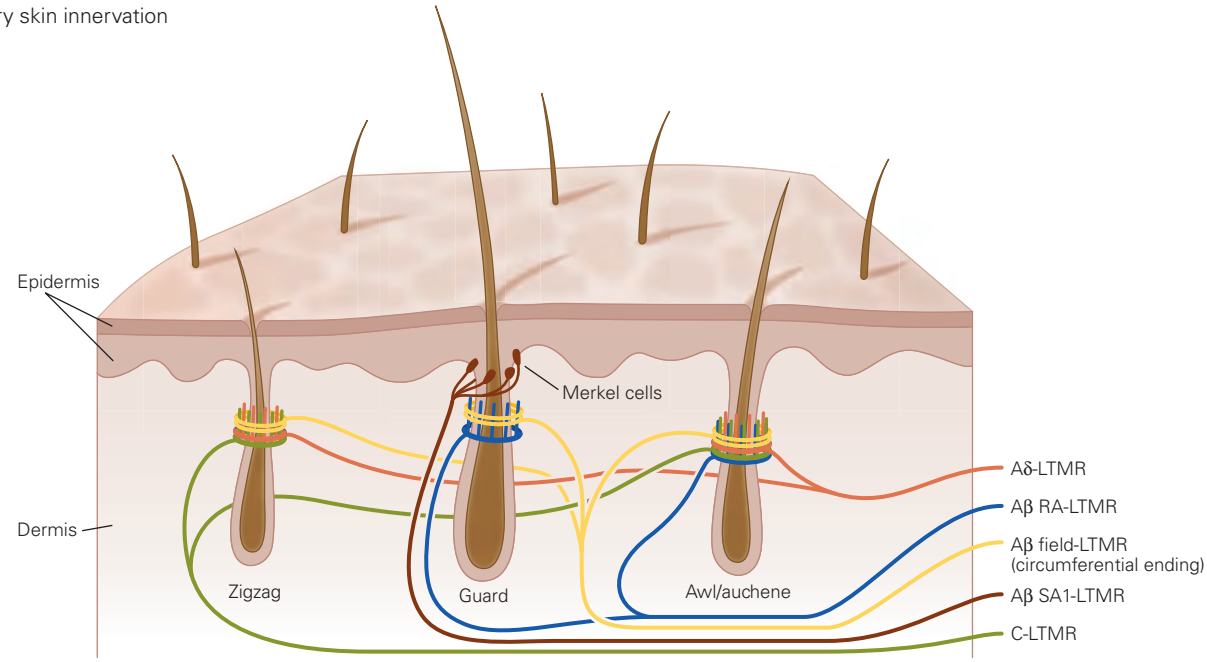
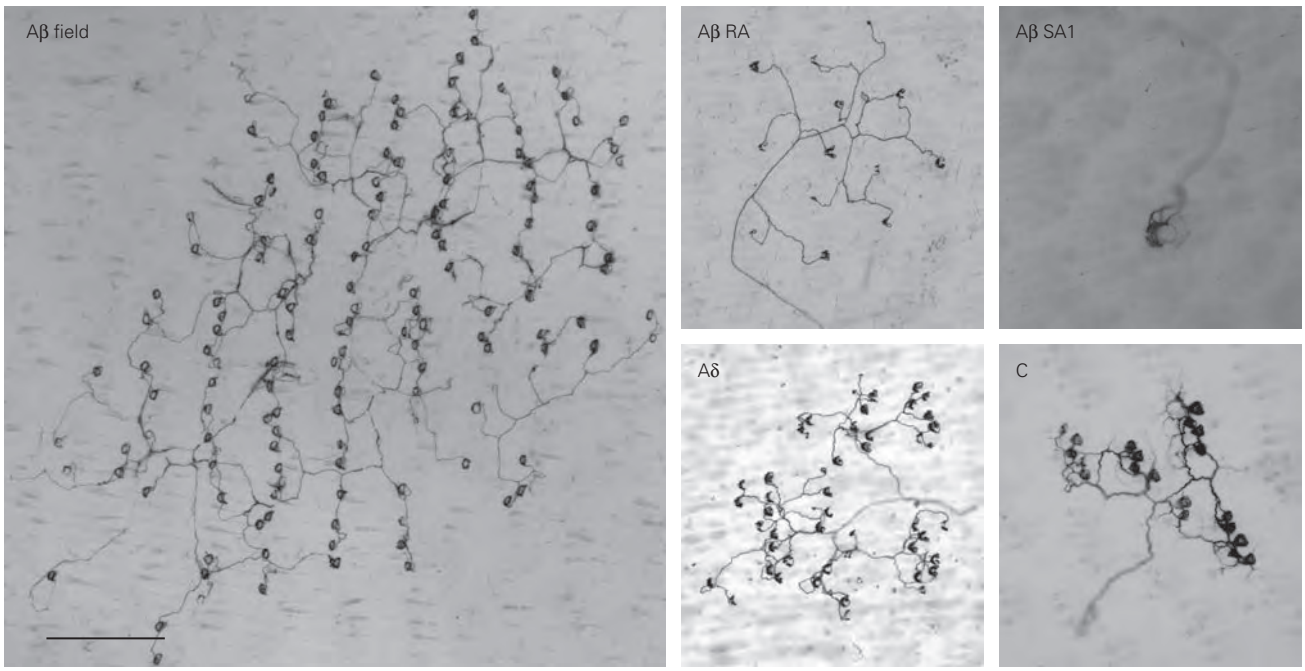
A Hairy skin innervation




B Receptive fields of low-threshold mechanoreceptors



smallest hair follicle receptive fields (see Figure 19–8B Aβ RA). The largest receptive fields in the skin are those of Aβ field receptors (see Figure 19–8B Aβ Field). These fibers form circumferential endings around hair follicles but do not respond to hair movement or air puffs. Instead, field receptors respond to stroking or stretching of the skin in their receptive fields. Field receptors are also excited by painful stimuli such as pulling hairs or strong pressure, suggesting that they may also mediate sensations of mechanical pain.

### Proprioceptors Measure Muscle Activity and Joint Positions

Mechanoreceptors in muscles and joints convey information about the posture and movements of the body and thereby play an important role in proprioception and motor control. Mechanical coupling of sensory nerve terminals to skeletal muscle, tendons, joint capsules, and the skin is thought to underlie proprioception. These receptors include two types of muscle-length sensors, the type Ia and II muscle spindle endings; one muscle force sensor, the Golgi tendon organ; joint-capsule receptors, which transduce tension in the joint capsule; and Ruffini endings that sense skin stretch over joints.

The muscle spindle consists of a bundle of thin muscle fibers, or intrafusal fibers, that are aligned parallel to the larger fibers of the muscle and enclosed within a capsule (Figure 18–9A). The intrafusal fibers are entwined by a pair of sensory axons that detect muscle stretch because of mechanoreceptive ion channels in the nerve terminals. Intrafusal muscles also receive inputs from motor axons that regulate contractile force and receptor sensitivity. (See Box 32–1 for details on muscle spindles.)

Although the receptor potential and firing rates of muscle spindle afferent fibers are proportional to muscle length (Figure 18–9B), these responses can be modulated by higher centers in the brain that regulate contraction of intrafusal muscles. Spindle afferent fibers are thus able to encode the amplitude and speed of internally generated voluntary movements as well as passive limb displacement by external forces (Chapter 32).

Golgi tendon organs, located at the junction between skeletal muscle and tendons, measure the forces generated by muscle contraction. (See Box 32–4 for details on Golgi tendon organs.) Although these receptors play an important role in reflex circuits modulating muscle force, they appear to contribute little to conscious sensations of muscle activity. Psychophysical experiments in which muscles are fatigued or partially paralyzed have shown that perceived muscle force is mainly related to centrally generated effort rather than to actual muscle force.

Recent studies by Ardem Patapoutian and colleagues suggest that Piezo2 mediates the signals transmitted by afferent fibers from muscle spindles and Golgi tendon organs, as these fibers express the Piezo2 protein in their distal terminals and cell body.

Joint receptors play little if any role in postural sensations of joint angle. Instead, perception of the angle of proximal joints such as the elbow or knee

**Figure 18–8** (Opposite) Innervation of the hairy skin by low-threshold mechanoreceptors.

**A.** Hairy skin of mammals is innervated by specific combinations of low-threshold mechanoreceptors (**LTMRs**); these multiple classes of nerve fibers allow touch information to be transmitted along multiple parallel nerve fibers to the central nervous system. Touch domes of Merkel cells are located at the epidermal–dermal boundary surrounding large-diameter guard hairs. The axons of Merkel cells are classified as Aβ SA1-LTMRs, and they compose approximately 3% of sensory fibers innervating hairy skin. Guard hair follicles are innervated by rapidly adapting touch fibers, classified as Aβ RA-LTMRs, which form longitudinal lanceolate (comb-like) endings surrounding the hair follicle. They compose another 3% of sensory fibers innervating hairy skin. Aβ RA-LTMR fibers also form lanceolate endings on medium size awl/auchene hairs; each fiber innervates multiple hair follicles in neighboring regions of skin. Awl/auchene hairs are innervated by lanceolate endings from three different classes of sensory fibers; Aβ RA-LTMRs (**blue**), Aδ-LTMRs (**red**, 7% of fibers), and C-LTMRs (**green**, 15%–27% of fibers). Zigzag, or down hairs, are the most numerous type; they are innervated by the smallest-diameter, slowest-conducting peripheral nerve fibers (Aδ- and C-LTMRs). All three types of hair follicles are also innervated by circumferential endings (**yellow**). (Reproduced with permission from Zimmerman, Bai, and Ginty 2014. Copyright © 2014 AAAS.)

**B.** Whole mount sections of skin illustrate the spread of LTMR sensory nerve terminals in hairy skin and the skin region that can activate an individual sensory fiber. All five classes innervate multiple hair follicles and have branched sensory nerve endings. Scale bar (which applies to all images) = 500 μm. Firing rates in each of these axons reflect inputs from multiple receptor end organs in the skin. Aβ field-LTMRs form circumferential endings around all classes of hair follicles; they have the largest receptive fields in hairy skin, innervating up to 180 hair follicles/fibers and spanning areas up to 6 $mm^2$. Aβ SA1-LTMRs have the smallest receptive fields but innervate all of the Merkel cells within a touch dome; each touch dome is innervated by only a single Aβ SA1-LTMR. Aβ RA- Aδ-, and C-LTMRs form lanceolate endings enclosing up to 40 individual hair follicles and span skin areas of 0.5 to 4 $mm^2$. (Reproduced, with permission, from Bai et al. 2015. Copyright © 2015 Elsevier Inc.)

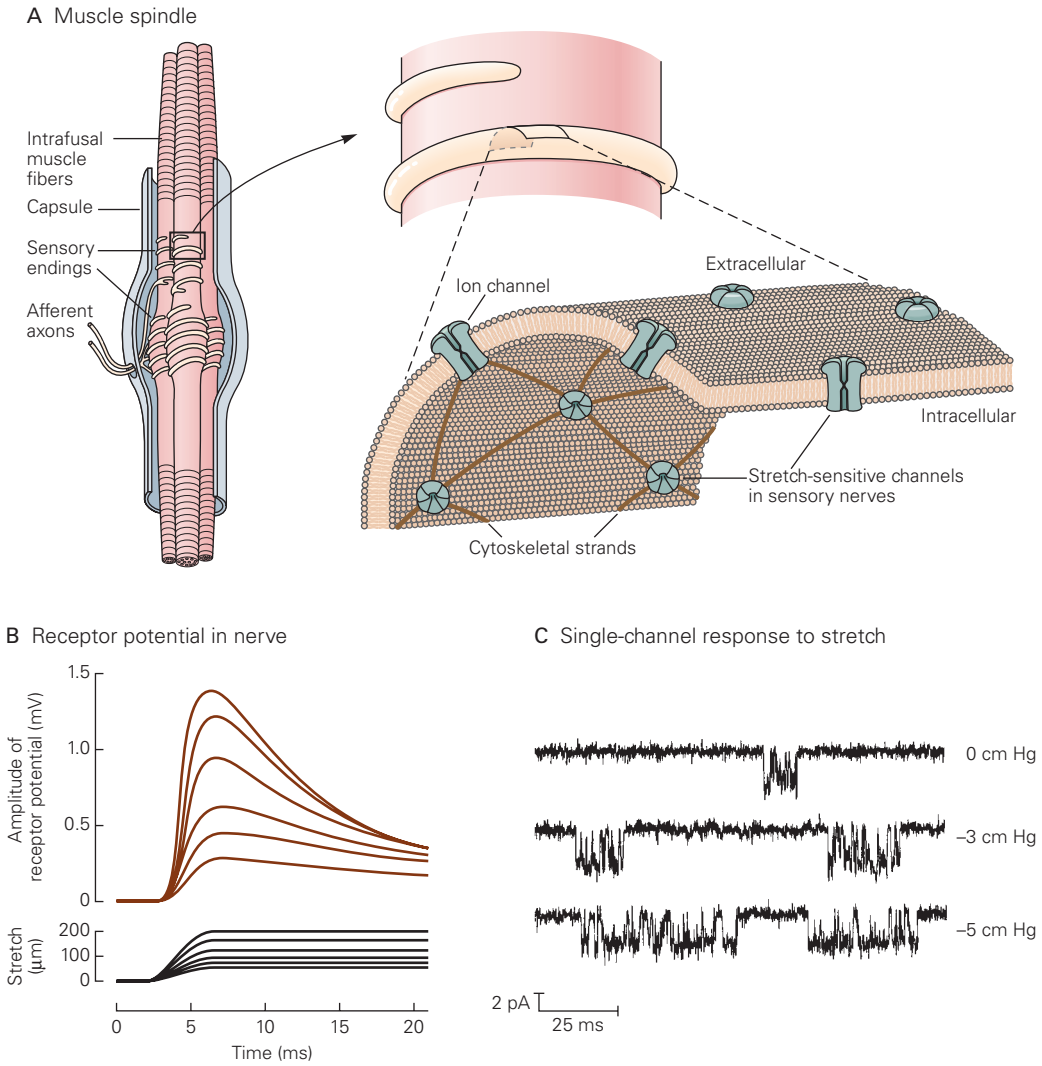



**Figure 18–9** The muscle spindle is the principal receptor for proprioception.

A. The muscle spindle is located within skeletal muscle and is excited by stretch of the muscle. It consists of a bundle of thin (intrafusal) muscle fibers entwined by a pair of sensory axons. It is also innervated by several motor axons (not shown) that produce contraction of the intrafusal muscle fibers. Stretch-sensitive ion channels in the sensory nerve terminals are linked to the cytoskeleton by the protein spectrin. (Adapted, with permission, from Sachs 1990.)

B. The depolarizing receptor potential recorded in a group Ia fiber innervating the muscle spindle is proportional to both the velocity and amplitude of muscle stretch parallel to the myofilaments. When stretch is maintained at a fixed length, the receptor potential decays to a lower value. (Adapted, with permission, from Ottoson and Shepherd 1971.)

C. Patch-clamp recordings of a single stretch-sensitive channel in myocytes. Pressure is applied to the receptor cell membrane by suction. At rest (0 cm Hg) the channel opens sporadically for short time intervals. As the pressure applied to the membrane increases, the channel opens more often and remains in the open state longer. This allows more current to flow into the receptor cell, resulting in higher levels of depolarization. (Adapted, with permission, from Guharay and Sachs 1984. Copyright © 1984 The Physiological Society.)

depends on afferent signals from muscle spindle receptors and efferent motor commands. Additionally, conscious sensations of finger position and hand shape depend on cutaneous stretch receptors as well as muscle spindles.

### Thermal Receptors Detect Changes in Skin Temperature

Although the size, shape, and texture of objects held in the hand can be apprehended visually as well as

by touch, the thermal qualities of objects are uniquely somatosensory. Humans recognize four distinct types of thermal sensation: cold, cool, warm, and hot. These sensations result from differences between the normal skin temperature of approximately 32°C (90°F) and the external temperature of the air or of objects contacting the body. Temperature sense, like the other *protopathic* modalities of pain and itch, is mediated by a *combinatorial code* of multiple receptor types, transmitted by small-diameter afferent fibers.

Although humans are exquisitely sensitive to sudden changes in skin temperature, we are normally unaware of the wide swings in skin temperature that occur as our cutaneous blood vessels expand or contract to discharge or conserve body heat. If skin temperature changes slowly, we are unaware of changes in the range 31° to 36°C (88–97°F). Below 31°C (88°F), the sensation progresses from cool to cold and, finally, beginning at 10° to 15°C (50–59°F), to pain. Above 36°C (97°F), the sensation progresses from warm to hot and then, beginning at 45°C (113°F), to pain.

Thermal sensations are mediated by free nerve endings in the epidermis. The temperature ranges signaled by these nerve fibers are determined by the molecular composition of receptor molecules expressed in the distal nerve terminals and cell bodies of small-diameter DRG neurons. Studies by David Julius and his colleagues revealed that thermal stimuli activate specific classes of *transient receptor potential (TRP) channels* in these neurons (Figure 18–10). TRP channels are encoded by genes belonging to the same gene superfamily as the voltage-gated channels that give rise to the action potential (Chapter 8). They form nonselective cation channels that mediate inward depolarizing current. TRP channels comprise four identical protein subunits, each of which contains six transmembrane α-helices,

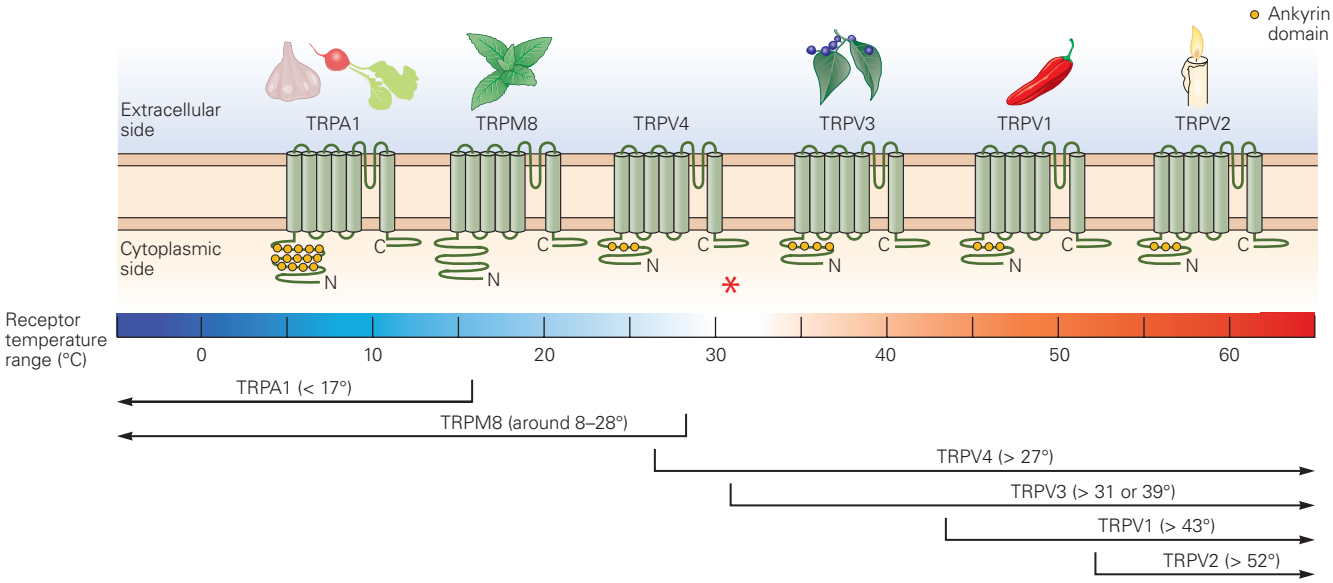



**Figure 18–10** **Transient receptor potential ion channels.** TRP channels consist of membrane proteins with six transmembrane α-helices. A pore is formed between the fifth (S5) and sixth (S6) helices from the four subunits. Most of these receptors contain ankyrin repeats in the N-terminal domains and a common 25-amino acid motif adjacent to S6 in the C-terminal domain. Individual TRP channels are composed of four identical TRP proteins. All TRP channels are gated by temperature and various chemical ligands, but different types respond to different temperature ranges and have different activation thresholds. At least six types of TRP receptors have been identified in sensory neurons; the thermal sensitivity of a neuron is determined by the particular TRP receptors expressed in its nerve terminals. At 32°C (90°F), the resting skin temperature (**asterisk**), only TRPV4 and some TRPV3 receptors are stimulated. TRPA1 and TRPM8 receptors are activated by cooling and cold stimuli. TRPM8 receptors also respond to menthol and various mints; TRPA1 receptors respond to allium-expressing plants such as garlic and radishes. TRPV3 receptors are activated by warm stimuli and also bind camphor. TRPV1 and TRPV2 receptors respond to heat and produce burning pain sensations. TRPV1 channels also respond to a variety of substances, temperatures, or forces that can elicit pain. Their sites of action on the receptor include binding sites for chili peppers' active ingredient (capsaicin), acids (lemon juice), spider venoms, and phosphorylation sites for second messenger-activated kinases. TRPV4 receptors are active at normal skin temperatures and respond to touch. (Adapted, with permission, from Jordt, McKemy, and Julius 2003; adapted from Dhaka, Viswanath, and Patapoutian 2006.)

with a pore-forming element between the fifth and sixth helices. Individual TRP receptors are distinguished by their sensitivity to heat or cold, showing sharp increases in conductance to cations when their thermal threshold is exceeded. Their names specify the genetic subfamily of TRP receptors and the member number. Examples include TRPV1 (for TRP vanilloid-1), TRPM8 (for TRP melastatin-8), and TRPA1 (for TRP ankyrin-1).

Two classes of TRP receptors are activated by cold temperatures and inactivated by warming. TRPM8 receptors respond to temperatures below 25°C (77°F); such temperatures are perceived as cool or cold. TRPA1 receptors have thermal thresholds below 17°C (63°F); this range is described as cold or frigid. Both TRPM8 and TRPA1 receptors are expressed in high-threshold cold receptor terminals, but only TRPM8 receptors are expressed in low-threshold cold receptor terminals.

Thermal signals from low-threshold cold receptors are transmitted by small-diameter, myelinated Aδ fibers with unmyelinated endings within the epidermis. These fibers express the transient receptor potential channel TRPM8 and respond to menthol applied to the skin. Cold receptors are approximately 100 times more sensitive to sudden drops in skin temperature than to gradual changes. This extreme sensitivity to change allows humans to detect a draft from a distant open window.

Four types of TRP receptors are activated by warm or hot temperatures and inactivated by cooling. TRPV3 receptors are expressed in warm type fibers; they respond to warming of the skin above 35°C (95°F) and generate sensations ranging from warm to hot. TRPV1 and TRPV2 receptors respond to temperatures exceeding 45°C (113°F) and mediate sensations of burning pain; they are expressed in heat nociceptors. TRPV4 receptors are active at temperatures above 27°C and signal normal skin temperatures.

Warm receptors are located in the terminals of C fibers that end in the dermis. Unlike the cold receptors, warm receptors act more like simple thermometers; their firing rates rise monotonically with increasing skin temperature up to the threshold of pain and then saturate at higher temperatures. Warm receptors are less sensitive to rapid changes in skin temperature than cold receptors. Consequently, humans are less responsive to warming than cooling; the threshold change for detecting sudden skin warming, even in the most sensitive subject, is about 0.1°C.

Heat nociceptors are activated by temperatures exceeding 45°C (113°F) and inactivated by skin cooling. The burning pain caused by high temperatures is transmitted by both myelinated Aδ fibers and unmyelinated C fibers.

The role of TRP receptors in thermal sensation was originally discovered by analyses of natural substances such as capsaicin and menthol that produce burning or cooling sensations when applied to the skin or injected subcutaneously. Capsaicin, the active ingredient in chili peppers, has been used extensively to activate nociceptive C fiber afferents that mediate sensations of burning pain. These studies indicate that the various TRP receptors also bind other molecules that induce painful sensations, such as toxins, venoms, and substances released by diseased or injured tissue. TRPA1 receptors bind pungent substances such as horseradish (wasabi), garlic, onions, and similar allium-expressing plants. These substances behave as irritants that may produce pain or itch through covalent modification of cysteines in the TRPA1 protein.

TRP channels are polymodal sensory integrators, because different sections of the protein respond directly to changes in temperature, pH, or osmolarity; to the presence of noxious substances such as capsaicin or toxins; or to phosphorylation by intracellular second messengers (see Figure 20–2). Their molecular structure and role in pain are detailed in Chapter 20.

### Nociceptors Mediate Pain

The receptors that respond selectively to stimuli that can damage tissue are called *nociceptors* (Latin *nocere*, to injure). They respond directly to mechanical and thermal stimuli and indirectly to other stimuli by means of chemicals released from cells in the traumatized tissue. Nociceptors signal impending tissue injury, and more important, they provide a constant reminder of tissues that are already injured and must be protected.

Abnormal function in major organ systems resulting from disease or trauma evokes conscious sensations of pain. Much of our knowledge of the neural mechanisms of pain is derived from studies of cutaneous nociceptors because the mechanisms are easier to study in cutaneous nerves than in visceral nerves. Nevertheless, the neural mechanisms underlying visceral pain are similar to those for pain arising from the surface of the body.

Nociceptors in the skin, muscle, joints, and visceral receptors fall into two broad classes based on the myelination of their afferent fibers. Nociceptors innervated by thinly myelinated Aδ fibers produce short-latency pain that is described as sharp and pricking. The majority are called mechanical nociceptors or *high-threshold mechanoreceptors* (HTMRs) because they are excited by sharp objects that penetrate, squeeze, or pinch the skin

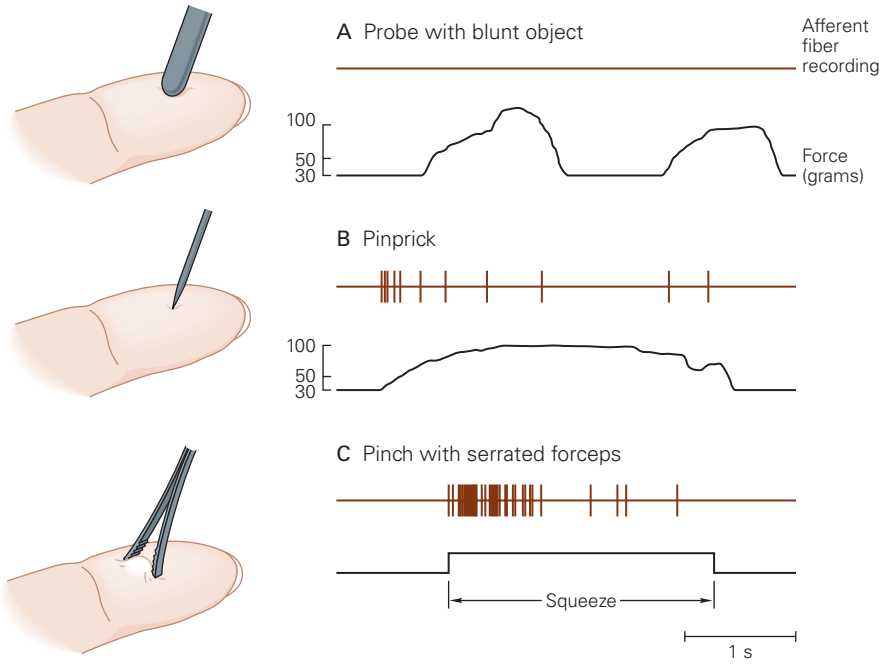



**Figure 18–11** Mechanical nociceptors respond to stimuli that puncture, squeeze, or pinch the skin. Sensations of sharp, pricking pain result from stimulation of Aδ fibers with free nerve endings in the skin. These receptors respond to sharp objects that puncture the skin (**B**), but not to strong pressure from a blunt probe (**A**). The strongest responses are produced by pinching the skin with serrated forceps that damage the tissue in the region of contact (**C**). (Adapted, with permission, from Perl 1968.)

(Figure 18–11) or by pulling hairs in hairy skin. Many of these fibers also respond to temperatures above 45°C (113°F) that burn the skin; these Aδ fibers also express the heat-sensitive TRPV2 channel.

Nociceptors innervated by C fibers produce dull, burning pain that is diffusely localized and poorly tolerated. The most common type encompasses polymodal nociceptors that respond to a variety of noxious mechanical, thermal, and chemical stimuli, such as pinch or puncture, noxious heat and cold, and irritant chemicals applied to the skin. As detailed in Chapter 20, most C-polymodal nociceptors express TRPV1 and/or TRPA1 receptors. Electrical stimulation of these fibers in humans evokes prolonged sensations of burning pain. In the viscera, nociceptors are activated by distension or swelling, producing sensations of intense pain.

### Itch Is a Distinctive Cutaneous Sensation

Itch is a common sensory experience that is confined to the skin, the ocular conjunctiva, and the mucosa. It has some properties in common with pain and, until recently, was thought to result from low firing rates in nociceptive fibers. Like pain, itch is inherently unpleasant whatever its intensity; even at the expense of inducing pain, we attempt to eliminate it by scratching.

Recent studies by Diana Bautista and Sarah Wilson indicate that C fibers that express both TRPV1 and TRPA1 receptors mediate itch sensations evoked by pruritic (itch-producing) agents. Itch induced by intradermal injection of histamine or by procedures that release endogenous histamine activates a subset of TRPV1-expressing neurons that also contain the H1 histamine receptor; these itch sensations are blocked by antihistamines. Histamine-independent itch appears to be mediated by C fiber DRGs that express TRPA1 channels. Itch sensations in this pathway are triggered by dry skin or by pruritogens that bind to members of the Mas-related G protein–coupled receptor (Mrgpr) family, such as the antimalarial drug chloroquine.

How can TRPA1 receptors mediate itch when they are also involved in sensing noxious cold temperatures (<15°C)? Why do some TRPV1-expressing fibers mediate itch sensations rather than sensations of noxious heat? The answer lies in the use of *combinatorial* codes by small-diameter sensory nerve fibers. For example, noxious cold is sensed when both TRPA1 and TRPM8

receptors are excited, but itch is perceived when TRPM8 receptors are silent. Likewise, heat pain is sensed when TRPV1-, TRPV2-, and TRPV3-expressing fibers are co-activated, but itch may be perceived when only TRPV1-expressing fibers respond and TRPV2 and TRPV3 receptors are silent. Similar combinatorial codes using multiple receptors are commonly used by other chemical senses such as olfaction and taste.

### Visceral Sensations Represent the Status of Internal Organs

Visceral sensations are important because they drive behaviors critical for survival, such as respiration, eating, drinking, and reproduction. The same molecular genetic strategies described earlier to study touch, pain, thermal senses, and proprioception in the dorsal root and trigeminal ganglia have been used to classify visceral afferents in the vagal sensory ganglia. Stephen Liberles and colleagues recently analyzed sensory responses in the vagal sensory ganglia (nodose/jugular complex) that receive mechanosensory or chemosensory information from the lungs, cardiovascular, immune, or digestive systems.

Vagal afferent fibers express a variety of G protein–coupled receptors (GPCRs) that have been labeled with fluorescent antibodies to identify their peripheral sensory receptor sites in specific viscera, as well as mark their distinctive central projections to specific zones in the nucleus of the solitary tract in the medulla. By expressing genetic markers of calcium transients (GCaMPs) in identified vagal ganglia neurons, Liberles and colleagues measured their physiological responses to mechanical stimuli such as stretch or their activation by nutrients or gastric hormones (serotonin, glucagon-like peptide 1, or cholecystokinin). The ability to label specific vagal afferents provides important tools for analyzing neural regulation of visceral function and tracing the pathways used to modulate these important bodily functions.

Although their cell bodies seem to be scattered randomly in the vagal nucleus, individual vagal neurons perform different sensory functions in specific organ systems. For example optogenetic stimulation of identified vagal sensory neurons reveals that there are at least two populations of vagal neurons controlling respiration. Neurons that express the GPCR *P2ry1* induce apnea, trapping the lung in expiration, while those expressing the GPCR *Npy2r* produce rapid shallow breathing. Stimulation of these neurons has no effect on heart rate or digestive function. Another set of GPCRs are used to label neurons that regulate gastrointestinal function. One set of gastric afferents are mechanoreceptors that sense distension of the stomach and upper intestine and modulate gastric motility, while other gastric afferents are chemoreceptors that sense specific nutrients in the gut and aid their absorption.

## Action Potential Codes Transmit Somatosensory Information to the Brain

In the previous sections, we learned that a variety of stimuli, such as mechanical forces, temperature, and various chemicals, interact with receptor molecules at the distal axon terminals of DRG neurons to produce local depolarization of the sensory endings. As noted in Chapter 17, these receptor potentials are transformed into a digital pulse code of action potentials for transmission to the central nervous system.

The sensory terminal regions of peripheral nerve fibers are usually unmyelinated and do not express the voltage-gated $Na^+$ and $K^+$ channels that underlie action potential generation. For example, the lanceolate endings of hair follicle afferents are unmyelinated (Figure 18–2H). This design optimizes information gathering in the receptive field by dedicating the highly branched terminal membrane area to sensory transduction channels such as Piezo2 or TRP receptors.

The most distal action potential ion channels in myelinated fibers are usually located near the initial myelin segment (see Figure 3–10) or at the intersection of branches in unmyelinated fibers. This has important consequences for information transmission. Depolarizing sensory signals from multiple branches can summate more easily if channels involved in action potential generation are absent from receptive terminals, because of the regenerative properties of action potentials and the subsequent inactivation of the voltage-gated $Na^+$ channels. Sensory messages arriving from later-activated receptors may be extinguished by collision with backward-propagating action potentials traveling along another branch of the fiber. Thus, the signals transmitted along a primary afferent axon may be a nonlinear reflection of the sensory stimulus, reflecting either spatial summation of excitation from multiple branches or winner-take-all suppression of late-generated activity. Sequential activation of different neurite branches can also aid detection of moving stimuli by generating long trains of action potentials if individual endings are stimulated at optimal rates so that their responses are not shunted by spikes generated earlier in other branches.

Action potential transmission along peripheral nerves depends on whether the axon is myelinated or

unmyelinated and on the expression of specific subclasses of voltage-dependent $Na_V$ and $K_V$ channels in each nerve fiber. Steven Waxman and colleagues reported that large-diameter Aα and Aβ fibers that innervate proprioceptors and low-threshold mechanoreceptors (LTMRs) express primarily $Na_V1.1$ and $Na_V1.6$ isoforms; these fibers generally fire action potentials at high rates, in part because they also express $K_V1.1$ and $K_V1.2$ channels that enable rapid repolarization of axons. Small-diameter peripheral nerves that mediate pain and itch sensations express $Na_V1.7$, $Na_V1.8$, and $Na_V1.9$ channels. The latter two $Na_V$ subtypes have kinetic and voltage sensitivities that promote repetitive firing, thereby enhancing painful sensations: $Na_V$ 1.8 channels inactivate incompletely during action potentials and recover rapidly following them; $Na_V$ 1.9 channels activate at relatively negative potentials and undergo negligible inactivation, resulting in persistent inward currents that can amplify subthreshold stimuli.

### Sensory Ganglia Provide a Snapshot of Population Responses to Somatic Stimuli

We conclude this survey of DRG neurons by examining the distribution of sensory responses within an individual mammalian somatosensory ganglion. Typically, peripheral nerve fibers have been studied one at a time, usually with optimal stimuli for particular receptor classes. However, even weak voices contribute to the neural chorale, and those have been largely ignored with classic single-cell recording techniques.

New in vivo functional imaging techniques provide useful tools for labeling, visualizing, and measuring ensemble responses to various types of somatosensory stimuli. For example, the $Ca^{2+}$ currents evoked by sensory stimuli provide an alternative to electrophysiological recordings of spike trains in individual neurons. In the experiment illustrated in Figure 18–12, the genetically encoded $Ca^{2+}$ sensor GCaMP6f was expressed in cells of the mouse trigeminal ganglia that also expressed the polymodal TRPV1 receptor, allowing researchers to visualize and quantify the activity of populations of neurons activated by a variety of somatosensory stimuli. Using a battery of tactile, noxious, and thermal stimuli first developed by William Willis to analyze somatosensory responses of neurons in the spinal cord, Nima Ghitani, Alexander Chesler, and colleagues recorded responses of 213 trigeminal neurons simultaneously. Their findings were quite remarkable. As shown in the heat map of Figure 18–12B1, neuronal responses are diverse, varying considerably in the intensity and duration of firing patterns to identical stimuli. Such ensemble recording techniques indicate that even at the receptor level there are no canonical responses to somatic stimuli, but rather common patterns of responses.

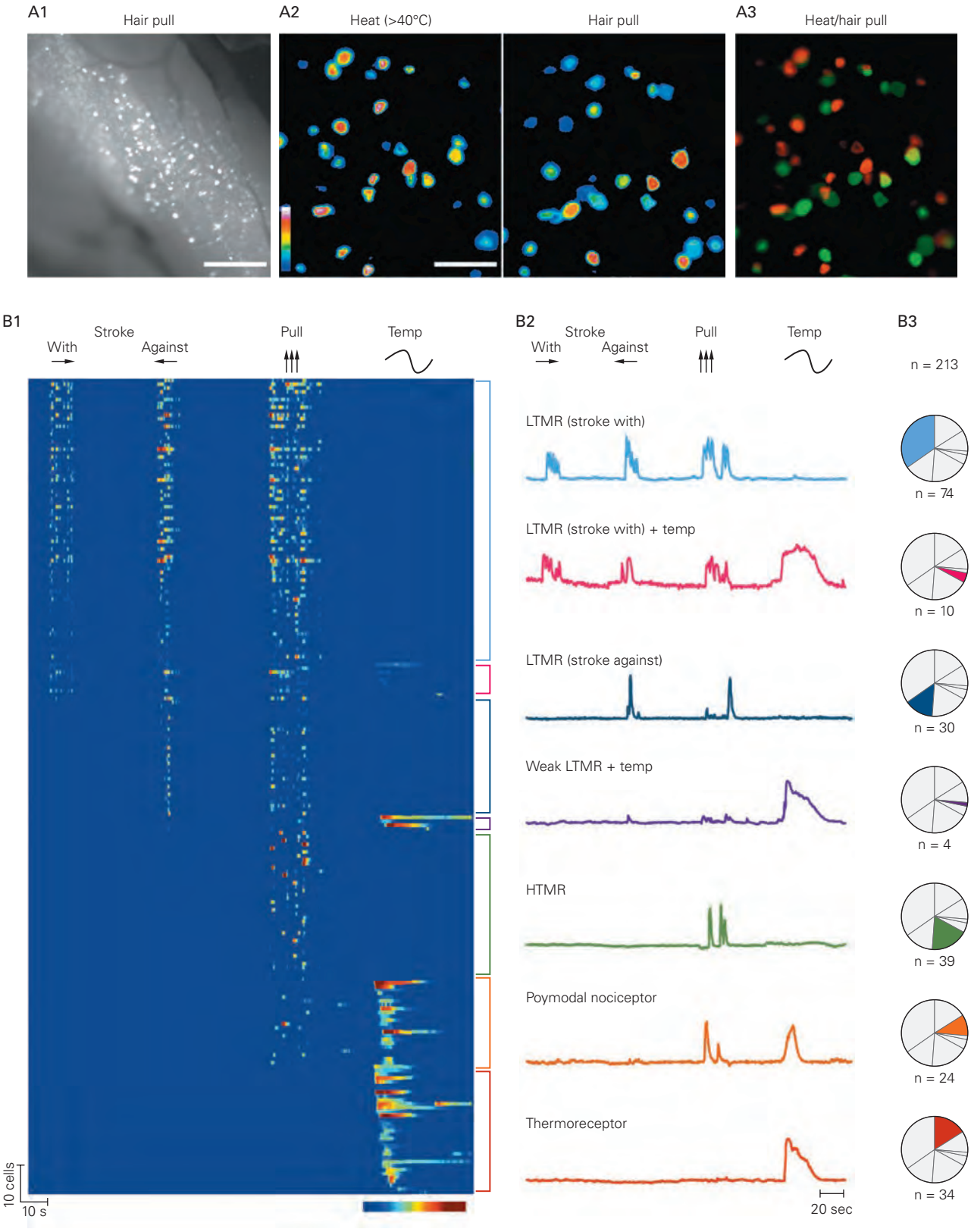
Furthermore, individual somatosensory neurons appear to be polysensory, responding to more than one modality, such as touch and pain. This study shows that individual trigeminal neurons distinguish noxious heat from mechanical pain (hair pull) and may respond, albeit weakly, to gentle touch or moderate thermal stimuli (Figure 18–12A). The most prevalent type of trigeminal ganglion neurons (49%) distinguish light touch (stroking the cheek) from thermal stimuli (Figure 18–12B). The next most common types are mechanical nociceptors (18%) or thermoreceptors (16%). Less common are polymodal types that respond to thermal and nociceptive stimuli (total 9%).

These new imaging techniques will enable neuroscientists to quantify sensory interactions in populations of somatosensory afferents, define combinatorial codes used by members of the active population, and thereby identify specific neural populations engaged in somatic sensation. Recording neurons simultaneously rather than one at a time is essential for decoding population activity and defining the circuits underlying diverse sensory modalities.

Lastly, we note that neurons in the dorsal root, trigeminal, and vagal ganglia do not appear to be spatially clustered or segregated functionally by modality such as mechanosensation or thermal or chemical events (Figure 18–12A). The principal organizational feature of these sensory ganglia is one of body topography: which particular area of skin or which muscle or visceral structure is innervated by particular sensory neurons. Such geographical specificity extends centrally to higher structures in the brain that analyze the sensory information and that organize specific behaviors.

### Somatosensory Information Enters the Central Nervous System Via Spinal or Cranial Nerves

As the peripheral nerve fibers exit the dorsal root ganglia and approach the spinal cord, the large- and small-diameter fibers separate into medial and lateral divisions, to form the *spinal nerves* that project to distinct locations in the spinal cord and brain stem. The medial division includes large myelinated Aα and Aβ fibers, which transmit proprioceptive and tactile information from the innervated body region. The lateral division of a spinal nerve includes small, thinly myelinated Aδ fibers and unmyelinated C fibers, which transmit noxious, thermal, pruritic, and visceral


A1
Hair pull
A2
Heat (>40°C)
Hair pull
A3
Heat/hair pull
B1
Stroke
With
Against
Pull
Temp
10 cells
10 s
B2
Stroke
With
Against
Pull
Temp
LTMR (stroke with)
LTMR (stroke with) + temp
LTMR (stroke against)
Weak LTMR + temp
HTMR
Poymodal nociceptor
Thermoreceptor
20 sec
B3
n = 213
n = 74
n = 10
n = 30
n = 4
n = 39
n = 24
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