

The Somatosensory System: Receptors and Central Pathways

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An Overall View

WE BEGIN THE STUDY OF THE INDIVIDUAL sensory systems with the somatosensory system (Greek *soma*, the body), the system in which sensory coding was first studied electrophysiologically. Somatic information is provided by receptors distributed throughout the body. One of the earliest investigators of the bodily senses, Charles Sherrington, noted that the somatosensory system serves three major functions: proprioception, exteroception, and interoception.

Proprioception is the sense of oneself (Latin *proprius*, one's own). Receptors in skeletal muscle, joint capsules, and the skin enable us to have conscious awareness of the posture and movements of our own body, particularly the four limbs and the head. Although one can move parts of the body without sensory feedback from proprioceptors, the movements are often clumsy, poorly coordinated, and inadequately adapted to complex tasks, particularly if visual guidance is absent.

Exteroception is the sense of direct interaction with the external world as it impacts on the body. The principal mode of exteroception is the sense of touch, which includes sensations of contact, pressure, stroking, motion, and vibration, and is used to identify objects. Some touch involves an active motor component—stroking, tapping, grasping, or pressing—whereby a part of the body is moved against another surface or organism. The sensory and motor components of touch are intimately connected anatomically in the brain and are important in guiding behavior.

Exteroception also includes the thermal senses of heat and cold. Thermal sensations are important controllers of behavior and homeostatic mechanisms needed to maintain the body temperature near 37°C (98.6°F). Finally,

exteroception includes the sense of pain, or nociception, a response to external events that damage or harm the body. Nociception is a prime motivator of actions necessary for survival, such as withdrawal or combat.

The third component of somatic sensation, *interoception*, is the sense of the function of the major organ systems of the body and its internal state. Although most of the events recorded by receptors in the viscera do not become conscious sensations, the information conveyed by these receptors is crucial for regulating autonomic functions, particularly in the cardiovascular, respiratory, digestive, and renal systems. Interoceptors are primarily chemoreceptors that monitor organ function through such indicators as blood gases and pH.

Abnormal function in major organ systems resulting from disease or trauma can evoke 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.

This diverse group of sensory functions may seem an unlikely combination to form a sensory system. We treat all of the somatic senses in one introductory chapter because they are mediated by one class of sensory neurons, the dorsal root ganglion neurons. Individual neurons in a dorsal root ganglion respond selectively to specific types of stimuli because of morphological and molecular specialization of their peripheral terminals.

In this chapter we consider the principles common to all dorsal root ganglion neurons and those that distinguish their individual sensory function. We begin with a description of the peripheral nerves and their organization, followed by a survey of the receptors responsible for each of the major bodily senses. We then consider their sensory pathways in the spinal cord and brain stem. The chapter concludes with a discussion of the central processing centers for each submodality in the thalamus. The physiological function of touch, pain, proprioception, and autonomic regulation are described in more detail in separate chapters.

The Primary Sensory Neurons of the Somatosensory System Are Clustered in the Dorsal Root Ganglia

Somatosensory information from the skin, muscles, joint capsules, and viscera is conveyed by dorsal root

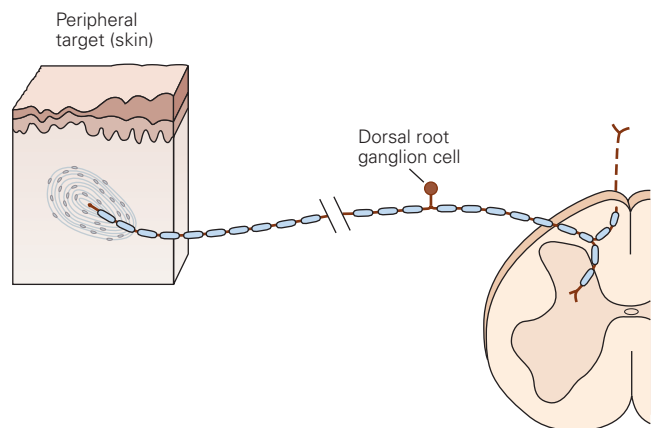


Figure 22-1 The dorsal root ganglion neuron is the primary sensory receptor cell of the somatosensory system. The neuron cell body is located in a dorsal root ganglion adjacent to the spinal cord. The axon has two branches, one projecting to the periphery, where its specialized terminal contains receptors for a particular form of stimulus energy, and one projecting to the spinal cord or brain stem, where the afferent signals are processed.

ganglion neurons innervating the limbs and trunk or by trigeminal sensory neurons that innervate cranial structures (the face, lips, oral cavity, conjunctiva, and dura mater). These sensory neurons perform two major functions: the transduction and encoding of stimuli into electrical signals and the transmission of those signals to the central nervous system.

The cell body of a dorsal root ganglion neuron lies in a ganglion on the dorsal root of a spinal or cranial nerve. Dorsal root ganglion neurons originate from the neural crest and are intimately associated with the nearby segment of the spinal cord.

Dorsal root ganglion neurons are a type of bipolar cell, called pseudo-unipolar cells. The axon of a dorsal root ganglion neuron has two branches, one projecting to the periphery and one projecting to the central nervous system (Figure 22-1). The peripheral terminals of different neurons innervate the skin, muscle, joint capsules, or viscera and contain receptors specialized for particular kinds of stimuli. They differ in receptor morphology and stimulus selectivity. The central branches terminate in the spinal cord or brain stem, forming the first synapses in somatosensory pathways. Thus the axon of each dorsal root ganglion cell serves as a single transmission line with one polarity between the receptor terminal and the central nervous system. This axon is called the *primary afferent fiber*.

Individual primary afferent fibers innervating a particular region of the body, such as the thumb or

fingers, are grouped together into bundles or fascicles of axons forming the *peripheral nerves*. They are guided during development to a specific location in the body by various trophic factors. The peripheral nerves also include motor axons innervating nearby muscles, blood vessels, glands, or viscera.

Damage to peripheral nerves or their targets in the brain may produce sensory deficits in more than one somatosensory submodality. Knowledge of where somatosensory modalities overlap morphologically, and where they diverge, facilitates diagnosis of neurological disorders and malfunction.

Peripheral Somatosensory Nerve Fibers Conduct Action Potentials at Different Rates

The diverse modalities of somatic sensation are mediated by peripheral nerve fibers that differ in diameter and conduction velocity. Mechanoreceptors for touch and proprioception are innervated by dorsal root ganglion neurons with large-diameter, myelinated axons that conduct action potentials rapidly. Thermal receptors, nociceptors, and other chemoreceptors have small-diameter axons that are either unmyelinated or thinly myelinated; these nerves conduct impulses more slowly. The difference in conduction velocity allows signals of touch and proprioception to reach the spinal cord and higher brain centers sooner than noxious or thermal signals.

Large-diameter fibers conduct action potentials more rapidly because the internal resistance to current flow along the axon is low, and the nodes of Ranvier are widely spaced along its length (see Chapter 6). The conduction velocity of large myelinated fibers (in meters per second) is approximately six times the axon diameter (in micrometers),

whereas thinly myelinated fibers conduct at five times the axon diameter. For unmyelinated fibers, the factor for converting axon diameter to conduction velocity is 1.5 to 2.5.

Peripheral nerve fibers are classified into functional groups based on properties related to axon diameter and myelination, conduction velocity, and whether they are sensory or motor. The first classification scheme was devised in 1894 by Charles Sherrington, who measured the diameter of myelin-stained axons in sensory nerves, and subsequently codified by David Lloyd (Table 22–1). They found two or three overlapping groups of axonal diameters (Figure 22–2). It was later discovered that in muscle nerves these anatomical groupings are functionally important. Group I axons innervate muscle-spindle receptors and Golgi tendon organs, which signal muscle length and contractile force. Group II fibers innervate secondary spindle endings and receptors in joint capsules; these receptors also mediate proprioception. Group III fibers, the smallest myelinated muscle afferents, and the unmyelinated group IV afferents signal disorders in muscles and joints that can be sensed as painful.

Cutaneous nerves contain two sets of myelinated fibers: Group II fibers innervate cutaneous mechanoreceptors that respond to touch, and group III fibers mediate thermal and noxious stimuli. Unmyelinated group IV cutaneous afferents, like those in muscle, also mediate thermal and noxious stimuli.

Another method for classifying peripheral nerve fibers is based on electrical stimulation of whole nerves. In this widely used diagnostic technique nerve conduction velocities are measured between pairs of stimulating and recording electrodes placed on the skin above a peripheral nerve. When studying conduction in the median or ulnar nerve, for example, the stimulation electrode might be placed on the wrist and

Table 22–1 Classification of Sensory Fibers in Peripheral Nerves¹

	Muscle nerve	Cutaneous nerve ²	Fiber diameter (μm)	Conduction velocity (m/s)
Myelinated				
Large diameter	I	Aα	12–20	72–120
Medium diameter	II	Aβ	6–12	36–72
Small diameter	III	Aδ	1–6	4–36
Unmyelinated	IV	C	0.2–1.5	0.4–2.0

¹Sensory fibers from muscle are classified according to their diameter, whereas those from the skin are classified by conduction velocity.

²The types of receptors innervated by each type of fiber are listed in Table 22–2.

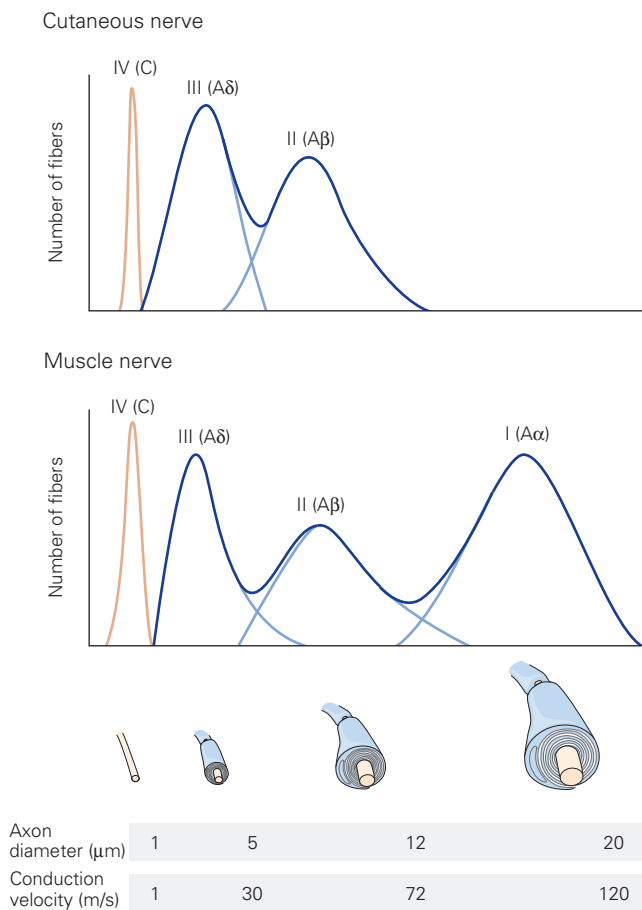


Figure 22-2 Peripheral nerves innervating skeletal muscle and the skin contain several types of sensory nerve fibers. The graphs illustrate the distribution of four groups of sensory nerve fibers innervating skeletal muscle and the skin. Each group has a characteristic axon diameter and conduction velocity. Light blue lines are the sum of fibers in each group in the zones of overlap. The conduction velocity of myelinated peripheral nerve fibers is approximately six times the fiber diameter. (Adapted, with permission, from Boyd and Davey 1968.)

the recording electrode on the upper arm. Brief electrical pulses applied through the stimulating electrode evoke action potentials in the nerve that are recorded a short time later in the arm. The recorded signal represents the summed action potentials of all of the nerve fibers excited by the stimulus pulse and is called the *compound action potential*. It increases in amplitude as more nerve fibers are stimulated; the summed activity is roughly proportional to the total number of active nerve fibers.

Electrical stimuli of increasing strength evoke action potentials in the largest axons first, for they

have the lowest electrical resistance, and then in progressively smaller axons. The earliest signal recorded in the compound action potential occurs in fibers with conduction velocities greater than 90 m/s. Called the $A\alpha$ wave (Figure 22-3), this signal reflects the action potentials generated in group I fibers and in motor neurons innervating skeletal muscle. The sensation is barely perceived by the subject in the region innervated.

A second signal, the $A\beta$ wave, appears as more large fibers are recruited. This component corresponds to group II fibers in skin or muscle nerves and becomes larger as the shock intensity is increased. At higher voltages, when axons in the smaller $A\delta$ range are recruited, the stimulus becomes painful, resembling an electric shock produced by static electricity. Voltages sufficient to activate unmyelinated C fibers evoke sensations of burning pain. Stimulation of motor neurons innervating muscle spindles evoke an intermediate wavelet called the $A\gamma$ wave, but this is usually difficult to discern because the conduction velocities of these motor neurons overlap those of $A\beta$ and $A\delta$ sensory axons.

The clinician takes advantage of the known distribution of the conduction velocities of afferent fibers in peripheral nerves to diagnose diseases that result in sensory-fiber degeneration or motor neuron loss. In certain conditions the loss of axons is selective; in the neuropathy characteristic of diabetes, for example, the large-diameter sensory fibers degenerate. Such a selective loss is reflected in a reduction in the appropriate peak of the compound action potential, a slowing of nerve conduction, and a corresponding diminution of sensory capacity. Similarly, in multiple sclerosis the myelin sheath of large-diameter fibers in the central nervous system degenerates, producing slowing of nerve conduction or failure of impulse transmission.

Rapid conduction in a peripheral nerve axon solves two problems. First, it provides the prompt sensory feedback required for motor control. The greatest velocities are in the afferent fibers from muscle that signal muscle length, contraction velocity, and force. Any delay in the feedback signal would cause instability, which probably explains why the fibers innervating spindles have the greatest diameters among peripheral axons.

Conduction-delay dispersion poses a second significant problem because conduction velocity varies among afferent fibers. Synchronous firing of a set of neurons becomes desynchronized by the time the action potentials reach the postsynaptic cells by an amount that is proportional to the mean conduction delay and the variation in conduction velocities. If the delay is great, either because the pathway is long or

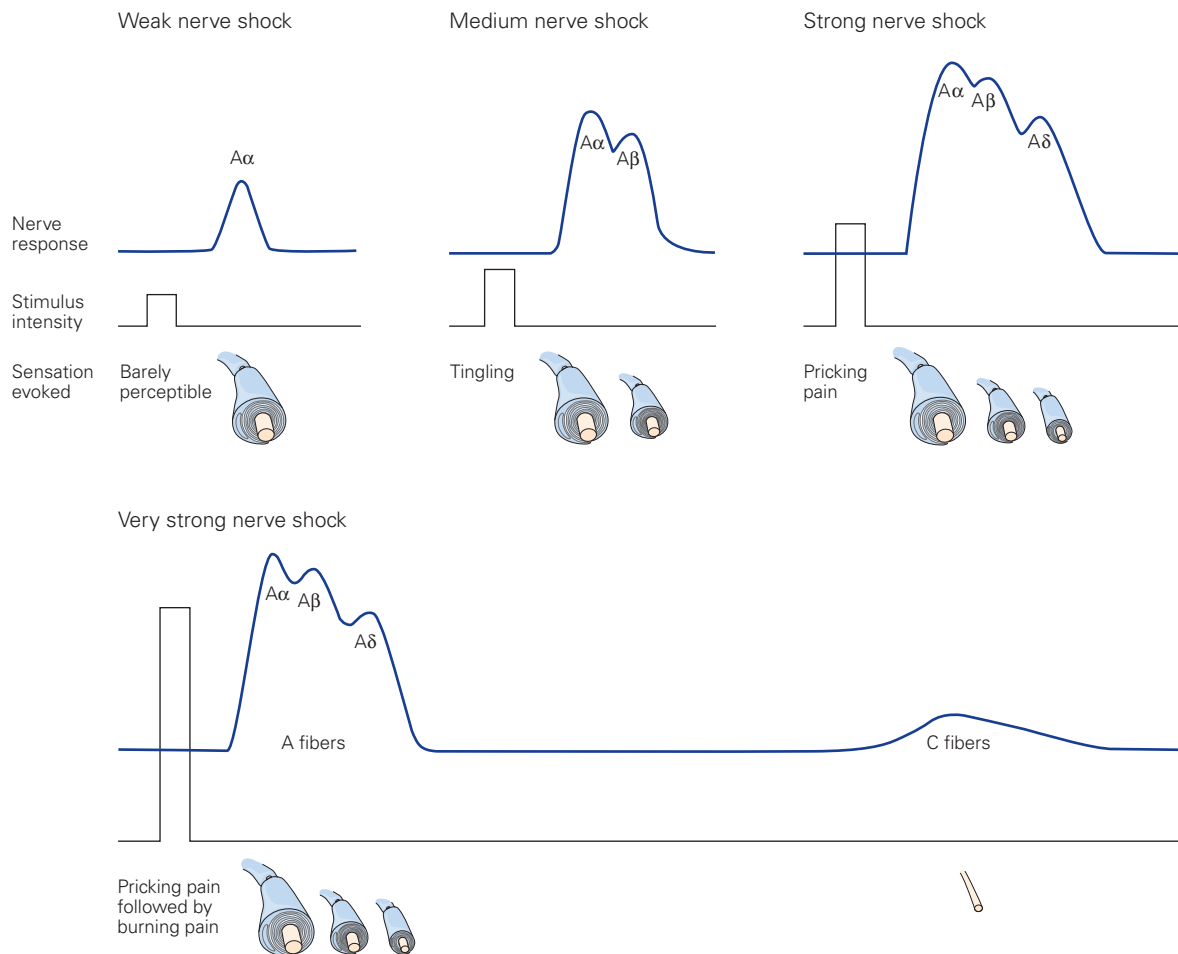


Figure 22-3 Conduction velocities of peripheral nerves are measured clinically from compound action potentials. Electrical stimulation of a peripheral nerve at varying intensities activates different types of nerve fibers. The action potentials of all the nerves stimulated by a particular amount of current are

summed to create the compound action potential. The distinct conduction velocities of different classes of sensory and motor axons produce multiple deflections. (Adapted, with permission, from Erlanger and Gasser 1938.)

because the conduction velocities are low, the desynchronization can be substantial.

As a general rule, conduction velocity throughout the nervous system is correlated with the need to maintain synchrony. The disparity in conduction times from a fingertip to the spinal cord can be calculated from the conduction velocities in Table 22-1 and by considering that the distance is approximately 0.8 m. In C fibers delays range from 0.8 s to 1.8 s, the mean delay is about 1.3 s, and the spike arrival times are distributed over about 1 s; thus events occurring more often than once per second are smeared together. In A α fibers delays range from 7.5 ms to 12.5 ms, the mean delay is 10 ms, and the arrival times vary by only 5 ms; events can therefore occur as often as 200 per second without smearing.

The comparable limits for A δ and A β fibers are approximately 8 Hz and 80 Hz. A blind person can scan his or her fingers across Braille dot patterns at remarkable rates of up to 100 mm/s with little loss of information because tactile information is conveyed by A β afferents, which maintain synchrony to within 12 ms.

Many Specialized Receptors Are Employed by the Somatosensory System

The particular receptor class expressed in the nerve terminal of a sensory neuron determines the type of stimulus detected by the neuron. The peripheral axons of the sensory neurons that mediate touch and

proprioception terminate in a nonneural capsule. They sense mechanical stimuli that indent or otherwise physically deform the receptive surface. In contrast the peripheral axons of neurons that detect noxious, thermal, or chemical events have unsheathed endings with multiple branches.

When a somatic receptor is activated by an appropriate stimulus, the terminal of the sensory neuron is typically depolarized. Stimuli of sufficient strength produce action potentials that are transmitted along the peripheral branch of the neuron's axon and into the central branch that terminates in the spinal cord or brain stem.

A variety of morphologically specialized receptors underlie the various somatosensory submodalities. For example, the median nerve that innervates the skin of the hand and some of the muscles controlling the hand contains tens of thousands of nerve fibers that can be classified into 30 functional types. Of these, 22 types are afferent fibers (sensory axons conducting

impulses toward the spinal cord), and eight types are efferent fibers (motor axons conducting impulses away from the spinal cord to skeletal muscle, blood vessels, and sweat glands). The afferent fibers convey signals from eight kinds of cutaneous mechanoreceptors that are sensitive to different kinds of skin deformation; five kinds of proprioceptors that signal information about muscle force, muscle length, and joint angle; four thermoreceptors that report the temperatures of objects touching the skin; four nociceptors that signal potentially injurious stimuli; and at least one kind of itch receptor. The major receptor groups within each submodality are listed in Table 22–2.

Mechanoreceptors Mediate Touch and Proprioception

Mechanoreceptors sense physical deformation of the tissue in which they reside. Mechanical distension,

Table 22–2 Receptor Types Active in Somatic Sensation

Receptor type	Fiber group ¹	Fiber name	Modality
Cutaneous and subcutaneous mechanoreceptors			Touch
Meissner corpuscle	A α , β	RA1	Stroking, flutter
Merkel disk receptor	A α , β	SA1	Pressure, texture
Pacinian corpuscle ²	A α , β	RA2	Vibration
Ruffini ending	A α , β	SA2	Skin stretch
Hair-tylotrich, hair-guard	A α , β	G1, G2	Stroking, fluttering
Hair-down	A δ	D	Light stroking
Field	A α , β	F	Skin stretch
C mechanoreceptor	C		Stroking, erotic touch
Thermal receptors			Temperature
Cool receptors	A δ	III	Skin cooling (<25°C [77°F])
Warm receptors	C	IV	Skin warming (>35°C [95°F])
Heat nociceptors	A δ	III	Hot temperature (>45°C [113°F])
Cold nociceptors	C	IV	Cold temperature (<5°C [41°F])
Nociceptors			Pain
Mechanical	A δ	III	Sharp, pricking pain
Thermal-mechanical (heat)	A δ	III	Burning pain
Thermal-mechanical (cold)	C	IV	Freezing pain
Polymodal	C	IV	Slow, burning pain
Muscle and skeletal mechanoreceptors			Limb proprioception
Muscle spindle primary	A α	Ia	Muscle length and speed
Muscle spindle secondary	A β	II	Muscle stretch
Golgi tendon organ	A α	Ib	Muscle contraction
Joint capsule receptors	A β	II	Joint angle
Stretch-sensitive free endings	A δ	III	Excess stretch or force

¹See Table 22–1.

²Pacinian corpuscles are also located in the mesentery, between layers of muscle, and on interosseous membranes.

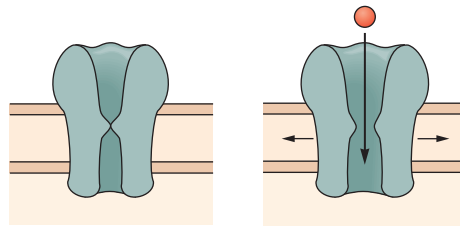
Figure 22–4 Ion channels in mechanoreceptor nerve terminals are activated by mechanical stimuli that stretch or deform the cell membrane. Mechanical displacement leads to channel opening, permitting the influx of cations. (Modified, with permission, from Lin and Corey 2005.)

A. Channels can be directly activated by forces conveyed through lipid tension in the cell membrane, such as osmotic swelling.

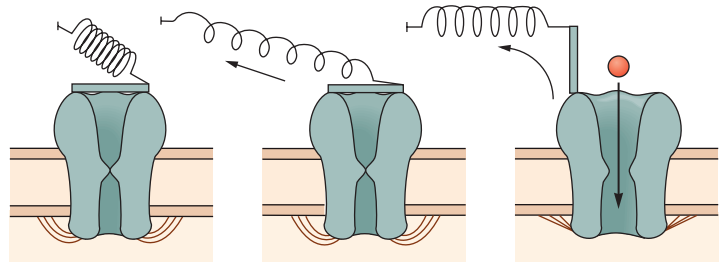
B. Forces conveyed through structural proteins linked to the ion channel can also directly activate channels. The linking proteins may be either extracellular (attached to the surrounding tissue) or intracellular (bound to the cytoskeleton) or both.

C. Channels can be indirectly activated by forces conveyed to a force sensor (a separate protein) in the membrane. An internal second messenger carries the sensory signal from the mechanosensitive protein to the channel.

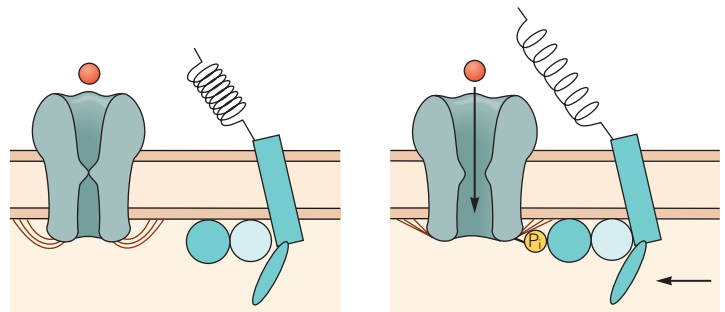
A Direct activation through lipid tension



B Direct activation through structural proteins



C Indirect action through membrane structural proteins



such as pressure on the skin or stretch of muscles, is transduced into electrical energy by the physical action of the stimulus on cation channels in the membrane. Mechanical stimulation deforms the receptor protein, thus opening stretch-sensitive ion channels and increasing Na^+ and Ca^{2+} conductances that depolarize the receptor neuron. Removal of the stimulus relieves mechanical stress on the receptor and allows stretch-sensitive channels to close.

Some mechanoreceptor ion channels are activated directly by forces applied to the tissue, permitting rapid activation and inactivation. For example, Pacinian corpuscle receptors in the skin can respond to vibration at frequencies as high as 500 Hz, firing one impulse for each vibratory cycle. This means that the receptor is capable of firing an impulse every 2 ms for sustained periods.

Various mechanisms for direct activation of mechanoreceptor ion channels have been proposed. Some mechanoreceptors appear to respond to forces conveyed through tension in the lipids of the plasma membrane (Figure 22–4A). This may be the mechanism for detection of cellular swelling, which plays an important role in osmoregulation.

Another mechanism for direct activation of mechanoreceptors is linking the channel to the surrounding tissue of the skin or to muscle cell membranes through structural proteins. The extracellular linkage is elastic and often represented as a spring, whereas the intracellular portion of the channel is anchored directly to proteins of the cytoskeleton (Figure 22–4B). Direct channel gating in this model may be produced by forces perpendicular or parallel to the receptor cell membrane that stretch the extracellular linkage protein.

This type of direct channel gating may be used by hair cells of the inner ear. Similar mechanical linkages between the skin and cutaneous mechanoreceptors have been postulated.

Likewise, mechanical coupling of sensory nerve terminals to skeletal muscle or tendons is thought to underlie proprioception. Unfortunately, because these receptors are embedded in nonneural tissue and thus difficult to isolate for biochemical analysis, the proteins involved in transduction have not been identified in mammals. Studies of invertebrates suggest that the transduction molecules for mechanosensation in skin and muscle may belong to the degenerin superfamily, which includes ion channels related to vertebrate epithelial Na^+ channels.

Some mechanoreceptor ion channels are activated indirectly through second-messenger pathways. In this case the force sensor in the receptor's cell membrane is a protein distinct from the ion channel (Figure 22-4C). A variety of intracellular messengers signal stimulation of the sensor to the ion channel, causing the channel to open. Unlike direct activation, the indirect pathway is slow to activate and inactivate, often outlasting the stimulus. The great advantage of the second-messenger mechanism of course is that the sensory signal is amplified; the conductance of many ionic channels can be affected by the activation of a single sensor molecule in the receptor cell. These properties are consistent with the responses of pain receptors sensitive to mechanical damage of the skin, such as pinch, or excessive distension of viscera. David Corey and co-workers have suggested that these sensations are mediated by TRPV4 receptors, a class of transient receptor potential (TRP) receptors that are also involved in thermal senses (see below).

The specialized, nonneural end organ that surrounds the nerve terminal of a mechanoreceptor nerve must be deformed in specific ways to excite the nerve. For example, individual receptors may respond selectively to pressure or motion, and may detect the direction of force applied to the skin, joints, or muscle fibers. The end organ can also amplify or modulate the sensitivity of the receptor to mechanical displacement.

The skin has eight types of mechanoreceptors that are responsible for the sense of touch (see Table 22-2). They are described briefly here and in greater detail in Chapter 23. The glabrous skin of the hands and feet contains four kinds of mechanoreceptors: Meissner corpuscles, Merkel cells, Pacinian corpuscles, and Ruffini endings (Figure 22-5). Two of these receptors are classified as slowly adapting (SA) because they continue to fire in response to steady pressure on the skin. The other two receptors are rapidly adapting (RA), responding to

motion on the skin but not to steady pressure. They also differ in receptor size and location within the skin.

Merkel cells are innervated by slowly adapting type 1 (SA1) fibers. They signal the amount of pressure applied to the skin and are particularly sensitive to edges, corners, and points. They distinguish textures and play key roles in the ability to read Braille. The Ruffini endings are innervated by slowly adapting type 2 (SA2) fibers. These receptors respond more vigorously to stretch than to indentation of skin, and consequently are particularly sensitive to the shape of large objects held in the hand. They also signal movements of the fingers and other joints that stretch the overlying skin.

Meissner corpuscles are innervated by rapidly adapting type 1 (RA1) fibers. These receptors detect the initial contact of the hand with objects, slippage of objects held in the hand, motion of the hand over textured surfaces, and low-frequency vibration. The Pacinian corpuscles are innervated by rapidly adapting type 2 (RA2) fibers. The receptor is a large, onion-like capsule that surrounds the axon terminal. It responds to motion in the nanometer range and mediates high-frequency vibration. The most important role of Pacinian corpuscles is detection of vibrations in tools, objects, or probes held in the hand.

The general hairy skin includes all of the mechanoreceptor organs of the glabrous skin except the Meissner corpuscle; the hair follicle afferents serve a function similar to that of Meissner corpuscles. Hair follicle afferents innervate 10 to 30 hairs spread over an area of 1 to 2 cm^2 and are sensitive to hair movement but not to static pressure. Other mechanoreceptors of the hairy skin include field receptors, which are very sensitive to skin movement, and low-threshold mechanoreceptors innervated by C fibers that respond to slow stroking of the skin and are thought to mediate erotic touch.

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. 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; and joint-capsule receptors, which transduce tension in the joint capsule.

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 22-6A). The intrafusal fibers

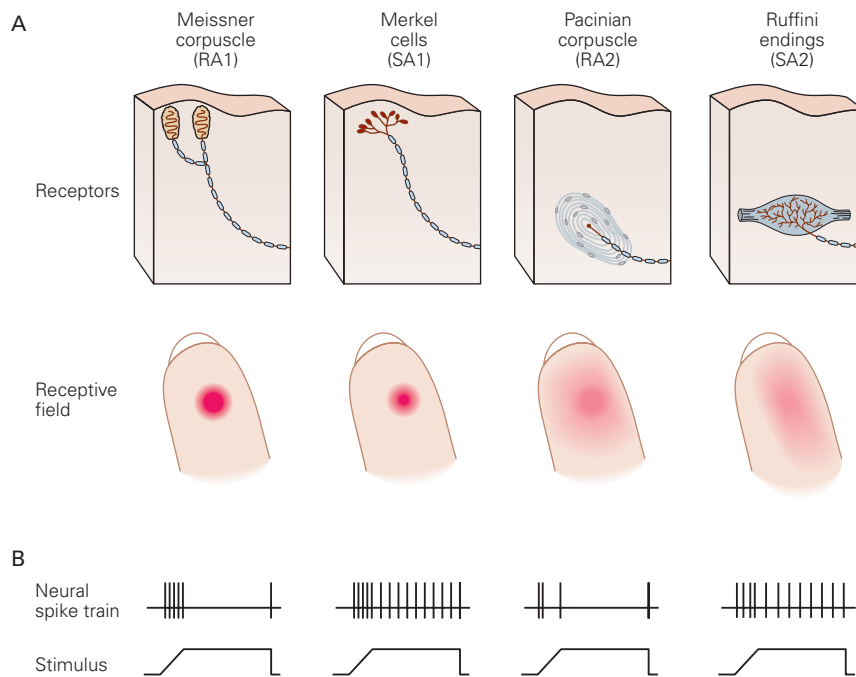


Figure 22-5 Touch is mediated by four types of mechanoreceptors in the human hand. The terminals of myelinated sensory nerves innervating the hand are surrounded by specialized structures that detect contact on the skin. The receptors differ in morphology, innervation patterns, location in the skin, receptive field size, and physiological responses to touch. (Adapted, with permission, from Johansson and Vallbo 1983.)

A. The superficial and deep layers of the glabrous (hairless) skin of the hand each contain distinct types of mechanoreceptors. The superficial layers contain small receptor cells: Meissner corpuscles and Merkel cells. The sensory nerve fibers innervating these receptors have branching terminals such that each fiber innervates multiple receptors of one type. The deep layers of the skin and subcutaneous tissue contain large receptors: Pacinian corpuscles and Ruffini endings. Each of these receptors

is innervated by a single nerve fiber, and each fiber innervates only one receptor. The receptive field of a mechanoreceptor reflects the location and distribution of its terminals in the skin. Touch receptors in the superficial layers of the skin have smaller receptive fields than those in the deep layers. (RA1, rapidly adapting type 1; RA2, rapidly adapting type 2; SA1, slowly adapting type 1; SA2, slowly adapting type 2.)

B. The nerve fibers innervating each type of mechanoreceptor respond differently when activated. The spike trains show responses of each type of nerve when its receptor is activated by constant pressure against the skin. The RA type fibers that innervate Meissner and Pacinian corpuscles adapt rapidly to constant stimulation while the SA type nerves that innervate Merkel cells and Ruffini endings adapt slowly.

are entwined by a pair of sensory axons that detect muscle stretch because of mechanoreceptive ion channels in the nerve terminals. Intrafusal muscles are also innervated by motor neurons that determine contractile force. (See Box 35-1 for details on muscle spindles.)

Although the receptor potential and firing rates of the sensory axons are proportional to muscle length (Figure 22-6B), these responses can be modulated by higher centers in the brain that regulate contraction of intrafusal muscles. In this manner the spindle afferents are able to signal the amplitude and speed of internally generated voluntary movements as well as passive limb displacement by external forces.

Golgi tendon organs, located between skeletal muscle and tendons, measure the forces generated

by muscle contraction. (See Box 35-3 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.

Joint receptors play little if any role in postural sensations of joint angle. Instead, the perception of the angle of proximal joints such as the elbow or knee depends on afferent signals from muscle spindle receptors and efferent motor commands. Likewise, conscious sensations of finger position and hand shape

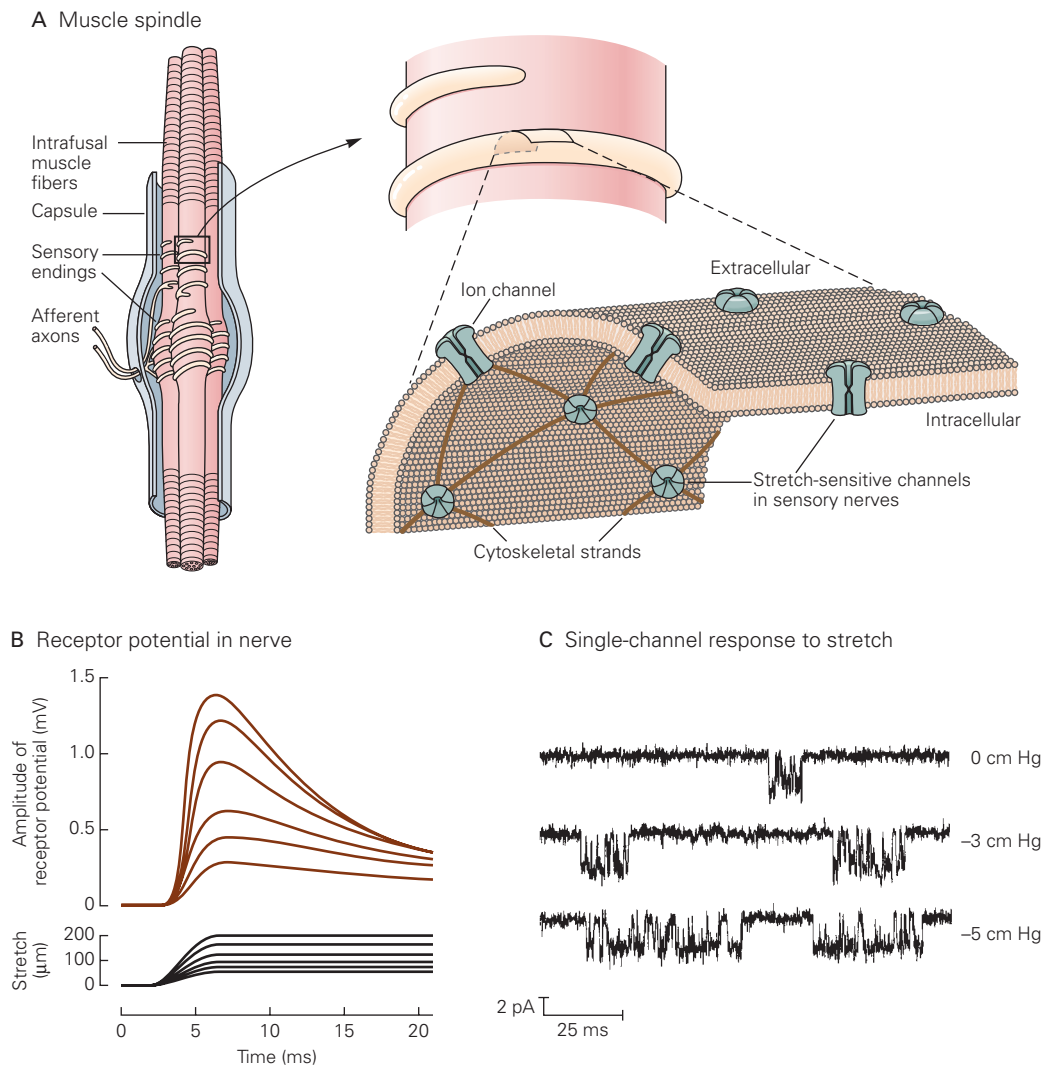


Figure 22-6 The muscle spindle is the principal receptor mediating proprioception.

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, and 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 (**upper record**) is proportional to both the velocity and amplitude of muscle stretch

parallel to the myofilaments (**lower record**). 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 (**top record**) the channel opens sporadically for short time intervals. As the pressure applied to the membrane increases (**lower records**) 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 Sachs 1990.)

depend on stretch receptors in the skin as well as muscle spindles and possibly joint receptors.

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 importantly, they provide a constant reminder of tissues that are already injured and must be protected.

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 A δ fibers produce short-latency pain that is described as sharp and pricking. The majority are called mechanical nociceptors because they are excited by sharp objects that penetrate, squeeze, or pinch the skin (Figure 22–7). Many of these A δ fibers also respond to noxious heat that can burn the skin.

Nociceptors innervated by C fibers produce dull, burning pain that is diffusely localized and poorly tolerated. The most common type are 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. 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.

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 external temperature of the air or of objects contacting the body and the normal skin temperature of approximately 32°C (90°F).

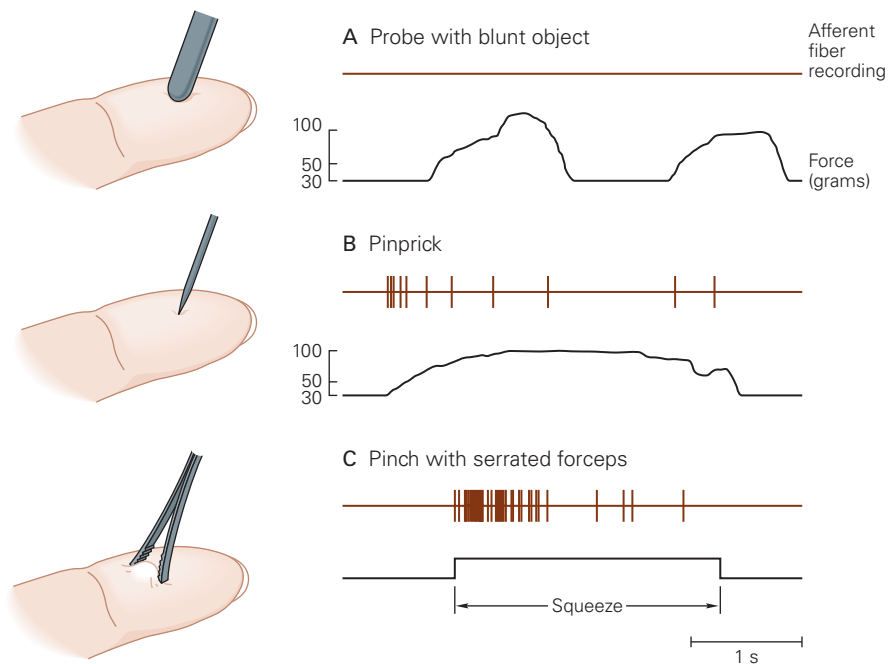


Figure 22–7 Mechanical nociceptors respond to stimuli that puncture, squeeze, or pinch the skin. Sensations of sharp, pricking pain result from stimulation of A δ fibers with free nerve endings in the skin. These receptors respond to sharp objects that puncture the skin (B) but not to strong pressure

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.)

Although we 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 open and close 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 result from the combined activity of six types of afferent fibers: low-threshold and high-threshold cold receptors, warm receptors, and two classes of heat nociceptors. The low-threshold cold receptor fibers are small-diameter, myelinated A δ fibers with unmyelinated endings within the epidermis. They 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. The high-threshold cold receptor fibers are much less sensitive to small cooling changes, but can signal rapid skin cooling even below 0°C (32°F).

The various qualities of cold sensations can be experienced by grasping an ice cube in a closed fist. Over the first five seconds or so the sensation progresses from cool to cold. After 10 seconds the sensation becomes progressively more painful. If the ice is held still longer, the sensation begins to include a deep, aching quality. The low-threshold and high-threshold receptors account for the initial sensations; the aching cold pain likely results from receptors within the veins.

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. Thus they cannot play a role in signaling heat pain. They are much less sensitive to rapid changes in skin temperature than are cold receptors. Consequently, humans are less responsive to warming than cooling; the threshold for detecting sudden skin warming, even in the most sensitive subject, is about 0.1 Centigrade degree.

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 A δ fibers and unmyelinated C fibers.

Recent studies by David Julius and his colleagues revealed that thermal stimuli activate specific classes of

TRP ion channels in the membrane. These nonselective cation receptor-channels are similar in structure to voltage-gated channels. They have four protein subunits, each of which contains six transmembrane domains, with a pore between the fifth and sixth segments. Both the C and N terminals are located in the cytoplasm. Individual TRP receptor-channels are distinguished by their sensitivity to heat or cold, showing sharp increases in conductance to cations when their thermal threshold is exceeded (Figure 22–8). 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 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.

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 activated by temperatures above 27°C and respond to normal skin temperatures. They may play a role in touch sensation.

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 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. These substances act by covalent modification of cysteines in the TRP channel protein.

Itch Is a Distinctive Cutaneous Sensation

Itch is a common sensory experience that is confined to the skin, the ocular conjunctiva, and the mucosa. Itch has some properties in common with pain and

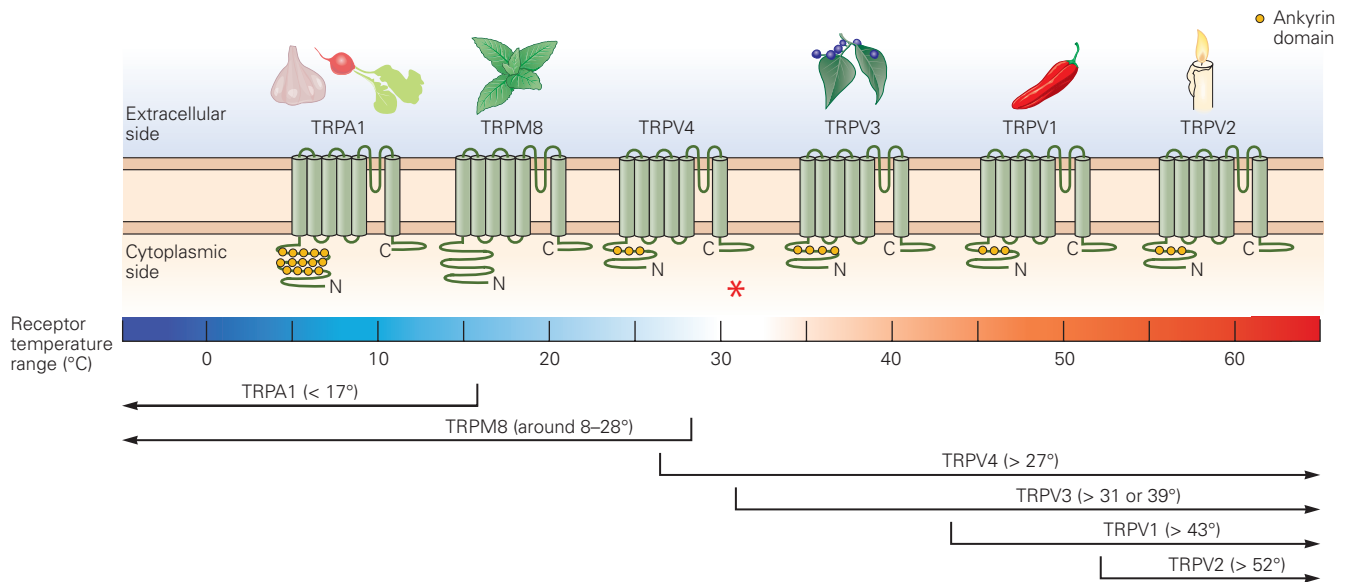


Figure 22–8 Transient receptor potential ion channels. Transient receptor potential (TRP) channels are membrane proteins with six transmembrane domains. A pore is formed between the fifth (S5) and sixth (S6) segments. Both C- and N-terminals are located in the cytoplasm. Most of these receptors contain ankyrin repeats in the N-terminal domains and a common 25-amino acid motif adjacent to S6 in the C-terminal domain. 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 alliums 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 but not TRPV2 receptors bind capsaicin, which mediates the burning sensations evoked by chili peppers. TRPV4 receptors are active at normal skin temperatures and respond to touch. (Adapted, with permission, from Jordt, McKemy, and Julius 2003; Dhaka, Viswanath, and Patapoutian 2006.)

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. When nerve conduction is blocked with pressure, itch persists until the slowest unmyelinated fibers stop firing.

Itch can be induced either by the injection of histamine or by procedures that release endogenous histamine, which suggests that the transducers are coupled to histamine receptors. Intradermal injection of a large dose of histamine produces intense itch that persists for tens of minutes but only mild pain, a strong indication that itch is not the result of low-level firing in polymodal nociceptors. Instead, itch appears to be mediated by a recently discovered class of C fibers with very slow conduction velocities (0.5 m/s) and physiological properties paralleling the time course of histamine-evoked itch.

Visceral Sensations Represent the Status of Various Internal Organs

Visceral sensations are important physiologically because they drive several types of behavior that are critical for survival, such as respiration, hunger, thirst, sexual arousal, and copulation. After about a minute without breathing, hunger for air, feelings of suffocation, and the need to relieve those sensations become all-consuming behavioral goals. These sensations allow us to hold our breath when needed with the knowledge that an internal sensory signal will tell us when it is no longer safe to do so. Thirst and hunger likewise provide the motivation to drink and eat; they come to dominate our behavior when we have been without water or food for periods that threaten our survival.

Visceral sensations that are linked directly to survival result from both peripheral and central sensors. Sensations associated with the need to breathe, for

example, arise from partial pressure of oxygen (PO_2) and partial pressure of carbon dioxide (PCO_2) sensors in the carotid bodies associated with the carotid arteries and from PCO_2 receptors in the respiratory centers of the medulla and hypothalamus (see Chapter 45). Damage to these medullary centers results in a loss of air hunger (Ondine's curse) and often death from failure of automatic breathing during sleep.

Hunger arises from an interaction between signals from hypothalamic chemoreceptors that respond to a variety of molecules in the blood and signals from the gut that indicate the presence or absence of food (see Chapter 49). Thirst results from central mechanisms whose site is uncertain and from peripheral signals from osmoreceptors in the liver and stretch receptors in the cardiopulmonary blood vessels that provide information on blood volume (see Chapter 49).

Nausea, which teaches animals—including us—which foods are unsafe to eat, depends on vagal serotonin receptors in the gut as well as the area postrema in the brain stem. Neurons within the area postrema are able to sense toxins in the blood and cerebrospinal fluid because the area lacks a blood-brain barrier (see Appendix D).

Sensations associated with sexual arousal and copulation, which are essential for survival of the species, arise from low-threshold mechanoreceptors in the genitalia and other body sites. Although the central component is not certain, functional imaging studies and experimental lesion studies suggest that the preoptic area and anterior hypothalamus are important components of arousal (see Chapter 47).

Somatosensory Information Enters the Central Nervous System Through Cranial and Spinal Nerves

Sensory information reaches the central nervous system either through the 31 spinal nerves, which enter through openings between the vertebrae of the spine, or through the 12 cranial nerves, which enter through openings in the cranium. The afferent and efferent axons within a spinal nerve arise from the dorsal and ventral roots of the spinal cord (see Figure 16–3), which are arrayed more or less continuously along the dorsal and ventral surfaces of each half of the cord (see Figure 16–2). To exit between the vertebrae, the roots gather into nerves that are named for the vertebrae below the foramen through which they pass (cervical nerves) or above (thoracic, lumbar, and sacral nerves).

The skin and deeper tissues innervated by the afferent fibers of a single spinal nerve constitute a

dermatome (Figure 22–9); the muscles innervated by the same nerve constitute a *myotome*. These are the skin and muscle regions affected by damage to a single spinal nerve. Because the dermatomes overlap, three adjacent spinal nerves often have to be blocked to anesthetize a particular area of skin.

Individual spinal nerves terminate on neurons located in specific zones of the spinal cord gray matter (see Figure 16–1). The spinal neurons that receive sensory input are either interneurons, which terminate upon other spinal neurons within the same or neighboring segment, or projection neurons that serve as the cells of origin of major ascending pathways to higher centers in the brain.

All but one of the spinal nerves contain both afferent and efferent nerve fibers; the exception is C1, which usually has only efferent axons. In contrast, 8 of the 12 cranial nerves are either pure motor or pure sensory nerves serving the special senses (olfactory, optic, and vestibulocochlear). The remaining four nerves (trigeminal, facial, glossopharyngeal, and vagus) are mixed nerves that together serve the same range of bodily senses as do the spinal nerves. Like the spinal nerves, the cell bodies of cranial nerves lie in ganglia near the point of entry to the central nervous system.

Each of the mixed cranial nerves has a distinct pattern of termination within the central nervous system and each is devoted principally to sensory information either from the viscera or from the skin and muscles (see Figure 45–5). The trigeminal nerve conveys sensory information from muscles of mastication and skin on the anterior half of the head. The facial and glossopharyngeal nerves innervate the taste buds of the tongue, the skin of the ear, and some of the skin of the tongue and pharynx. The glossopharyngeal and vagus nerves provide some cutaneous information, but their main sensory role is visceral. Cutaneous and proprioceptive information from all four nerves enters the trigeminal nuclei; visceral information flows into the nucleus of the solitary tract.

Somatosensory Information Flows from the Spinal Cord to the Thalamus Through Parallel Pathways

The nerve fibers that convey the various somatosensory submodalities from each dermatome are bundled together in the peripheral nerves as they enter the dorsal root ganglia. However, as the fibers exit the ganglia and approach the spinal cord, the large- and small-diameter fibers separate into medial and lateral divisions.

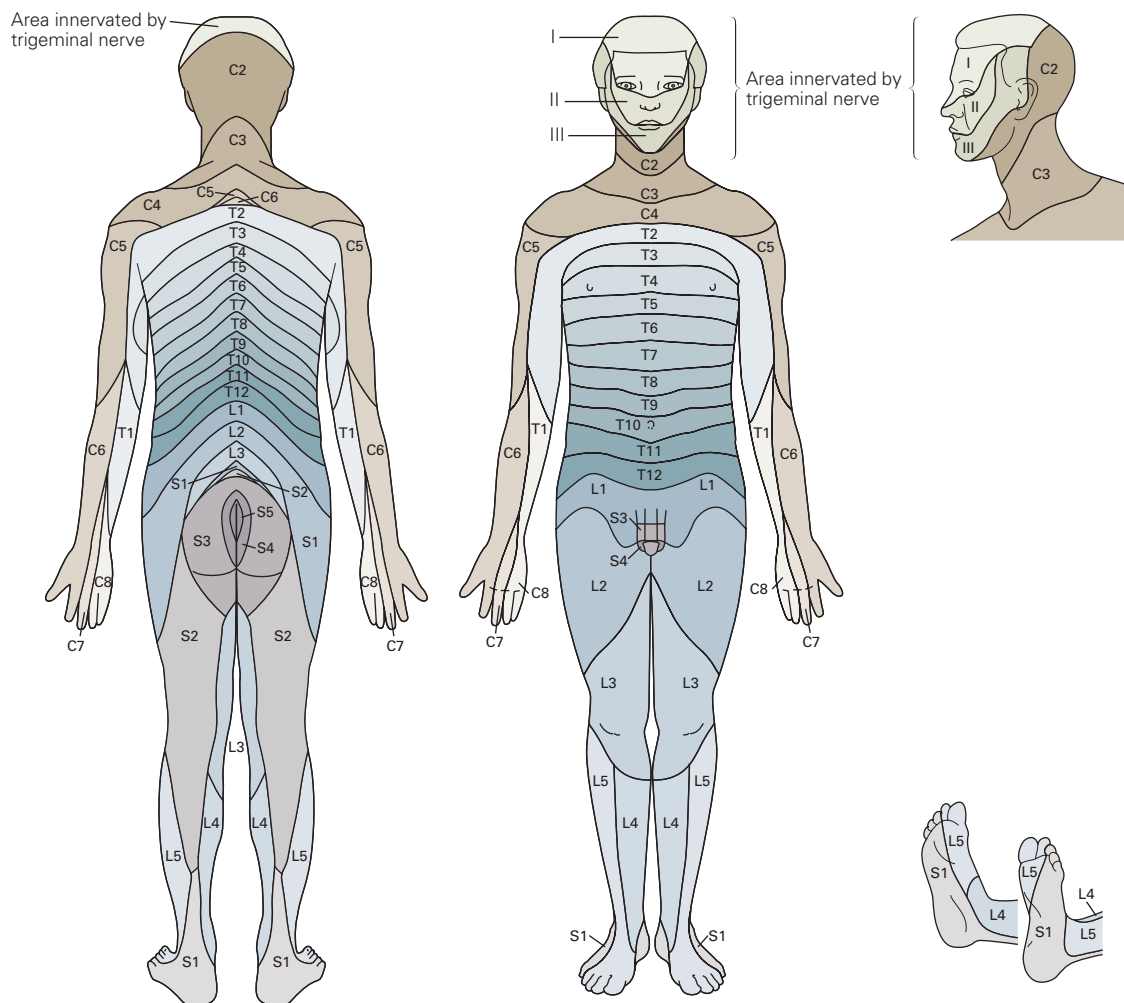


Figure 22-9 The distribution of dermatomes. A dermatome is the area of skin and deeper tissues innervated by a single dorsal root. The dermatomes of the 31 pairs of dorsal root nerves are projected onto the surface of the body and labeled by the foramen through which each nerve enters the spinal cord. The 8 cervical (C), 12 thoracic (T), 5 lumbar (L), 5 sacral (S), and single coccygeal roots are numbered rostrocaudally for each division of the vertebral column. The facial skin, cornea, scalp, dura, and intra-oral regions are innervated by the

ophthalmic (I), maxillary (II), and mandibular (III) divisions of the trigeminal nerve (cranial nerve V). Level C1 has no dorsal root, only a ventral (or motor) root. Dermatome maps provide an important diagnostic tool for locating injury to the spinal cord and dorsal roots. However, the boundaries of the dermatomes are less distinct than shown here because the axons comprising a dorsal root originate from several different peripheral nerves, and each peripheral nerve contributes fibers to several adjacent dorsal roots.

The medial division includes large, myelinated $A\alpha$ and $A\beta$ fibers that transmit proprioceptive and cutaneous information from a dermatome. The lateral division includes small thinly myelinated $A\delta$ and unmyelinated C fibers that transmit noxious, thermal, and visceral information from the same dermatome. After entering the spinal cord the afferent fibers become further segregated according to modality and terminate on different functional sets of neurons in the

gray matter of the same or adjacent spinal segments. In addition, the $A\alpha$ and $A\beta$ fibers send a major branch to the medulla through the dorsal columns.

The gray matter in each spinal segment is divided into three functionally distinct regions: the dorsal and ventral horns and an intermediate zone. As a general rule the largest fibers ($A\alpha$) terminate in or near the ventral horn, the medium-size fibers ($A\beta$) from the skin and muscle terminate in intermediate layers of

the dorsal horn, and the smallest fibers ($A\delta$ and C) terminate in the most dorsal portion of the spinal gray matter.

The spinal gray matter is further subdivided into 10 laminae (or layers), numbered I to X from dorsal to ventral, based on differences in cell and fiber composition. Lamina I consists of a thin layer of neurons capping the dorsal horn of the spinal cord and pars caudalis of the spinal trigeminal nucleus. Individual neurons of lamina I receive monosynaptic inputs from small myelinated fibers ($A\delta$) or unmyelinated C fibers of a single type (Figure 22–10) and therefore transmit information about noxious, thermal, or visceral stimuli. Inputs from warm, cold, itch, and pain receptors have been identified in lamina I, and some neurons have unique cellular morphologies. Lamina I neurons generally have small receptive fields localized to one dermatome.

Neurons in laminae II and III are interneurons that receive inputs from $A\delta$ and C fibers, and make

excitatory or inhibitory connections to neurons in lamina I, IV, and V that project to higher brain centers. The dendrites of neurons in laminae III to V are the main targets of the large myelinated sensory ($A\beta$) fibers from cutaneous mechanoreceptors (Figure 22–10). Neurons in lamina V typically respond to more than one modality—low-threshold mechanical stimuli, visceral stimuli, or noxious stimuli—and have therefore been named *wide-dynamic-range neurons*.

Visceral C fibers have widespread projections in the spinal cord that terminate ipsilaterally in laminae I, II, V, and X; some also cross the midline and terminate in lamina V and X of the contralateral gray matter. The extensive spinal distribution of visceral C fibers appears to be responsible for the poor localization of visceral pain sensations. Afferents from the pelvic viscera make important connections to cells in the central gray matter (lamina X) of spinal segments L5 and S1. Lamina X neurons in turn project their axons along the midline of the dorsal columns to

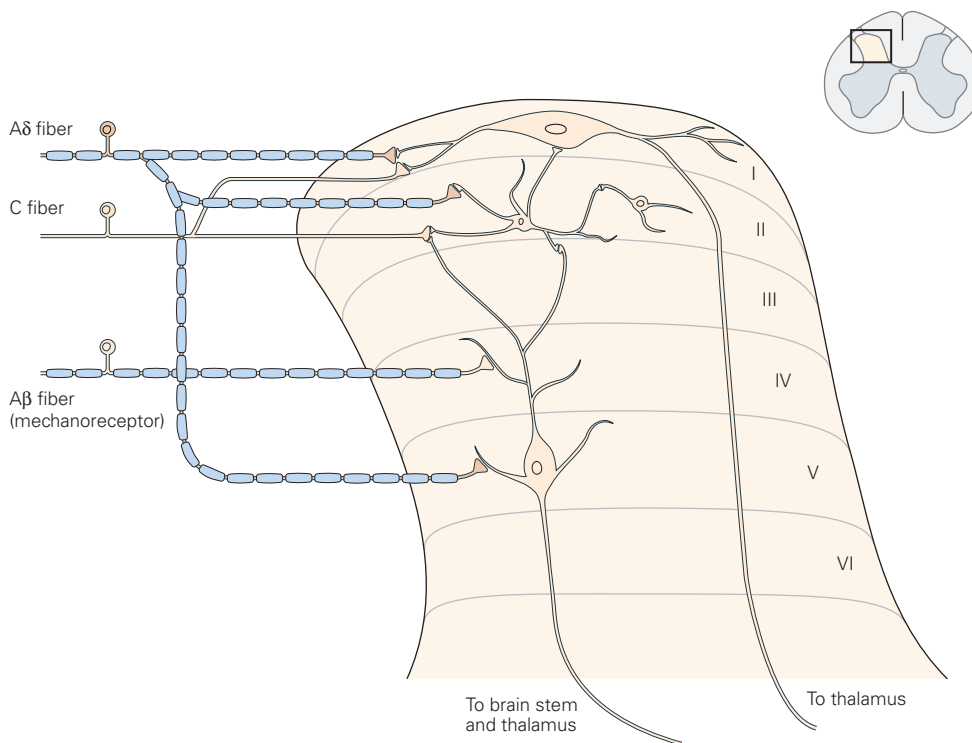


Figure 22–10 The spinal gray matter in the dorsal horn and intermediate zone is divided into six layers of cells (laminae I–VI) each with functionally distinct populations of neurons. The axons of neurons in laminae I and V make up the majority of fibers in the spinothalamic tract (see Figure 22–11). Neurons in lamina I receive nociceptive or thermal inputs from receptors

innervated by $A\delta$ or C fibers, and from interneurons in lamina II; their axons are the fastest conducting fibers in the spinothalamic tract. Neurons in lamina V respond to nociceptive and tactile information because they receive inputs from both $A\beta$ and $A\delta$ fibers as well as from interneurons in laminae II, III, and IV. (Adapted, with permission, from Fields 1987.)

the nucleus gracilis in a postsynaptic dorsal column pathway for visceral pain.

Primary afferent fibers that terminate in the deepest laminae in the ventral horn feed back information from proprioceptors that is required for somatic motor control, such as spinal reflexes (see Chapter 35).

Functional separation of sensory afferents is maintained in the pathways to higher centers in the brain. Somatosensory information is conveyed to the thalamus and cerebral cortex by two ascending pathways. The dorsal column–medial lemniscal system transmits tactile and proprioceptive information, and the spinothalamic tract pain and thermal information. A third pathway, the dorsolateral tract, conveys somatosensory information from the lower half of the body to the cerebellum.

The Dorsal Column–Medial Lemniscal System Relays Tactile and Proprioceptive Information

The dorsal column on each side contains the central branches of A α and A β afferents as they ascend to the medulla and thus form the major ascending pathway for tactile and proprioceptive information to the brain stem nuclei from which somatosensory information is conveyed to the cerebral cortex. They represent the most prominent anatomical feature of the dorsal funiculus of the spinal cord.

Each dorsal column is bounded medially by the median septum and laterally by the dorsal horn of the gray matter (Figure 22–11). Each contains about a million fibers as it enters the brain stem and terminates within the ipsilateral dorsal column nuclei. Of these fibers 90% are axons of dorsal root ganglion cells, and the remaining 10% are axons of spinal neurons. The postsynaptic dorsal column axons that course along the midline adjacent to the medial septum provide a specialized rapid pathway for visceral pain.

Fibers from the spinal nerves are added successively to the medial edge of the dorsal column, beginning with the fibers from the upper cervical segment and ending with the most caudal spinal nerve in the layer next to the midline. This lateral-to-medial arrangement reflects the fact that during development the most rostral spinal segments are formed earlier than the more caudal ones. In this way the dorsal column is arranged in layers, one for each dermatome. Because the dermatomes overlap extensively, adjacent layers do not convey a continuous somatotopic representation of the skin. However, when the fibers reach the brain stem they are sorted into a coherent map of the receptor sheet, with the anogenital skin of the ipsilateral side of the body most medial and the skin of the ipsilateral neck and head most lateral.

Caudal to T7 the dorsal column on each side is called the *gracile* (slender) *fascicle*. At about T7 a sulcus appears, and the remaining spinal nerves contribute to a second column called the *cuneate* (wedge-shaped) *fascicle*. The division between gracile and cuneate fascicles is important only because they terminate in anatomically distinct nuclei in the caudal brain stem, the gracile and cuneate nuclei (Figure 22–11). Together with the external cuneate nucleus and other minor nuclei, they form the dorsal column nuclei.

The gracile and cuneate nuclei are shaped like sausages with a rostrocaudal orientation. Primary afferent fibers terminate on neurons throughout the rostrocaudal extent of each nucleus so that a rod-like collection of cells extending the length of the nucleus represents one small skin region, and the neurons in any cross section represent the entire body. The somatic representation in that neural map is of a headless homunculus lying on his back with his sacrum toward the midline and his hands and feet extended dorsally. Tactile and proprioceptive information from the head, face, and mouth is represented in the adjacent principal trigeminal nucleus.

Somatosensory submodalities are segregated in the dorsal column nuclei: Individual neurons receive synaptic inputs from afferents of a single type and neurons of distinct types are spatially separated. The rostral third of the dorsal column nuclei is dominated by neurons that process proprioceptive information; nearly 75% receive sensory information from muscle afferents. Tactile inputs predominate in the middle third where nearly 90% of the neurons process cutaneous information. The neurons in the caudal third are evenly divided between cutaneous and proprioceptive modalities.

There is also a dorsal-ventral gradient both in the dorsal columns and in the dorsal column nuclei; proprioceptive neurons are more common ventrally and cutaneous neurons more common dorsally. This division may simply reflect the fact that the hands and feet, which have dense cutaneous innervation but relatively little musculature, are represented dorsally, whereas the trunk and proximal limbs, with more muscle and less skin innervation, are represented ventrally.

Lateral and rostral to the cuneate nucleus proper is the external cuneate nucleus, which receives proprioceptive afferents from the arm and hand. The external cuneate nucleus projects to both the cerebellum and thalamus.

Axons of neurons in the dorsal column nuclei form the *medial lemniscus*, which crosses the midline in the medulla and is joined medially by the homologous projection from the trigeminal nuclei (Figure 22–11). In transit the somatotopic representation becomes inverted; within the thalamus the somatotopic map

displays the head medially, the sacrum laterally, and the hands and feet ventrally. Because of the crossing of the fibers in the medial lemniscus, the left side of the brain receives somatosensory input from the mechanoreceptors on the right side of the body, and vice versa.

Cutaneous information from the dorsal column and trigeminal nuclei enters the lateral and medial ventral posterior nuclei of the thalamus, which form a single functional entity. Proprioceptive information enters the superior ventral posterior nucleus, which lies just above the other two (see Figure 16–5).

The Spinothalamic System Conveys Noxious, Thermal, and Visceral Information

The *spinothalamic tract* is the principal pathway transmitting noxious, thermal, and visceral information to the thalamus and cerebral cortex (Figure 22–11). It originates from neurons in laminae I, V, and VII, the main targets of the small-diameter fibers with sensory information destined for conscious perception. These neurons have distinctive physiological properties based on their sensory inputs.

More than 50% of spinal projections to the thalamus originate from neurons in lamina I, neurons that receive inputs from nociceptors, thermal receptors, visceral afferents, or itch receptors. Lamina I has the characteristics of a modality-segregated sensory relay nucleus for somatic and visceral information transmitted by small-diameter myelinated fibers (A δ) or unmyelinated C fibers of a single type. The second major origin of fibers in the spinothalamic tract is wide-dynamic-range neurons in lamina V that respond to various combinations of tactile, visceral, thermal, and noxious stimuli.

It is reasonable to suppose, based on the neurophysiological responses of neurons in lamina I and V,

that thermal sensations originate in fibers arising in lamina I whereas pain originates in fibers from either system. The pattern of sensation evoked by stimulation also reflects the projection patterns of spinothalamic tract neurons, for most but not all cross the midline to ascend in the contralateral tract (82% of the stimulus sites produced contralateral sensation, 12% ipsilateral, and 6% bilateral sensations).

The third major source of spinothalamic tract fibers is neurons in lamina VII and in deeper parts of the spinal gray matter. Lamina VII neurons receive inputs from large areas of the body, including the viscera, and therefore have very large receptive fields. This severely limits their ability to localize sensory stimuli. Further, they project to nuclei in the thalamus that are more involved in affective responses to stimuli than in identification and localization of stimuli.

The axons of most neurons in lamina I cross the midline, just ventral to the central canal, and ascend in the contralateral *lateral spinothalamic tract* located in the lateral funiculus. Axons of lamina V neurons cross the spinal cord and ascend in the contralateral *ventral spinothalamic tract*. They convey mixed information from visceroreceptors, nociceptors, and low-threshold mechanoreceptors to the thalamus.

As in the medial lemniscus, fibers in the spinothalamic tract are arranged somatotopically. Fibers originating in the lumbar and sacral segments are located laterally, whereas those from the cervical spinal segments are positioned medially. The spinothalamic tract is joined by axons from the trigeminal nucleus caudalis.

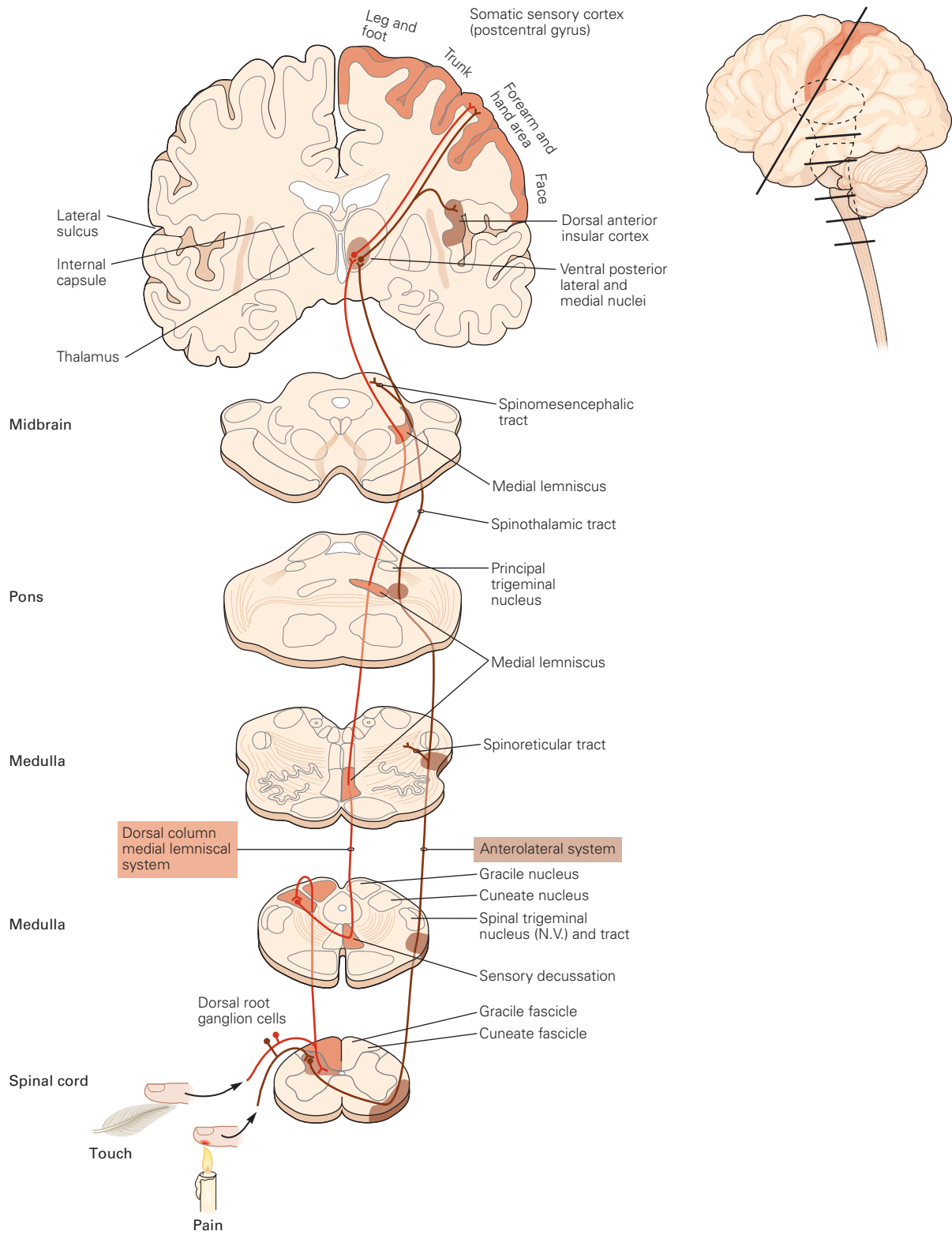
As a result of the decussation of spinothalamic fibers in the spinal cord, noxious and thermal information from each dermatome is transmitted contralaterally in the anterolateral column, whereas touch and proprioception are transmitted ipsilaterally in the dorsal column. Unilateral injury to the spinal

Figure 22–11 (Opposite) Somatosensory information from the limbs and trunk is conveyed to the thalamus and cerebral cortex by two ascending pathways. Brain slices along the neuraxis from the spinal cord to the cerebrum illustrate the anatomy of the two principal pathways conveying somatosensory information to the cerebral cortex. The two pathways are separated until they reach the pons, where they are juxtaposed.

Dorsal column—medial lemniscal system. Tactile and limb proprioception signals are conveyed to the spinal cord and brain stem by large-diameter myelinated fibers and transmitted to the thalamus in this system. In the spinal cord the fibers for touch and proprioception divide, one branch going to the spinal gray matter and the other ascending in the ipsilateral dorsal column to the medulla. The second-order fibers from

the dorsal column nuclei cross the midline in the medulla and ascend in the medial lemniscus toward the thalamus, where they terminate in the lateral and medial ventral posterior nuclei. These nuclei convey tactile and proprioceptive information to the primary somatic sensory cortex.

Anterolateral system. Pain, itch, temperature, and visceral information is conveyed to the spinal cord by small-diameter myelinated and unmyelinated fibers that terminate in the dorsal horn. This information is conveyed across the midline within the spinal cord and transmitted to the brain stem and the thalamus in the contralateral anterolateral system. Anterolateral fibers terminating in the brain stem comprise the spinoreticular and spinomesencephalic tracts; the remaining anterolateral fibers form the spinothalamic tract.



cord may therefore produce deficits in tactile and proprioceptive sensations on the same side of the body as the lesion, and impairments in thermal or painful sensations on the side opposite the lesion. The somatosensory submodalities of touch, proprioception, temperature, and pain are reunited on the contralateral side of the neuraxis higher in the brain stem as the medial lemniscus and spinothalamic tract approach the thalamus (Figure 22–11).

Information carried by small-diameter sensory fibers may also reach the cerebral cortex through several polysynaptic routes other than the spinothalamic tract. These paths include the spinomesencephalic, spinoreticular, and spinolimbic tracts that project to brain stem nuclei such as the parabrachial nucleus (Figure 22–11). These brain stem nuclei in turn project to the thalamus and to other sites that may have a sensory role, such as the hypothalamus and amygdala. Although many of these pathways originate from neurons in lamina I and V, and have physiological properties similar to spinothalamic tract neurons, they arise from a different group of neurons. Neurons that project to sites other than the thalamus may be involved in homeostasis and autonomic regulation.

Finally, as noted above, the most medial fibers in the dorsal column relay signals from nociceptors in the pelvic and abdominal viscera. We know that the postsynaptic dorsal column pathway originates with cells in the central gray matter of the sacral and mid-thoracic spinal cord and terminates in the gracile nucleus. Morphine infusion at these loci in animals blocks transmission of visceral pain signals. This pathway is important clinically because midline myelotomy at T10 relieves pelvic cancer pain in patients with colorectal distension.

The Thalamus Has a Number of Specialized Somatosensory Regions

The thalamus is an egg-shaped cluster of nuclei in the center of the brain that acts as a center of communication between many subcortical brain centers and the neocortex. The locations of nuclei within the thalamus correspond roughly with the hemispheric locations of the regions of the cerebral cortex with which they communicate (see Figure 16–5).

The Ventral Posterior Nucleus Relays Tactile and Proprioceptive Information

The fibers of the medial lemniscus, which convey tactile and proprioceptive signals, terminate in the ventral

posterior nucleus of the thalamus. The medial zone of the nucleus receives trigeminal nerve fibers from the head and face. The lateral zone receives fibers from the dorsal column nuclei; these inputs are arranged somatotopically, with the forelimb medial and the trunk and legs lateral. Individual body parts are represented by rod-shaped clusters of neurons aligned along the anterior-posterior axis of the thalamus.

The ventral posterior nucleus—called nucleus ventralis caudalis in humans—has traditionally been thought of as a single nucleus in which the fibers carrying cutaneous signals terminate in a large central and caudal region while those conveying proprioceptive information terminate in a dorsal and rostral region. More recently, Jon Kaas and his colleagues have argued that the two regions represent separate nuclei: the ventral posterior nucleus proper, which receives the cutaneous information conveyed by medial lemniscal and trigeminal axons, and the ventral posterior superior nucleus, which processes proprioceptive information. These nuclei send their outputs to different subregions of the cerebral cortex. The ventral posterior nucleus transmits cutaneous information primarily to area 3b of the primary somatosensory cortex, whereas the ventral posterior superior nucleus conveys proprioceptive information principally to area 3a in the postcentral gyrus. (The cortical areas for touch and proprioception are described in Chapter 23.)

Noxious, Thermal, and Visceral Information Is Processed in Several Thalamic Nuclei

The information for pain, temperature, itch, and the visceral senses takes a more complex path through the thalamus. Because virtually all of the research on this subject is concerned with the pathways for pain (see Chapter 24), inferences about the pathways for the other bodily senses relayed by the laminae I and V systems are tentative and controversial.

The axons of neurons in lamina V terminate in the ventral posterior nucleus and overlap some of the tactile inputs from the same body region. Nociceptive neurons in the nucleus project primarily to area 3a in the postcentral gyrus and are thought to play a role in localization of painful sensations.

The lamina I system terminates heavily in a concentrated region of thalamus rich in neurons that are immunoreactive to calbindin, a calcium-binding protein found in some cortical and thalamic neurons. This region spans the posterior part of the ventral posterior nucleus and the posterior part of the adjacent ventral medial nucleus. The gustatory and visceral inputs from the nucleus of the solitary tract, which terminate

in the parabrachial nuclei, also are arrayed topographically in the ventral medial nucleus.

Neurons in the ventral medial nucleus project to the insula, where they terminate in a topographic array. Functional imaging studies show that this region is a primary cortical region for thermal sensations. Because the insula also responds to visceral inputs arising from the spinal nucleus and nucleus of the solitary tract, it is sometimes called the interoceptive or visceral cortex.

An Overall View

The bodily senses mediate a wide range of experiences that are important for normal bodily function and for survival. Although diverse, they share common pathways and common principles of organization. The most important of those principles is specificity: Each of the bodily senses arises from a specific type of receptor distributed throughout the body.

Mechanoreceptors are sensitive to specific aspects of local tissue distortion, thermoreceptors to particular temperature ranges and shifts in temperature, and chemoreceptors to particular molecular structures.

The information from each type of somatosensory receptor is conveyed in discrete pathways that constitute submodalities. Information from all of the somatosensory submodalities is carried to the spinal cord or brain stem by the axons of neurons with cell bodies that generally lie in ganglia close to the point of entry. The axons are gathered together in nerves, which form the peripheral nervous system. Axon diameter and myelination, both of which determine the speed of action potential conduction, vary in different sensory pathways according to the need for speedy information.

When the axons enter the central nervous system they separate to form five separate sensory pathways with different properties. In three of those systems (the medial lemniscal, lamina I spinothalamic, and solitary tract systems) the pathways for submodalities appear to be segregated until they reach the cerebral cortex.

The medial lemniscal system includes the large myelinated axons and is organized for high-fidelity temporal and spatial information processing. Fibers from lamina I and the nucleus of the solitary tract convey information about temperature and impending and actual tissue damage, and a wide range of visceral stimuli from the small myelinated and unmyelinated axons. The lamina V spinothalamic system combines information from different submodalities at the first synapse in the pathway; the responses of neurons in lamina V correlate closely with reports of pain intensity.

The lamina VII spinothalamic system gathers information from widespread parts of the body and apparently plays a significant role in emotional responses to sensory stimuli. These afferent systems terminate in different regions of the thalamus with different functions and different cortical targets.

As described in the next few chapters, afferent nerves conveying specific somatosensory submodalities remain segregated as they reach the cerebral cortex. Information carried by large-diameter axons is conveyed to the postcentral gyrus of the neocortex and then to cortical regions concerned with motor control and cognition. Information that originated in the small-diameter axons travels to the primary somatosensory cortex but also to cortical regions concerned with autonomic functions and the emotions, such as the insula and anterior cingulate cortex.

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