients who lack large mechanoreceptive afferents cannot be tickled (Cole et al. 2006). These two findings seem to provide strong evidence for the interpretation that tickle sensation is not dependent on unmyelinated CT afferents but rather on Aβ afferents.
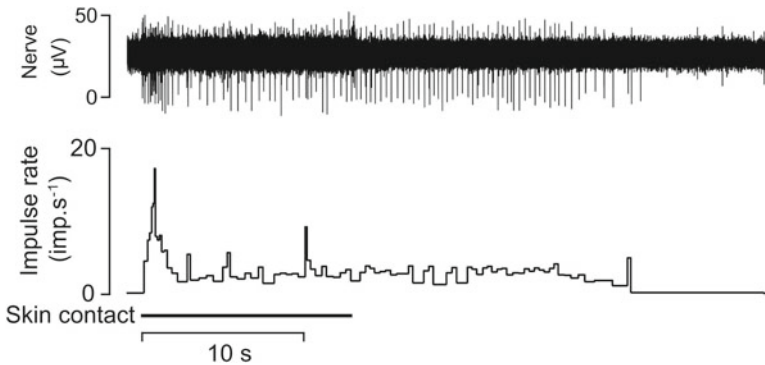
Fig. 1.12 After-discharge at low temperature. Sustained indentation indicated by bar was followed by an unusually long-lasting after-discharge which usually occurs with low temperature only. Skin temperature 15 °C
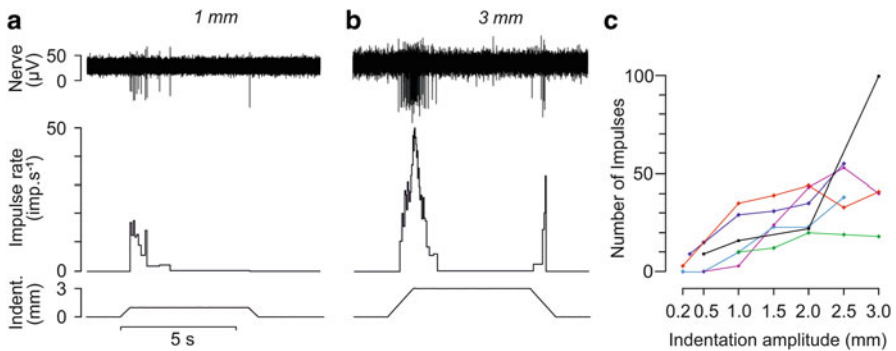

Fig. 1.13 Dependence of CT response on indentation amplitude. (**a**, **b**) Sample records from an afferent stimulated with two different indentation amplitudes. Note off responses. (**c**) Stimulus response curves for six CT afferents demonstrating effect of indentation amplitudes

Response to Amplitude of Skin Deformation

As with other kinds of cutaneous mechanoreceptive units, CT afferents are sensitive to the amount of local skin indentation as illustrated in Fig. 1.13. However, a difference is that CT afferents tend to respond less consistently to local indentations than Aβ mechanoreceptive afferents. Hence, stimulus response relation curves often emerge as irregular, nonmonotonous, and highly varying between individual CT units (Fig. 1.13c). No attempt has been made to explore which factors may account for the poor consistency of the CT response in man. However, it is noteworthy that the finding shown in Fig. 1.13c seems to clash with data from a study of CLTMR afferents in the cat where high correlations are reported between indentation amplitude and unit response (Iggo and Kornhuber 1977). To what extent this difference is related to heterogeneity of CLTMRs in furry animals remains to be explored.

Response to Hair Movements

Qualitative observations indicate that human CT afferents do not regularly respond to hair movements. A small response may be seen with large hair movements, possibly due to deformation of the skin outside the hair follicle. Whether CTs are excited by movements of the small vellus hairs has not been specifically tested, although it seems unlikely because air puffs are generally not effective (Ackerley et al. 2014a, b). These observations are in marked contrast to findings on CLTMR response in furry animals. A number of electrophysiological studies emphasize response to hair movements (Iggo 1960; Iggo and Kornhuber 1977; Douglas and Ritchie 1957) although there is a single exception (Bessou et al. 1971). Moreover, recent morphological studies using molecular-genetic labeling show that CLTMR regularly innervate hair follicles in rodents (Li et al. 2011; Zimmerman et al. 2014).

Psychoneural Analyses Indicate Hedonic Potential of the CT System

In response to a moving touch stimulus most mechanoreceptive afferents respond with higher impulse rate the faster the movement. However, this is not true with CT afferents. A unique feature of particular significance for the hedonic touch hypothesis is their relatively poor response to fast-moving stimuli (Nordin 1990; Vallbo et al. 1999). Figure 1.14 illustrates that human CTs respond with a similar impulse rate when a probe is moving across the skin at a low speed and at a five times higher speed. A more detailed analysis of CT impulse rate as a function of speed of a touch stimulus moving over the skin surface is illustrated in Fig. 1.15a.
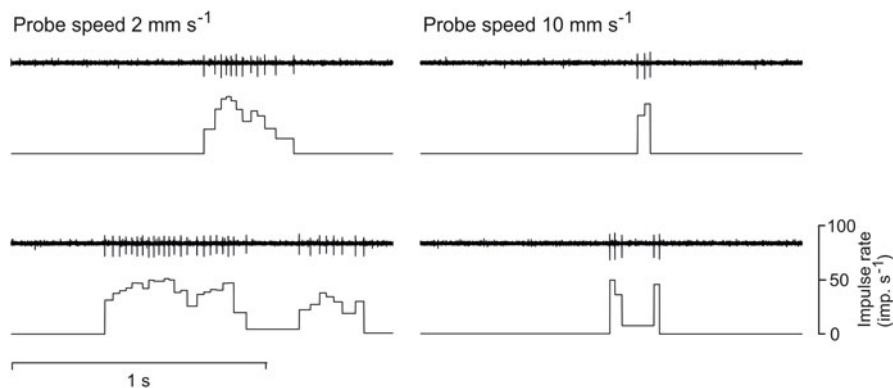

Fig. 1.14 Low sensitivity of CT afferents to speed of a moving stimulus. Responses of two afferents (upper and lower records) to touch stimuli moving over the skin surface at two different speeds. Indentation force was 2 mN. Stimulus delivered with a rounded probe
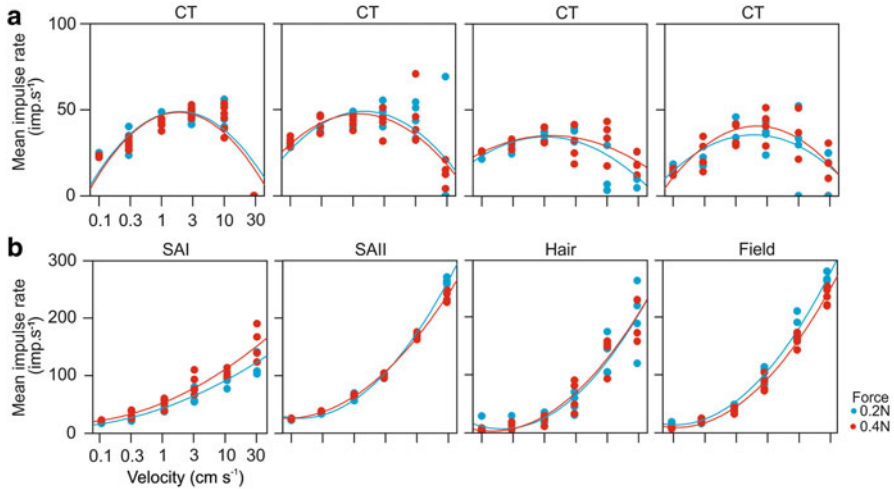
Fig. 1.15 Responses to moving touch stimuli. Contrast between Aβ and CT afferents. CT exhibit tuning to intermediate speeds of movement, whereas all types of Aβ afferents exhibit monotonous increase of impulse rate with speed of movement. Panels show data from individual units. Two different indentation forces (0.2 and 0.4 N) as indicated by *color code*. Stimulus was delivered with of a soft water color brush moving along the skin surface. Note difference in Y-scales with CT and Aβ units

The response increases to a peak at stroking velocities in the range 1–10 cm s^{-1}, whereas it levels off at higher and lower speeds. Hence, human CT afferents are tuned to a relatively slow speed of movements across the skin (Löken et al. 2009; Ackerley et al. 2014a, b). In contrast, impulse rates in Aβ mechanoreceptive afferents increase monotonously with the speed of a touch stimulus moving over the skin surface as illustrated in Fig. 1.15b for four different types of tactile afferents in the hairy skin.

For most people, a caring hand slowly moving over your skin surface gives a more pleasant sensation than a fast movement (Essick et al. 1999). A pertinent question is to what extent our feeling of pleasantness may match the impulse rate of the CT afferents. Figure 1.16 illustrates that subjects' estimates of pleasantness (middle diagram) are similarly tuned to the speed of movement as the response of CT afferents (left-hand diagram). The correlation between the two measures is highly significant (right-hand diagram) (Pearson's linear regression, $R^2 = 0.70$, $P < 0.001$) (Löken et al. 2009). On the other hand, there is a striking mismatch between the estimate of pleasantness and impulse rates of the myelinated tactile afferents as is obvious from data in Figs. 1.15 and 1.16. The difference between firing of CT and Aβ mechanoreceptive afferents in relation to subjects' estimates of pleasantness provides a direct support for the role of CT afferents as a system of significance for boosting the hedonic aspect of skin contact.

It is noticeable that the tuning of unmyelinated tactile afferents to relatively slow velocity of stimuli moving across the skin surface was described in the cat already in
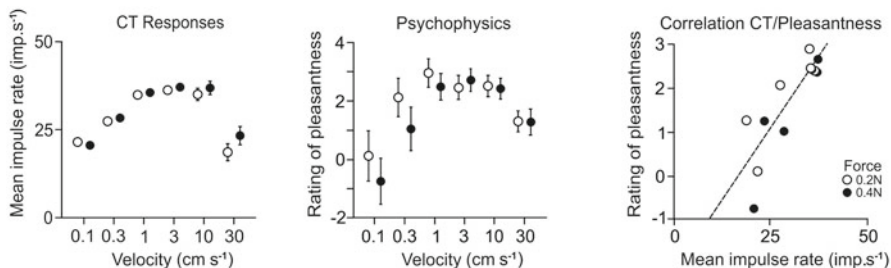
Fig. 1.16 Psychoneural relations between CT afference and pleasantness. Plot in *left-hand panel* demonstrates tuning of CT afferents ($n=16$) to intermediate velocities of soft brush stroking. *Middle panel* shows subjects' estimates of pleasantness as a function of speed of soft brush stroking ($n=10$). *Right-hand panel* demonstrates that the correlation between subjects' estimates of pleasantness and CT impulse rates is highly significant (Pearson's linear regression $R^2=0.70$, $P=0.00063$)

1971 by Bessou et al. They pointed out that "the receptors respond more vigorously to an object moving at certain slow speeds across the skin than to one which moves more rapidly. … Whether central sensory systems utilize this peculiarity of responses is unknown." Obviously, time was not ripe at that time for a discussion of this observation in relation to the emotional impact of skin-to-skin contact. In fact, hypotheses of affective touch were never considered in animal studies of unmyelinated tactile afferents. In contrast, up to the 1990s, studies of cutaneous mechanoreceptive mechanisms were highly focused on discriminative touch (Kanel et al. 2013).

The hedonic effect of a caressing movement is dependent not only on the mechanical and kinetic characteristics of the stimulus but also on the temperature of the touching object. Obviously, in most situations one would not feel a cold or a hot object as very pleasant. The significance of the temperature was explored to assess whether CT response and estimates of pleasantness would be consistent with the affective touch hypothesis. When responses to slowly moving objects of three different temperatures were tested, a very pertinent response pattern emerged that seems not only consistent with the hedonic touch hypothesis but also, in fact, directly supporting it (Ackerley et al. 2014a, b). Left-hand diagram of Fig. 1.17 illustrates that a slowly moving object of neutral temperature was more effective than a warmer or cooler object in activating CT afferents. Moreover, subjects' feelings of pleasantness were optimal when the temperature of the moving object was neutral but suboptimal when the moving object was warmer or cooler (middle diagram). In fact, the correlation between CT firing and subjects' estimates of pleasantness was highly significant with neutral temperature (right-hand diagram), whereas the correlation was nonsignificant when the object was cooler or warmer (not illustrated). With Aβ afferents there was no such effect of temperature because their response was basically identical at the three different temperatures.

To sum up, two key features of caressing gestures were tested in the studies illustrated in Figs. 1.15, 1.16, and 1.17. The findings demonstrate significant correlations between CT activity and estimates of pleasantness when two different stimulus parameters were varied, that is, the speed of an object moving over the skin surface
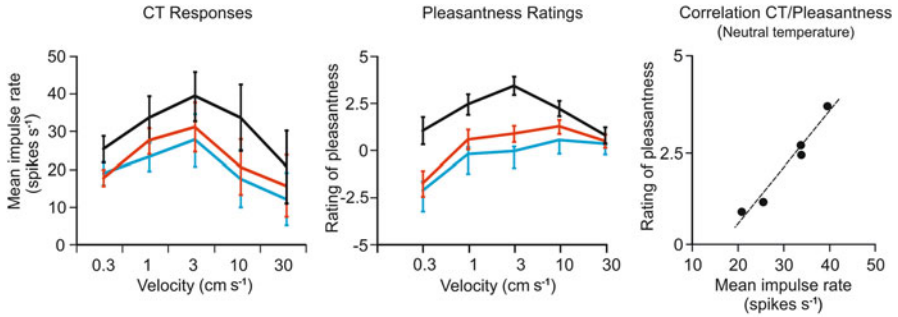
Fig. 1.17 Dependence of psychoneural relation on temperature of moving touch stimuli. Left-hand plot shows CT response ($n = 8$) to an object moving over the receptive field at different speeds. Three different object temperatures are color coded: *black*—neutral, *red*—warm, and *blue*—cool. *Middle plot* shows subject's estimates of pleasantness with the same stimuli. *Right-hand plot* shows correlation between estimates of pleasantness and CT firing rates with the object having neutral temperature. The correlation was highly significant ($R^2 = 0.96$, $p = 0.003$). whereas correlations were insignificant with warm or cool object stimulation (not shown)

as well as the temperature of the moving object. It seems that these two sets of correlations provide a strong support for the hedonic touch hypothesis which argues that the role of CT afferents, within the realm of perception, is to boost the feeling of pleasantness when touched by a friendly human being.

Functional Role of the CT System

The human CT system has attracted a remarkable interest in recent years. In contrast, its homolog in furry animals, that is, the CLTM system, was not much discussed until the CT system was identified in man. The interest in the human CT system is probably not only due to a new sensory system having been discovered. Even more important might be the nature of the hypothesis advanced regarding the functional role of the CT system, that is, the affective touch or social touch hypothesis. This working hypothesis ascribes to the CT system a unique role very much different from ideas previously considered among sensory physiologists.

The role of the CT system is not primarily to satisfy the need of a wide range of factual information about distinct features of mechanical events at the skin surface. This kind of information is amply provided by the fast Aβ system. The role of the CT system is rather to capture the particular features of skin deformation which indicate gentle bodily contact with an amiable individual. Thereby the system would boost the emotional effects of closeness to a friendly conspecific. The system would be of significance in supporting feelings of pleasure (reward), confidence, comfort, and security as you are close to your parents, lover, kin, or friends. Moreover, it may have a role in hormonal responses as well as in bonding individuals emotionally together.

The attraction as well as the problems with this hypothesis is to a great extent related to the idea that the CT system is conceptually deeply embedded in the complex emotional system of the human brain.

The hypothesis claims tight links between sensory input provided by a seemingly superfluous sensory system, on the one hand, and emotional responses which would contribute to the mental and physical well-being of the organism, on the other. Hence, the hypothesis puts the CT system side by side with a number of other small fiber systems which have the role to report the state of physical and chemical variables in the body which are essential for the control systems guarding the well-being of the individual (Craig 2002, 2008).

Scientists engaged in the CT system are facing demanding and exceptional problems due to the nature of the central effects ascribed to the CT system. The effects are obscure and diffuse compared to those commonly discussed in relation other cutaneous afferent systems. The complex mechanisms involved in emotional response to intersubject skin contacts make the task of pinpointing the exact role of the CT system particularly demanding. This is partly due to the response to touch by another individual being highly dependent on a number of contextual factors, for example, the social relation between the two and the actual emotional state of the person being touched. Moreover, the fact that another sensory system, that is, the Aβ system, is always activated along with the CT system and has the potential to capture all details of cutaneous stimuli, even those that seem relevant for social touch, is another complication for understanding and clarifying the exact role of the CT system.

With regard to the strict sensory effect, it is important to emphasize that selective stimulation of human CT afferents does not produce a clear and vivid sensation of pleasant touch as demonstrated in neuronopathy patients (Olausson et al. 2002). These patients report weak, vague, and inconsistent sensations of touch, sometimes reported as pleasurable, when innocuous skin stimuli are delivered. Hence, it seems obvious that the full sensation of pleasant touch by a close and amiable individual is dependent on sensory input in the two tactile systems. When considering the affective touch idea as a working hypothesis, it seems important to point out that only two alternative hypotheses have been discussed during the 75 years since the unmyelinated system was first identified in furry animals and then later in humans First, the tickle hypothesis, which has been refuted by observations in microneurography experiments showing lack of correspondence between CT activity and tickle sensation, and neuronopathy patients who lack large myelinated afferents are not aware of being tickled, indicating that the sensation of tickle is dependent on large myelinated afferents rather than unmyelinated nerve fibers. The other alternative hypothesis that has been aired in informal discussions is that the CT system might be essential in shaping somatotopic maps in the sensory cortex. The idea stems from studies in nonhuman species indicating that unmyelinated mechanoreceptive afferents may play an essential role in these complex processes (Calford and Tweedale 1991). Importantly, these studies emphasize that the C afferents involved in body surface mapping are sensitive to capsaicin, suggesting nociceptive afferents. Animal studies indicate that CLTMR are not sensitive to capsaicin (Foster and Ramage 1981; Kenins 1982; Vrontou et al. 2013) as is true with human CTs (Wiklund-Fernström 2004).

To sum up, there is essentially no experimental support for the two alternatives to the social touch hypothesis. Rather, available data speak against them. In contrast, a number of observations are consistent with the social touch hypothesis. Evidence from psychoneural correlation studies strongly suggest that CT activation is associated with hedonic effects. Moreover, supporting findings are provided by studies of CLTMR system in rodents. Particularly interesting is the demonstration that pharmacogenetic activation of one part of the CLTMR system has a positively reinforcing effect on behavior suggesting an anxiolytic potential (Vrontou et al. 2013).

At present, the affective touch hypothesis is the most promising and most stimulating interpretation of the functional role of the CT system. In spite of the difficulties to design conclusive tests, it seems important to explore further the CT afferents and their central connections. The more we know about the system the more we will be able to test and refine the social touch hypothesis—or any alternative idea that might eventually be proposed to explain the survival value of a seemingly superfluous tactile system.

References

Ackerley R, Backlund Wasling H, Liljencrantz J, Olausson H, Johnson RD, Wessberg J (2014a) Human C-tactile afferents are tuned to the temperature of a skin-stroking caress. J Neurosci 34(8):2879–2883

Ackerley R, Saar K, McGlone F, Backlund Wasling H (2014b) Quantifying the sensory and emotional perception of touch: differences between glabrous and hairy skin. Front Behav Neurosci 8:34

Adriensen H, Gybels J, Handwerker HO, van Hees J (1983) Response properties of the thin myelinated (A-delta) fibers in the human skin. J Neurophysiol 49:111–122

Bessou P, Burgess PR, Perl ER, Taylor CB (1971) Dynamic properties of mechanoreceptors with unmyelinated (C) fibers. J Neurophysiol 34:116–131

Brown AG, Iggo A (1967) A quantitative study of cutaneous receptors and afferent fibres in the cat and rabbit. J Physiol 193(3):707–733

Burgess PR, Petit D, Warren RM (1968) Receptor types in cat hairy skin supplied by myelinated fibers. J Neurophysiol 31(6):833–848

Calford MB, Tweedale R (1991) C-fibres provide a source of masking inhibition to primary somatosensory cortex. Proc R Soc Lond B Biol Sci 243:269–275

Cole J, Bushnell MC, McGlone F, Elam M, Lamarre Y, Vallbo A et al (2006) Unmyelinated tactile afferents underpin detection of low-force monofilaments. Muscle Nerve 34:105–107

Cole J (1995) Pride and a daily marathon. The MIT Press, Cambridge

Craig AD (2002) How do you feel? Interoception: the sense of the physiological condition of the body. Nat Rev Neurosci 3:655–666

Craig AD (2008) Interoception and emotion. In: Lewis M, Haviland-Jones JM, Barrett LF (eds) Handbook of emotions, 3rd edn. Guilford Publications, New York, pp 272–288

Douglas WW, Ritchie JM (1957) Non-medullated fibres in the saphenous nerve which signal touch. J Physiol 139:385–399

Douglas WW, Ritchie JM (1962) Mammalian nonmyelinated nerve fibers. Physiol Rev 42:297–334

Edin BB (2001) Cutaneous afferents provide information about knee joint movements in humans. J Physiol 531:289–297

Erlanger J, Gasser HS (1924) The compound nature of the action current of nerve as disclosed by the cathode ray ocillograph. Am J Physiol 70:624–666

Essick G, James A, McGlone FP (1999) Psychophysical assessment of the affective components of non-painful touch. NeuroReport 10:2083–2087

Franz DN, Iggo A (1968) Conduction failure in myelinated and non-myelinated axons at low temperatures. J Physiol 199(2):319–345

Forget R, Lamarre Y (1987) Rapid elbow flexion in the absence of proprioceptive and cutaneous feedback. Hum Neurobiol 6:27–37

Foster RW, Ramage AG (1981) The action of some chemical irritants on somatosensory receptors of the cat. Neuropharmacology 20(2):191–198

Fourneret P, Paillard J, Lamarre Y, Cole J, Jeannerod M (2002) Lack of conscious recognition of one's own actions in a haptically deafferented patient. Neuroreport 13(4): 541–547

Georgopoulos AP (1976) Functional properties of primary afferent units probably related to pain mechanisms in primate glabrous skin. J Neurophysiol 39(1):71–83

Guest S, Essick GK, Mehrabyan A, Dessirier J-M, McGlone F (2014) Effect of hydration on the tactile and thermal sensitivity of the lip. Physiol Behav 123:127–135

Hagbarth K-E, Vallbo ÅB (1968) Discharge characteristics of human muscle afferents during muscle stretch and contraction. Exp Neurol 22:674–694

Hallin RG, Torebjörk HE (1974) Methods to differentiate electrically induced afferent and sympathetic C unit responses in human cutaneous nerves. Acta Physiol Scand 92(3):318–31

Iggo A (1960) Cutaneous mechanoreceptors with afferent C fibres. J Physiol 152:337–353

Iggo A, Kornhuber HH (1977) A quantitative study of C-mechanoreceptors in hairy skin of the cat. J Physiol 271:549–565

Iggo A, Muir AR (1969) The structure and function of a slowly adapting touch corpuscle in hairy skin. J Physiol 200(3):763–796

Inglis JT, Leeper JB, Burke D, Gandevia SC (1996) Morphology of action potentials recorded from human nerves using microneurography. Exp Brain Res 110(2):308–314

Johansson RS, Trulsson M, Olsson KÅ, Westberg K-G (1988) Mechanoreceptor activity from the human face and oral mucosa. Exp Brain Res 72:204–208

Johansson RS, Vallbo AB (1980) Spatial properties of the population of mechanoreceptive units in the glabrous skin of the human hand. Brain Res 184(2):353–366

Johansson RS, Vallbo ÅB (1983) Tactile sensory coding in the glabrous skin of the human hand. Trends Neurosci 6:27–32

Kandel ER, Schwartz JH, Jessel TM, Siegelbaum SA, Hudspeth AJ (eds) (2013) Principles of neural science, 5th edn. McGraw-Hill, New York

Kenins P (1982) Responses of single nerve fibres to capsaicin applied to the skin. Neurosci Lett 29(1):83–88

Kumazawa T, Perl ER (1977) Primate cutaneous sensory units with unmyelinated (C) afferent fibers. J Neurophysiol 40:1325–1338 (They point out that CT are scarce in distal arm regions)

Li L, Rutlin M, Abraira VE, Cassidy C, Kus L, Gong S, Jankowski MP, Luo W, Heintz N, Koerber HR, Woodbury CJ, Ginty DD (2011) The functional organization of cutaneous low-threshold mechanosensory neurons. Cell 147(7):1615–1627

Liu Q, Vrontou S, Rice FL, Zylka MJ, Dong X, Anderson DJ (2007) Molecular genetic visualization of a rare subset of unmyelinated sensory neurons that may detect gentle touch. Nat Neurosci 10:946–948

Löken LS, Wessberg J, Olausson H (2007) Unmyelinated tactile (CT) afferents are present in the human peroneal and radial nerves. Society for Neuroscience Abstracts Online 827.2

Löken LS, Wessberg J, Morrison I, McGlone F, Olausson H (2009) Coding of pleasant touch by unmyelinated afferents in humans. Nat Neurosci 12:547–548

MacKenzie RA, Burke D, Skuse NF, Lethlean AK (1975) Fibre function and perception during cutaneous nerve block. J Neurol Neurosurg Psychiatry 38:865–873

McGlone F, Wessberg J, Olausson H (2014) Discriminative and affective touch: sensing and feeling. Neuron 82:737–755

McGlone F, Olausson H, Boyle JA, Jones-Gotman M, Dancer C, Guest S, Essick G (2012) Touching and feeling: differences in pleasant touch processing between glabrous and hairy skin in humans. Eur J Neurosci 35:1782–1788

Morrison I, Löken LS, Olausson H (2010) The skin as a social organ. Exp Brain Res 204:305–314

Nagi SS, Mahns DA (2013) Mechanical allodynia in human glabrous skin mediated by low-threshold cutaneous mechanoreceptors with unmyelinated fibres. Exp Brain Res 231:139–151

Nordin M (1990) Low-threshold mechanoreceptive and nociceptive units with unmyelinated (C) fibers in the human supraorbital nerve. J Physiol 426:229–240

Ochoa J, Torebjork E (1983) Sensations evoked by intraneural microstimulation of single mechanoreceptor units innervating the human hand. J Physiol 342:633–654

Olausson H, Lamarre Y, Backlund H, Morin C, Wallin BG, Starck G, Ekholm S, Strigo I, Worsley K, Vallbo AB, Bushnell MC (2002) Unmyelinated tactile afferents signal touch and project to insular cortex. Nat Neurosci 5:900–904

Olausson H, Wessberg J, Morrison I, McGlone F, Vallbo Å (2010) The neurophysiology of unmyelinated tactile afferents. Neurosci Biobehav Rev 34:185–191

Schmidt R, Schmelz M, Forster C, Ringkamp M, Torebjörk E, Handwerker H (1995) Novel classes of responsive and unresponsive C nociceptors in human skin. J Neurosci 15(1):333–341

Shea VK, Perl ER (1985) Sensory receptors with unmyelinated (C) fibers innervating the skin of the rabbit's ear. J Neurophysiol 54(3):491–501

Torebjörk HE, Hallin RG (1973) Perceptual changes accompanying controlled preferential blocking of A and C fibre responses in intact human skin nerves. Exp Brain Res. 16(3):321–332

Trulsson M, Francis ST, Kelly EF, Westling G, Bowtell R, McGlone F (2001) Cortical responses to single mechanoreceptive afferent microstimulation revealed with fMRI. Neuroimage 13(4):613–622

Vallbo ÅB (1976) Prediction of propagation block on the basis of impulse shape in single unit recordings from human nerves. Acta Physiol Scand 97:66–74

Vallbo ÅB, Hagbarth K-E (1968) Activity from skin mechanoreceptors recorded percutaneously in awake human subjects. Exp Neurol 21:270–289

Vallbo AB, Olausson H, Wessberg J (1999) Unmyelinated afferents constitute a second system coding tactile stimuli of the human hairy skin. J Neurophysiol 81:2753–2763

Vallbo AB, Olausson H, Wessberg J, Kakuda N (1995) Receptive filed characteristics of tactile units with myelinated afferents in hairy skin of human subjects. J Physiol 483(3):783–795

Vallbo A, Olausson H, Wessberg J, Norrsell U (1993) A system of unmyelinated afferents for innocuous mechanoreception in the human skin. Brain Res 628:301–304

Vallbo AB, Olsson KA, Westberg K-G, Clark F (1984) Microstimulation of single tactile afferents from the human hand. Sensory attributes related to unit type and properties of receptive fields. Brain 107:727–749

Vrontou S, Wong AM, Rau KK, Koerber HR, Anderson DJ (2013) Genetic identification of C fibers that detect massage-like stroking of hairy skin in vivo. Nature 493:669–673, CrossRef Medline

Wessberg J, Olausson H, Fernström KW, Vallbo AB (2003) Receptive field properties of unmyelinated tactile afferents in the human skin. J Neurophysiol 89:1567–1575

Westling GK (1972) A solid state amplifier for recording of single unit impulses with tungsten electrodes inn human nerves. Appendix (pp 294–297) to Vallbo ÅB. Single unit recording from human peripheral nerves: muscle receptor discharge in resting muscles and during voluntary contractions, pp 283-297. In: Somjen GG (ed) Neurophysiology studied in man. Excerpta Medica, Amsterdam

Wiklund-Fernström K (2004) Physiological properties of unmyelinated low-threshold tactile (CT) afferents in the human hairy skin. Thesis, Göteborg University; ISBN: 91-626-6190-5

Zimmerman A, Bai L, Ginty DD (2014) The gentle touch receptors of mammalian skin. Science 346(6212):950–954

Zotterman Y (1939) Touch, pain and tickle: an electro-physiological investigation on cutaneous sensory nerves. J Physiol 95:1–28