Each sensory receptor has an **adequate stimulus**, a particular form of energy to which it is most responsive. For example, thermoreceptors are more sensitive to temperature changes than to pressure, and mechanoreceptors respond preferentially to stimuli that deform the cell membrane. Although receptors are specific for one form of energy, they can respond to most other forms if the intensity is high enough. Photoreceptors of the eye respond most readily to light, for instance, but a blow to the eye may cause us to “see stars,” an example of mechanical energy of sufficient force to stimulate the photoreceptors.

Sensory receptors can be incredibly sensitive to their preferred form of stimulus. For example, a single photon of light stimulates certain photoreceptors, and a single odorant molecule may activate the chemoreceptors involved in the sense of smell. The minimum stimulus required to activate a receptor is known as the **threshold**, just as the minimum depolarization required to trigger an action potential is called the threshold [p. 257].

How is a physical or chemical stimulus converted into a change in membrane potential? The stimulus opens or closes ion channels in the receptor membrane, either directly or indirectly (through a second messenger). In most cases, channel opening results in net influx of Na⁺ or other cations into the cell, depolarizing the membrane. In a few cases, the response to the stimulus is hyperpolarization when K⁺ leaves the cell. In the case of vision, the stimulus (light) closes cation channels to hyperpolarize the receptor.

The change in sensory receptor membrane potential is a graded potential [p. 258] called a **receptor potential**. In some cells, the receptor potential initiates an action potential that travels along the sensory fiber to the CNS. In other cells, receptor potentials influence neurotransmitter secretion by the receptor cell, which in turn alters electrical activity in an associated sensory neuron.

### A Sensory Neuron Has a Receptive Field

Somatic sensory and visual neurons are activated by stimuli that fall within a specific physical area known as the neuron’s **receptive field**. For example, a touch-sensitive neuron in the skin responds to pressure that falls within its receptive field. In the simplest case, one receptive field is associated with one sensory neuron (the **primary sensory neuron** in the pathway), which in turn synapses on one CNS neuron (the **secondary sensory neuron**). However, receptive fields frequently overlap with neighboring receptive fields. (Primary and secondary sensory neurons are also known as **first-order** and **second-order neurons**.)

In addition, sensory neurons of neighboring receptive fields may exhibit **convergence** [p. 282], in which multiple presynaptic neurons provide input to a smaller number of postsynaptic neurons (Fig. 10-2). Convergence allows multiple simultaneous subthreshold stimuli to sum at the postsynaptic (secondary) neuron. When multiple primary sensory neurons converge on a single secondary sensory neuron, their individual receptive fields merge into a single, large **secondary receptive field**, as in Figure 10-2.

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**TABLE 10-2** Types of Sensory Receptors

<table>
<thead>
<tr>
<th>TYPE OF RECEPTOR</th>
<th>EXAMPLES OF STIMULI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chemoreceptors</td>
<td>Oxygen, pH, various organic molecules such as glucose</td>
</tr>
<tr>
<td>Mechanoreceptors</td>
<td>Pressure (baroreceptors), cell stretch (osmoreceptors), vibration, acceleration, sound</td>
</tr>
<tr>
<td>Photoreceptors</td>
<td>Photons of light</td>
</tr>
<tr>
<td>Thermoreceptors</td>
<td>Varying degrees of heat</td>
</tr>
</tbody>
</table>

---

*Concept Check*

1. What advantage do myelinated axons provide?
2. What accessory role does the outer ear (the pinna) play in the auditory system?
3. For each of the somatic and visceral stimuli listed in Table 10-1, which of the following receptor types is the appropriate transducer: mechano-, chemo-, photo-, or thermoreceptors?

*Answers: p. 383*

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**Sensory Transduction Converts Stimuli into Graded Potentials**

How do receptors convert diverse physical stimuli, such as light or heat, into electrical signals? The first step is **transduction**, the conversion of stimulus energy into information that can be processed by the nervous system [p. 182]. In many receptors, the opening or closing of ion channels converts mechanical, chemical, thermal, or light energy directly into a change in membrane potential. Some sensory transduction mechanisms include signal transduction and second messenger systems [p. 184] that initiate the change in membrane potential.

---

*Note:* The image contains a table that is not transcribed, but it is mentioned in the text. The table should be reviewed for context and accuracy.
The receptive fields of three primary sensory neurons overlap to form one large secondary receptive field.

**FIGURE 10-2  Receptive fields of sensory neurons.** Convergence of primary sensory neurons allows simultaneous subthreshold stimuli to sum at the secondary sensory neuron and initiate an action potential. (In this illustration, only part of the secondary sensory neuron is shown.)

The size of secondary receptive fields determines how sensitive a given area is to a stimulus. For example, sensitivity to touch is demonstrated by a two-point discrimination test. In some regions of skin, such as that on the arms and legs, two pins placed within 20 mm of each other are interpreted by the brain as a single pinprick. In these areas, many primary neurons converge on a single secondary neuron, so the secondary receptive field is very large (Fig. 10-3a ). In contrast, more sensitive areas of skin, such as the fingertips, have smaller receptive fields, with as little as a 1:1 relationship between

(a) Convergence of many primary sensory neurons creates a very large secondary receptive field. Two stimuli that fall within the same secondary receptive field are perceived as a single point, because only one signal goes to the brain.

(b) When fewer neurons converge, secondary receptive fields are much smaller. The two stimuli activate separate pathways and are perceived as distinct stimuli.

**FIGURE 10-3  Two-point discrimination varies with the size of the secondary receptive field.** (a) Less-sensitive regions of the skin are found on the arms and legs. In these regions, two stimuli 20 mm apart cannot be felt separately. (b) In more sensitive regions, such as the fingertips, two stimuli separated by as little as 2 mm will be perceived as two distinct stimuli.
primary and secondary sensory neurons. In these regions, two pins separated by as little as 2 mm can be perceived as two separate touches (Fig. 10-3b).

The CNS Integrates Sensory Information

Sensory information from much of the body enters the spinal cord and travels through ascending pathways to the brain. Some sensory information goes directly into the brain stem via the cranial nerves (p. 310). Sensory information that initiates visceral reflexes is integrated in the brain stem or spinal cord and usually does not reach conscious perception. An example of an unconscious visceral reflex is the control of blood pressure by centers in the brain stem.

Each major division of the brain processes one or more types of sensory information (Fig. 10-4). For example, the midbrain receives visual information, and the medulla oblongata receives input for sound and taste. Information about balance and equilibrium is processed primarily in the cerebellum. These pathways, along with those carrying somatosensory information, project to the thalamus, which acts as a relay and processing station before passing the information on to the cerebrum.

Only olfactory (olfacere, to sniff) information is not routed through the thalamus. The sense of smell, a type of chemoreception, is considered to be one of the oldest senses, and even the most primitive vertebrate brains have well-developed regions for processing olfactory information. Information about odors travels from the nose through the first cranial nerve and olfactory bulb to the olfactory cortex in the cerebrum. Perhaps it is because of this direct input to the cerebrum that odors are so closely linked to memory and emotion. Most people have experienced encountering a smell that suddenly brings back a flood of memories of places or people from the past.

One interesting aspect of CNS processing of sensory information is the perceptual threshold, the level of stimulus intensity necessary for you to be aware of a particular sensation. Stimuli bombard your sensory receptors constantly, but your brain can filter out and “turn off” some stimuli. You experience a change in perceptual threshold when you “tune out” the radio while studying or when you “zone out” during a lecture. In both cases, the noise is adequate to stimulate sensory neurons in the ear, but neurons higher in the pathway dampen the perceived signal so that it does not reach the conscious brain.
Decreased perception of a stimulus is accomplished by inhibitory modulation [\( \text{p. 42} \)], which diminishes a suprathreshold stimulus until it is below the perceptual threshold. Inhibitory modulation often occurs in the secondary and higher neurons of a sensory pathway. If the modulated stimulus suddenly becomes important, such as when the professor asks you a question, you can consciously focus your attention and overcome the inhibitory modulation. At that point, your conscious brain seeks to retrieve and recall recent sound input from your subconscious so that you can answer the question.

**Coding and Processing Distinguish Stimulus Properties**

If all stimuli are converted to action potentials in sensory neurons and all action potentials are identical, how can the central nervous system tell the difference between, say, heat and pressure, or between a pinprick to the toe and one to the hand? The attributes of the stimulus must somehow be preserved once the stimulus enters the nervous system for processing. This means that the CNS must distinguish four properties of a stimulus: (1) its nature, or modality, (2) its location, (3) its intensity, and (4) its duration.

**Sensory Modality** The modality of a stimulus is indicated by which sensory neurons are activated and by where the pathways of the activated neurons terminate in the brain. Each receptor type is most sensitive to a particular modality of stimulus. For example, some neurons respond most strongly to touch; others respond to changes in temperature. Each sensory modality can be subdivided into qualities. For instance, color vision is divided into red, blue, and green according to the wavelengths that most strongly stimulate the different visual receptors.

In addition, the brain associates a signal coming from a specific group of receptors with a specific modality. This 1:1 association of a receptor with a sensation is called labeled line coding. Stimulation of a cold receptor is always perceived as cold, whether the actual stimulus was cold or an artificial depolarization of the receptor. The blow to the eye that causes us to “see” a flash of light is another example of labeled line coding.

**Location of the Stimulus** The location of a stimulus is also coded according to which receptive fields are activated. The sensory regions of the cerebrum are highly organized with respect to incoming signals, and input from adjacent sensory receptors is processed in adjacent regions of the cortex. This arrangement preserves the topographical organization of receptors on the skin, eye, or other regions in the processing centers of the brain.

For example, touch receptors in the hand project to a specific area of the cerebral cortex. Experimental stimulation of that area during brain surgery is interpreted as a touch to the hand, even though there is no contact. Similarly, the phantom limb pain reported by some amputees occurs when secondary sensory neurons in the spinal cord become hyperactive, resulting in the sensation of pain in a limb that is no longer there.

Auditory information is an exception to the localization rule, however. Neurons in the ears are sensitive to different frequencies of sound, but they have no receptive fields and their activation provides no information about the location of the sound. Instead, the brain uses the timing of receptor activation to compute a location, as shown in Figure 10-5. A sound originating directly in front of a person reaches both ears...
Simultaneously. A sound originating on one side reaches the closer ear several milliseconds before it reaches the other ear. The brain registers the difference in the time it takes for the sound stimuli to reach the two sides of the auditory cortex and uses that information to compute the sound’s source.

**Lateral inhibition**, which increases the contrast between activated receptive fields and their inactive neighbors, is another way of isolating the location of a stimulus. Figure 10-6 shows this process for a pressure stimulus to the skin. A pin pushing on the skin activates three primary sensory neurons, each of which releases neurotransmitters onto its corresponding secondary neuron. However, the three secondary neurons do not all respond in the same fashion. The secondary neuron closest to the stimulus (neuron B) suppresses the response of the secondary neurons lateral to it (that is, on either side), where the stimulus is weaker, and simultaneously allows its own pathway to proceed without interference. The inhibition of neurons farther from the stimulus enhances the contrast between the center and the sides of the receptive field, making the sensation more easily localized. In the visual system, lateral inhibition sharpens our perception of visual edges.

The pathway in Figure 10-6 also demonstrates **population coding**, the way multiple receptors function together to send the CNS more information than would be possible from a single receptor. By comparing the input from multiple receptors, the CNS can make complex calculations about the quality and spatial and temporal characteristics of a stimulus.

**CONCEPT CHECK**

4. In Figure 10-6, what kind(s) of ion channel might open in neurons A and C that would depress their responsiveness: Na⁺, K⁺, Cl⁻, or Ca²⁺?

**Answers:** p. 383

**Intensity and Duration of the Stimulus** The intensity of a stimulus cannot be directly calculated from a single sensory neuron action potential because a single action potential is “all-or-none.” Instead, stimulus intensity is coded in two types
of information: the number of receptors activated (another example of population coding) and the frequency of action potentials coming from those receptors (frequency coding).

Population coding for intensity occurs because the threshold for the preferred stimulus is not the same for all receptors. Only the most sensitive receptors (those with the lowest thresholds) respond to a low-intensity stimulus. As a stimulus increases in intensity, additional receptors are activated. The CNS then translates the number of active receptors into a measure of stimulus intensity.

For individual sensory neurons, intensity discrimination begins at the receptor. If a stimulus is below threshold, the primary sensory neuron does not respond. Once stimulus intensity exceeds threshold, the primary sensory neuron begins to fire action potentials. As stimulus intensity increases, the receptor potential amplitude (strength) increases in proportion, and the frequency of action potentials in the primary sensory neuron increases, up to a maximum rate (Fig. 10-7).

Similarly, the duration of a stimulus is coded by the duration of action potentials in the sensory neuron. In general, a longer stimulus generates a longer series of action potentials in the primary sensory neuron. However, if a stimulus persists, some receptors adapt, or cease to respond. Receptors fall into one of two classes, depending on how they adapt to continuous stimulation.

**Tonic receptors** are slowly adapting receptors that fire rapidly when first activated, then slow and maintain their firing as long as the stimulus is present (Fig. 10-8a). Pressure-sensitive baroreceptors, irritant receptors, and some tactile receptors and proprioceptors fall into this category. In general, the stimuli that activate tonic receptors are parameters that must be monitored continuously by the body.

In contrast, **phasic receptors** are rapidly adapting receptors that fire when they first receive a stimulus but cease firing if the strength of the stimulus remains constant (Fig. 10-8b). Phasic receptors are attuned specifically to changes in a parameter. Once a stimulus reaches a steady intensity, phasic receptors
adapt to the new steady state and turn off. This type of response allows the body to ignore information that has been evaluated and found not to threaten homeostasis or well-being.

Our sense of smell is an example of a sense that uses phasic receptors. For example, you can smell your cologne when you put it on in the morning, but as the day goes on your olfactory receptors adapt and are no longer stimulated by the cologne molecules. You no longer smell the fragrance, yet others may comment on it. Adaptation of phasic receptors allows us to filter out extraneous sensory information and concentrate on what is new, different, or essential. In general, once adaptation of a phasic receptor has occurred, the only way to create a new signal is to either increase the intensity of the excitatory stimulus or remove the stimulus entirely and allow the receptor to reset.

The molecular mechanism for sensory receptor adaptation depends on the receptor type. In some receptors, K+ channels in the receptor membrane open, causing the membrane to repolarize and stopping the signal. In other receptors, Na+ channels quickly inactivate. In yet other receptors, biochemical pathways alter the receptor's responsiveness.

Accessory structures may also decrease the amount of stimulus reaching the receptor. In the ear, for example, tiny muscles contract and dampen the vibration of small bones in response to loud noises, thus decreasing the sound signal before it reaches auditory receptors.

To summarize, the specificity of sensory pathways is established in several ways:

1. Each receptor is most sensitive to a particular type of stimulus.
2. A stimulus above threshold initiates action potentials in a sensory neuron that projects to the CNS.
3. Stimulus intensity and duration are coded in the pattern of action potentials reaching the CNS.
4. Stimulus location and modality are coded according to which receptors are activated or (in the case of sound) by the timing of receptor activation.
5. Each sensory pathway projects to a specific region of the cerebral cortex dedicated to a particular receptive field. The brain can then tell the origin of each incoming signal.

**CONCEPT CHECK**

5. How do sensory receptors communicate the intensity of a stimulus to the CNS?

6. What is the adaptive significance of irritant receptors that are tonic instead of phasic?

Answers: p. 383

**SOMATIC SENSES**

There are four somatosensory modalities: touch, proprioception, temperature, and nociception, which includes pain and itch. We discuss details of proprioception in Chapter 13.
Pathways for Somatic Perception Project to the Somatosensory Cortex and Cerebellum

Receptors for the somatic senses are found both in the skin and in the viscera. Receptor activation triggers action potentials in the associated primary sensory neuron. In the spinal cord, many primary sensory neurons synapse onto interneurons that serve as the secondary sensory neurons. The location of the synapse between a primary neuron and a secondary neuron varies according to the type of receptor (Fig. 10-9). Neurons associated with receptors for nociception, temperature, and coarse touch synapse onto their secondary neurons shortly after entering the spinal cord. In contrast, most fine touch, vibration, and proprioceptive neurons have very long axons that project up the spinal cord all the way to the medulla (Fig. 10-3).

All secondary sensory neurons cross the midline of the body at some point, so that sensations from the left side of the body are processed in the right hemisphere of the brain and vice versa. The secondary neurons for nociception, temperature, and coarse touch cross the midline in the spinal cord, then ascend to the brain. Fine touch, vibration, and proprioceptive neurons cross the midline in the medulla.

In the thalamus, secondary sensory neurons synapse onto tertiary sensory neurons, which in turn project to the somatosensory region of the cerebral cortex. In addition, many
sensory pathways send branches to the cerebellum so that it can use the information to coordinate balance and movement.

The somatosensory cortex [p. 315] is the part of the brain that recognizes where ascending sensory tracts originate. Each sensory tract has a corresponding region of the cortex, so that all sensory pathways for the left hand terminate in one area, all pathways for the left foot terminate in another area, and so on (Fig. 10-10 e). Within the cortical region for a particular body part, columns of neurons are devoted to particular types of receptors. For example, a cortical column activated by cold receptors in the left hand may be found next to a column activated by pressure receptors in the skin of the left hand. This columnar arrangement creates a highly organized structure that maintains the association between specific receptors and the sensory modality they transmit.

Some of the most interesting research about the somatosensory cortex has been done on patients during brain surgery for epilepsy. Because brain tissue has no pain fibers, this type of surgery can be performed with the patient awake under local anesthesia. The surgeon stimulates a particular region of the brain and asks the patient about sensations that occur. The ability of the patient to communicate with the surgeon during this process has expanded our knowledge of brain regions tremendously.

Experiments can also be done on nonhuman animals by stimulating peripheral receptors and monitoring electrical activity in the cortex. We have learned from these experiments that the more sensitive a region of the body is to touch and other stimuli, the larger the corresponding region in the cortex. Interestingly, the size of the regions is not fixed. If a particular body part is used more extensively, its topographical region in the cortex will expand. For example, people who are visually handicapped and learn to read Braille with their fingertips develop an enlarged region of the somatosensory cortex devoted to the fingertips.

In contrast, if a person loses a finger or limb, the portion of the somatosensory cortex devoted to the missing structure begins to be taken over by sensory fields of adjacent structures. Reorganization of the somatosensory cortex “map” is an example of the remarkable plasticity [p. 282] of the brain. Unfortunately, sometimes the reorganization is not perfect and can result in sensory sensations, including pain, that the brain interprets as being located in the missing limb (phantom limb pain).

**Touch Receptors Respond to Many Different Stimuli**

Touch receptors are among the most common receptors in the body. These receptors respond to many forms of physical contact, such as stretch, steady pressure, fluttering or stroking movement, vibration, and texture. They are found both in the
Somatic Senses

Merkel receptors
Meissner's corpuscle
Free nerve ending
Sensory nerves

Free nerve ending of hair root senses hair movement.
Pacinian corpuscle
Ruffini corpuscle
Merkel receptors

Merkel receptors sense steady pressure and texture.
Meissner's corpuscle responds to flutter and stroking movements.

Free nerve ending
Hair root
Hair
Pacinian corpuscle senses vibration.
Ruffini corpuscle responds to skin stretch.
Sensory nerves carry signals to spinal cord.

FIGURE 10-11 Touch receptors in the skin. Different types of touch receptors are scattered throughout the superficial and deep layers of the skin.

skin (Fig. 10-11) and in deeper regions of the body. We discuss touch receptors associated with muscles, joints, or internal organs in later chapters.

Touch receptors come in many forms (Tbl. 10-4). Some are free nerve endings, such as those that wrap around the base of hairs. Others are more complex. Most touch receptors are difficult to study because of their small size. However, Pacinian corpuscles, which respond to vibration, are some of the largest receptors in the body, and much of what we know about somatosensory receptors comes from studies on these structures.

Pacinian corpuscles are composed of nerve endings encapsulated in layers of connective tissue (see Fig. 10-1b). They are found in the subcutaneous layers of skin and in muscles, joints, and internal organs. The concentric layers of connective tissue in the corpuscles create large receptive fields. Pacinian corpuscles respond best to high-frequency vibrations, whose energy is transferred through the connective tissue capsule to the nerve ending, where the energy opens mechanically gated ion channels. Pacinian corpuscles are rapidly adapting phasic receptors, and this property allows them to respond to a change in touch but then ignore it.

Properties of the remaining touch receptors depicted in Figure 10-11—Meissner's corpuscles, Ruffini corpuscles, and Merkel receptors—are summarized in Table 10-4.

<table>
<thead>
<tr>
<th>RECEPTOR</th>
<th>STIMULUS</th>
<th>LOCATION</th>
<th>STRUCTURE</th>
<th>ADAPTATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Free nerve endings</td>
<td>Various touch and pressure stimuli</td>
<td>Around hair roots and under surface of skin</td>
<td>Unmyelinated nerve endings</td>
<td>Variable</td>
</tr>
<tr>
<td>Meissner's corpuscles</td>
<td>Flutter, stroking</td>
<td>Superficial layers of skin</td>
<td>Encapsulated in connective tissue</td>
<td>Rapid</td>
</tr>
<tr>
<td>Pacinian corpuscles</td>
<td>Vibration</td>
<td>Deep layers of skin</td>
<td>Encapsulated in connective tissue</td>
<td>Rapid</td>
</tr>
<tr>
<td>Ruffini corpuscles</td>
<td>Stretch of skin</td>
<td>Deep layers of skin</td>
<td>Enlarged nerve endings</td>
<td>Slow</td>
</tr>
<tr>
<td>Merkel receptors</td>
<td>Steady pressure, texture</td>
<td>Superficial layers of skin</td>
<td>Enlarged nerve endings</td>
<td>Slow</td>
</tr>
</tbody>
</table>
Classes of Somatosensory Nerve Fibers

<table>
<thead>
<tr>
<th>FIBER TYPE</th>
<th>FIBER CHARACTERISTICS</th>
<th>SPEED OF CONDUCTION</th>
<th>ASSOCIATED WITH</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aβ (beta)</td>
<td>Large, myelinated</td>
<td>30-70 m/sec</td>
<td>Mechanical stimuli</td>
</tr>
<tr>
<td>Aδ (delta)</td>
<td>Small, myelinated</td>
<td>12-30 m/sec</td>
<td>Cold, fast pain, mechanical stimuli</td>
</tr>
<tr>
<td>C</td>
<td>Small, unmyelinated</td>
<td>0.5-2 m/sec</td>
<td>Slow pain, heat, cold, mechanical stimuli</td>
</tr>
</tbody>
</table>

Temperature Receptors Are Free Nerve Endings

Temperature receptors are free nerve endings that terminate in the subcutaneous layers of the skin. Cold receptors are sensitive primarily to temperatures lower than body temperature. Warm receptors are stimulated by temperatures in the range extending from normal body temperature (37°C) to about 45°C. Above that temperature, pain receptors are activated, creating a sensation of painful heat.

The receptive field for a thermoreceptor is about 1 mm in diameter, and the receptors are scattered across the body. There are considerably more cold receptors than warm ones. Temperature receptors slowly adapt between 20° and 40° C. Their initial response tells us that the temperature is changing, and their sustained response tells us about the ambient temperature. Outside the 20–40° C range, where the likelihood of tissue damage is greater, the receptors do not adapt. Temperature receptors play an important role in thermoregulation, which is discussed in Chapter 22.

Nociceptors Initiate Protective Responses

Nociceptors [nocere, to injure] are receptors that respond to a variety of strong noxious stimuli (chemical, mechanical, or thermal) that cause or have the potential to cause tissue damage. Activation of nociceptors initiates adaptive, protective responses, such as the reflexive withdrawal of a hand from a hot stove touched accidentally. Nociceptors are not limited to the skin. Discomfort from overuse of muscles and joints helps us avoid additional damage to these structures. Two sensations may be perceived when nociceptors are activated: pain and itch.

Nociceptors are sometimes called pain receptors, even though pain is a perceived sensation rather than a stimulus. Nociceptive pain is mediated by free nerve endings whose ion channels are sensitive to a variety of chemical, mechanical, and thermal stimuli. For example, the membrane channels called vanilloid receptors (also called transient receptor potential V₁ or TRPV₁ channels) respond to damaging heat from a stove or other source, as well as to capsaicin, the chemical that makes hot chili peppers burn your mouth. At the opposite end of the temperature spectrum, researchers recently identified a membrane protein that responds both to cold and to menthol, one reason mint-flavored foods feel cool.

Nociceptor activation is modulated by local chemicals that are released upon tissue injury, including K⁺, histamine, and prostaglandins released from damaged cells; serotonin released from platelets activated by tissue damage; and the peptide substance P, which is secreted by primary sensory neurons. These chemicals, which also mediate the inflammatory response at the site of injury, either activate nociceptors or sensitize them by lowering their activation threshold. Increased sensitivity to pain at sites of tissue damage is called inflammatory pain.

Nociceptors may activate two pathways: (1) reflexive protective responses that are integrated at the level of the spinal cord and (2) ascending pathways to the cerebral cortex that become conscious sensation (pain or itch). Primary sensory neurons from nociceptors terminate in the dorsal horn of the spinal cord (see Fig. 10-9). There they synapse onto secondary sensory neurons that project to the brain or onto interneurons for local circuits.

Irritant responses that are integrated in the spinal cord initiate rapid unconscious protective reflexes that automatically remove a stimulated area from the source of the stimulus. For example, if you accidentally touch a hot stove, an automatic withdrawal reflex causes you to pull back your hand even before you are aware of the heat. This is one example of the spinal reflexes discussed in Chapter 9 [ p. 307].

The lack of brain involvement in many protective reflexes has been demonstrated in the classic “spinal frog” preparation, in which the animal’s brain has been destroyed. If the frog’s foot is placed in a beaker of hot water or strong acid, the withdrawal reflex causes the leg to contract and move the foot away from the stimulus. The frog is unable to feel pain because the brain, which translates sensory input into perception, is not functional.

Pain and Itching Are Mediated by Nociceptors

Afferent signals from nociceptors are carried to the CNS in three types of primary sensory fibers: Aβ (A-beta) fibers, Aδ (A-delta) fibers, and C fibers (Tbl. 10-5). The most common
sensation carried by these pathways is pain, but when histamine or some other stimulus activates a subtype of C fiber, we perceive the sensation we call itch (pruritus). Itch comes only from nociceptors in the skin and is characteristic of many rashes and other skin conditions. However, itch can also be a symptom of a number of systemic diseases, including multiple sclerosis, hyperparathyroidism, and diabetes mellitus.

The higher pathways for itch are not as well understood as the pathways for pain, but there is an antagonistic interaction between the two sensations. When something itches, we scratch it, creating a mildly painful sensation that seems to interrupt the itch sensation. And many of the opiate painkillers, such as morphine, relieve pain but in some people they also induce the side effect of itching.

Pain is a subjective perception, the brain's interpretation of sensory information transmitted along pathways that begin at nociceptors. Pain is also highly individual and may vary with a person's emotional state. The discussion here is limited to the sensory experience of pain.

Fast pain, described as sharp and localized, is rapidly transmitted to the CNS by small, myelinated Aβ fibers. Slow pain, described as duller and more diffuse, is carried on small, unmyelinated C fibers. The timing distinction between the two is most obvious when the stimulus originates far from the CNS, such as when you stub your toe. You first experience a quick stabbing sensation (fast pain), followed shortly by a dull throbbing (slow pain).

The ascending pathways for nociception cross the body's midline in the spinal cord and ascend to the thalamus and sensory areas of the cortex (see Fig. 10-9). The pathways also send branches to the limbic system and hypothalamus. As a result, pain may be accompanied by emotional distress (suffering) and a variety of autonomic reactions, such as nausea, vomiting, or sweating.

Our perception of pain is subject to modulation at several levels in the nervous system. It can be magnified by past experiences or suppressed in emergencies when survival depends on ignoring injury. In such emergencies, descending pathways that travel through the thalamus inhibit nociceptor neurons in the spinal cord. Artificial stimulation of these inhibitory pathways is one of the newer techniques being used to control chronic pain.

Pain can also be suppressed in the dorsal horn of the spinal cord, before the stimuli are sent to ascending spinal tracts. Normally, tonically active inhibitory interneurons in the spinal cord inhibit ascending pathways for pain (Fig. 10-12a). C fibers from nociceptors synapse on these inhibitory interneurons. When activated by a painful stimulus, the C fibers simultaneously excite the ascending path and block the tonic inhibition (Fig. 10-12b). This action allows the pain signal from the C fiber to travel unimpeded to the brain.

In the gate control theory of pain modulation, Aβ fibers carrying sensory information about mechanical stimuli help block pain transmission (Fig. 10-12c). The Aβ fibers synapse on the inhibitory interneurons and enhance the interneuron's inhibitory activity. If simultaneous stimuli reach the inhibitory neuron from the Aβ and C fibers, the integrated response is partial inhibition of the ascending pain pathway so that pain perceived by the brain is lessened. The gate control theory explains why rubbing a bumped elbow or shin lessens your pain: the tactile stimulus of rubbing activates Aβ fibers and helps decrease the sensation of pain.

Pain can be felt in skeletal muscles (deep somatic pain) as well as in the skin. Muscle pain during exercise is associated
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with the onset of anaerobic metabolism and is often perceived as a burning sensation in the muscle (as in “go for the burn!”). Some investigators have suggested that the exercise-induced metabolite responsible for the burning sensation is K+, known to enhance the pain response. Muscle pain from ischemia (lack of adequate blood flow that reduces oxygen supply) also occurs during myocardial infarction (heart attack).

Pain in the heart and other internal organs (visceral pain) is often poorly localized and may be felt in areas far removed from the site of the stimulus (Fig. 10-13a). For example, the pain of cardiac ischemia may be felt in the neck and down the left shoulder and arm. This referred pain apparently occurs because multiple primary sensory neurons converge on a single ascending tract (Fig. 10-13b). According to this model, when painful stimuli arise in visceral receptors, the brain is unable to distinguish visceral signals from the more common signals arising from somatic receptors. As a result, it interprets the pain as coming from the somatic regions rather than the viscera.

Chronic pain of one sort or another affects millions of people in this country every year. This type of pain is often much greater than nociceptor activation would indicate and reflects damage to or long-term changes in the nervous system. Chronic pain is a pathological pain and is also called neuropathic pain. One of the most common forms of neuropathic pain is diabetic neuropathy, which develops as a consequence of chronically elevated blood glucose concentrations. Scientists do not yet fully understand what causes glucose neurotoxicity or neuropathic pain, which makes its treatment difficult.

The alleviation of pain is of considerable interest to health professionals. Analgesic drugs [analgesia, painlessness] range from aspirin to potent opiates such as morphine. Aspirin inhibits prostaglandins, decreases inflammation, and presumably slows the transmission of pain signals from the site of injury. The opiate drugs act directly on CNS opioid receptors that are part of an analgesic system that responds to endogenous opiate molecules [p. 278]. Activation of opioid receptors blocks

**FIGURE QUESTION**

A man goes to his physician and complains of pain that radiates down his left arm. This suggests to the physician that the man may have a problem with what organ?

Skin (usual stimulus)
Kidney (uncommon stimulus)
Secondary Ascending sensory neuron path to somatosensory cortex of brain

(b) One theory of referred pain says that nociceptors from several locations converge on a single ascending tract in the spinal cord. Pain signals from the skin are more common than pain from internal organs, and the brain associates activation of the pathway with pain in the skin. Adapted from H.L. Fields, *Pain* (McGraw Hill, 1987).
Chemoreception: Smell and Taste

NATURAL PAINKILLERS

Many drugs we use today for pain relief are derivatives of plant or animal molecules. One of the newest painkillers in this group is ziconotide, a synthetic compound related to the poison used by South Pacific cone snails to kill fish. This drug works by blocking calcium channels on nociceptive neurons. Ziconotide, approved in 2004 for the treatment of severe chronic pain, is highly toxic. To minimize systemic side effects, it must be injected directly into the cerebrospinal fluid surrounding the spinal cord. Ziconotide relieves pain but may also cause hallucinations and other psychiatric symptoms, so it is a last-resort treatment. Other painkilling drugs from biological sources include aspirin, derived from the bark of willow trees (genus Salix), and opiate drugs such as morphine and codeine that come from the opium poppy, Papaver somniferum. These drugs have been used in Western and Chinese medicine for centuries, and even today you can purchase willow bark as an herbal remedy.

CONCEPT CHECK

7. What is the adaptive advantage of a spinal reflex?
8. Rank the speed of signal transmission through the following fiber types, from fastest to slowest: (a) small diameter, myelinated fiber; (b) large diameter, myelinated fiber; (c) small diameter, unmyelinated fiber.
9. Your sense of smell uses phasic receptors. What other receptors (senses) adapt to ongoing stimuli?  Answer: p. 383

CHEMORECEPTION: SMELL AND TASTE

The five special senses—smell, taste, hearing, equilibrium, and vision—are concentrated in the head region. Like somatic senses, the special senses rely on receptors to transform information about the environment into patterns of action potentials that can be interpreted by the brain. Smell and taste are both forms of chemoreception, one of the oldest senses from an evolutionary perspective. Unicellular bacteria use chemoreception to sense their environment, and primitive animals without formalized nervous systems use chemoreception to locate food and mates. It has been hypothesized that chemoreception evolved into chemical synaptic communication in animals.

Olfaction Is One of the Oldest Senses

Imagine waking up one morning and discovering a whole new world around you, a world filled with odors that you never dreamed existed—scents that told you more about your surroundings than you ever imagined from looking at them. This is exactly what happened to a young patient of Dr. Oliver Sacks (an account is in The Man Who Mistook His Wife for a Hat and Other Clinical Tales). Or imagine skating along the sidewalk without a helmet, only to fall and hit your head. When you regain consciousness, the world has lost all odor: no smell of grass or perfume or garbage. Even your food has lost much of its taste, and you now eat only to survive because eating has lost its pleasure.

We do not realize the essential role that our sense of smell plays in our lives until a head cold or injury robs us of the ability to smell. Olfaction [olfacere, to sniff] allows us to discriminate among thousands of different odors. Even so, our noses are not nearly as sensitive as those of many other animals whose survival depends on olfactory cues. The olfactory bulb, the extension of the forebrain that receives input from the primary olfactory neurons, is much better developed in vertebrates whose survival is more closely linked to chemical monitoring of their environment (Fig. 10-14). The human olfactory system consists of primary sensory neurons (olfactory receptor cells) whose axons form the olfactory nerve (cranial nerve I [p. 310]). The olfactory nerve synapses with secondary sensory neurons in the olfactory bulb, which then processes the incoming information (Figure 10-14b). Secondary and higher-order neurons project from the olfactory bulb through the olfactory tract to the olfactory cortex