Second Edition

Basic Neuroscience

Anatomy & Physiology

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demonstrated that such modulators are important in at least some of the memory processes, which we discuss in Chapter 19.

Excitatory and Inhibitory Receptors

Some postsynaptic receptors, when activated, cause excitation of the postsynaptic neuron and others cause inhibition. The importance of having inhibitory as well as excitatory types of receptors is that this gives an additional dimension to nervous function, allowing restraint of nervous action as well as excitation.

The different molecular and membrane mechanisms employed by the different receptors to cause excitation or inhibition include the following:

Excitation

1. Opening of sodium channels to allow large numbers of positive electrical charges to flow to the interior of the postsynaptic cell. This raises the membrane potential in the positive direction up toward the threshold level for excitation. It is by far the most widely used means of causing excitation.
2. Depressed conduction through potassium or chloride channels, or both. This decreases the diffusion of positively charged potassium ions out of the postsynaptic neuron or decreases the diffusion of negatively charged chloride ions to the inside. In either instance, the effect is to make the internal membrane potential more positive than normally, which is excitatory.
3. Various changes in the internal metabolism of the cell to excite cell activity, or in some instances increase in the number of excitatory membrane receptors or decrease in the number of inhibitory membrane receptors.

Inhibition

1. Opening of potassium ion channels through the receptor molecule. This allows rapid diffusion of positively charged potassium ions from inside the postsynaptic neuron to the outside, thereby carrying positive charges outward and increasing the negativity inside, which is inhibitory.
2. Increase in the conductance of chloride ions through the receptor. This allows negative chloride ions to diffuse to the interior, which is also inhibitory.
3. Activation of receptor enzymes that inhibit cellular metabolic functions or that increase the number of inhibitory synaptic receptors or decrease the number of excitatory receptors.

CHEMICAL SUBSTANCES THAT FUNCTION AS SYNAPTIC TRANSMITTERS

More than 40 different chemical substances have been proved or postulated to function as synaptic transmitters. Most of these are listed in Tables 7–1 and 7–2, which give two different groups of synaptic transmitters. One is composed of small-molecule, rapidly acting transmitters. The other comprises a large number of neuropeptides of much larger molecular size and much more slowly acting.

TABLE 7–1 Small-Molecule, Rapidly Acting Transmitters

Class I
Acetylcholine
Class II: *The Amines*
Norepinephrine
Epinephrine
Dopamine
Serotonin
Histamine
Class III: *Amino Acids*
Gamma-aminobutyric acid (GABA)
Glycine
Glutamate
Aspartate

The small-molecule, rapidly acting transmitters are the ones that cause most of the acute responses of the nervous system, such as transmission of sensory signals to and inside the brain and motor signals back to the muscles. The neuropeptides, on the other hand, usually cause more prolonged actions, such as long-term changes in numbers of receptors, long-term closure of certain ion channels, and possibly even long-term changes in numbers of synapses.

The Small-Molecule, Rapidly Acting Transmitters

Almost without exception, the small-molecule types of transmitters are synthesized in the cytosol of the pre-

TABLE 7–2 Neuropeptide, Slowly Acting Transmitters

A.	*Hypothalamic-releasing hormones*
	Thyrotropin-releasing hormone
	Luteinizing hormone-releasing hormone
	Somatostatin (growth hormone-inhibitory factor)
B.	*Pituitary peptides*
	ACTH
	β-Endorphin
	α-Melanocyte-stimulating hormone
	Prolactin
	Luteinizing hormone
	Thyrotropin
	Growth hormone
	Vasopressin
	Oxytocin
C.	*Peptides that act on gut and brain*
	Leucine enkephalin
	Methionine enkephalin
	Substance P
	Gastrin
	Cholecystokinin
	Vasoactive intestinal polypeptide (VIP)
	Neurotensin
	Insulin
	Glucagon
D.	*From other tissues*
	Angiotensin II
	Bradykinin
	Carnosine
	Sleep peptides
	Calcitonin

TABLE 8–1 Classification of Sensory Receptors

- Mechanoreceptors
  - Skin tactile sensibilities (epidermis and dermis)
    - Free nerve endings
    - Expanded tip endings
      - Merkel's discs
      - Several other variants
    - Spray endings
      - Ruffini's endings
    - Encapsulated endings
      - Meissner's corpuscles
      - Krause's corpuscles
    - Hair end-organs
  - Deep tissue sensibilities
    - Free nerve endings
    - Expanded tip endings
    - Spray endings
      - Ruffini's endings
    - Encapsulated endings
      - Pacinian corpuscles
      - A few other variants
    - Muscle endings
      - Muscle spindles
      - Golgi tendon receptors
  - Hearing
    - Sound receptors of cochlea
  - Equilibrium
    - Vestibular receptors
  - Arterial pressure
    - Baroreceptors of carotid sinuses and aorta
- Thermoreceptors
  - Cold
    - Cold receptors
  - Warmth
    - Warm receptors
- Nociceptors
  - Pain
    - Free nerve endings
- Electromagnetic receptors
  - Vision
    - Rods
    - Cones
- Chemoreceptors
  - Taste
    - Receptors of taste buds
  - Smell
    - Receptors of olfactory epithelium
  - Arterial oxygen
    - Receptors of aortic and carotid bodies
  - Osmolality
    - Probably neurons in or near supraoptic nuclei
  - Blood CO_2
    - Receptors in or on surface of medulla and in aortic and carotid bodies
  - Blood glucose, amino acids, fatty acids
    - Receptors in hypothalamus

the type of sensation felt when a nerve fiber is stimulated is determined by the point in the nervous system to which the fiber leads. For instance, if a pain fiber is stimulated, the person perceives pain regardless of what type of stimulus excites the fiber. The stimulus can be electricity, heat, crushing, or stimulation of the pain nerve ending by damage to the tissue cells. Yet the person still perceives pain. Likewise, if a touch fiber is stimulated by exciting a touch receptor electrically or in any other way, the person perceives touch because touch fibers lead to specific touch areas in the brain. Similarly, fibers from the retina of the eye terminate in the vision areas of the brain, fibers from the ear terminate in the auditory areas of the brain, and temperature fibers terminate in the temperature areas.

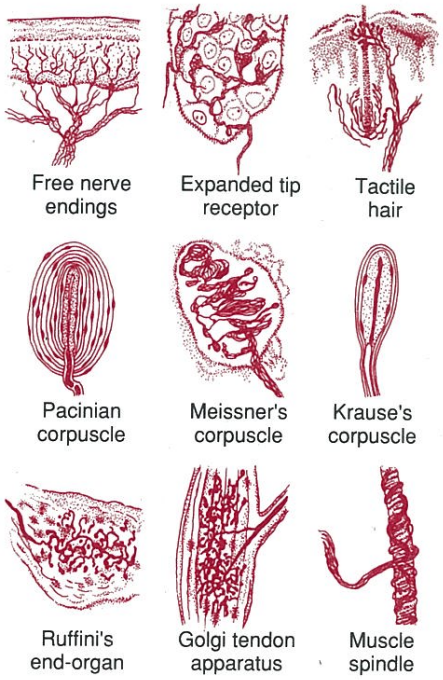


Figure 8–1. Several types of somatic sensory nerve endings.

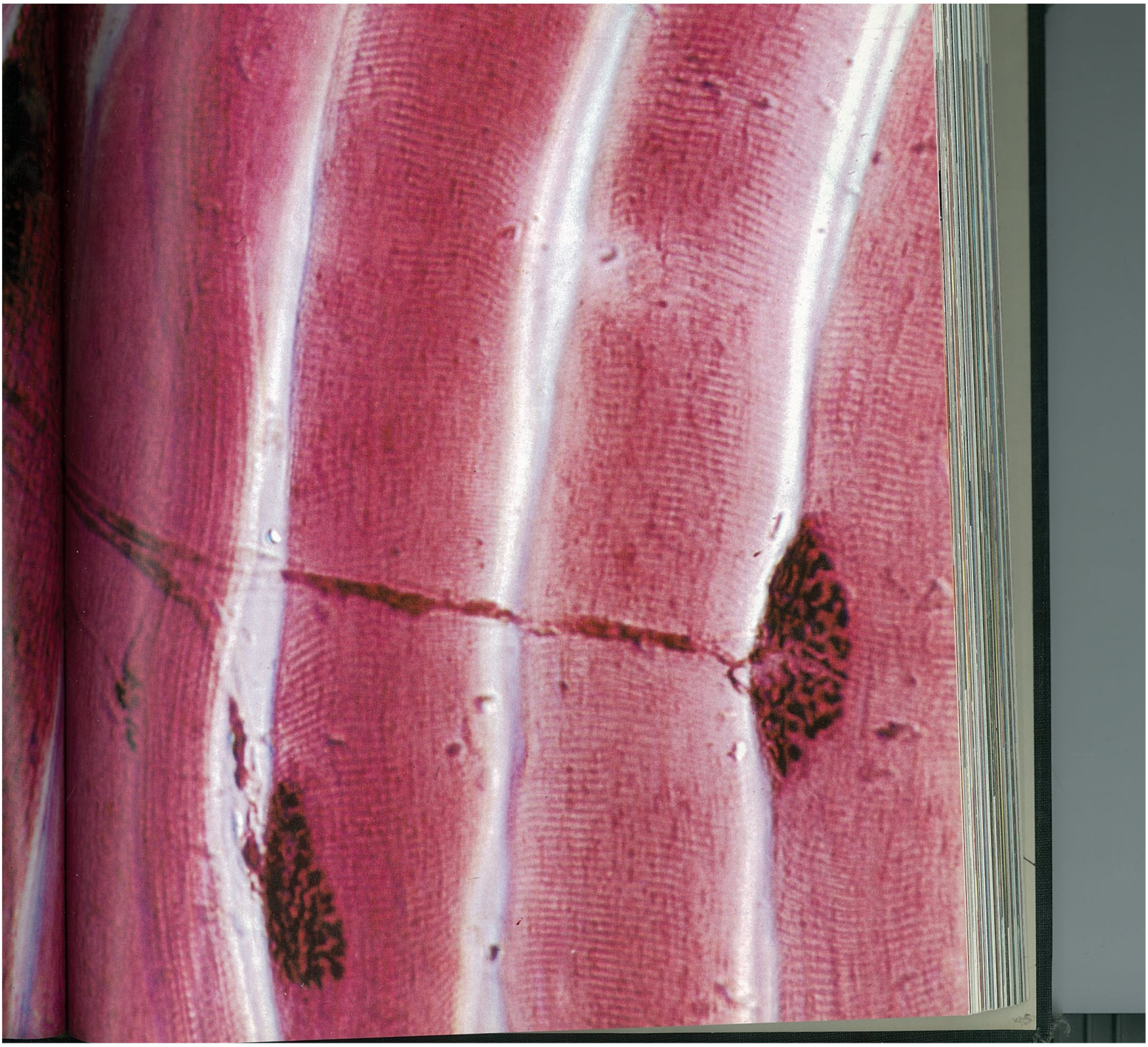
This specificity of nerve fibers for transmitting only one modality of sensation is called the *"labeled line" principle.*

■ TRANSDUCTION OF SENSORY STIMULI INTO NERVE IMPULSES

LOCAL CURRENTS AT NERVE ENDINGS—RECEPTOR POTENTIALS

All sensory receptors have one feature in common. Whatever the type of stimulus that excites the receptor, its immediate effect is to change the membrane potential of the receptor. This change in potential is called a *receptor potential.*

Mechanisms of Receptor Potentials. Different receptors can be excited in several different ways to cause receptor potentials: (1) by mechanical deformation of the receptor, which stretches the membrane and opens ion channels; (2) by application of a chemical to the membrane, which also opens ion channels; (3) by change of the temperature of the membrane, which alters the permeability of the membrane; and (4) by the effects of electromagnetic radiation such as light on the receptor, which either directly or indirectly changes the membrane characteristics and allows ions to flow through membrane channels. It will be recognized that these four different means of exciting receptors correspond in general with the different types of



sity—are all transmitted in more rapidly conducting types of sensory nerve fibers. On the other hand, the cruder types of signals, such as crude pressure, poorly localized touch, and especially tickle, are transmitted via much slower nerve fibers that require much less space in the nerve bundle than the faster fibers.

DETECTION OF VIBRATION

All the different tactile receptors are involved in detection of vibration, though different receptors detect different frequencies of vibration. Pacinian corpuscles can signal vibrations from 30 to 800 cycles/sec, because they respond extremely rapidly to minute and rapid deformations of the tissues, and they also transmit their signals over type Aβ nerve fibers, which can transmit more than 1000 impulses/sec.

Low frequency vibrations up to 80 cycles/sec, on the other hand, stimulate other tactile receptors—especially Meissner's corpuscles, which are less rapidly adapting than pacinian corpuscles.

TICKLE AND ITCH

Recent neurophysiological studies have demonstrated the existence of very sensitive, rapidly adapting, mechanoreceptive free nerve endings that elicit only the tickle and itch sensations. Furthermore, these endings are found almost exclusively in the superficial layers of the skin, which is also the only tissue from which the tickle and itch sensations usually can be elicited. These sensations are transmitted by very small type C, unmyelinated fibers similar to those that transmit the aching, slow type of pain.

The purpose of the itch sensation is presumably to call attention to mild surface stimuli such as a flea crawling on the skin or a fly about to bite, and the elicited signals then excite the scratch reflex or other maneuvers that rid the host of the irritant.

Itch can be relieved by the process of scratching if this removes the irritant or if the scratch is strong enough to elicit pain. The pain signals are believed to suppress the itch signals in the cord by the process of lateral inhibition, which will be described later.

■ THE TWO SENSORY PATHWAYS FOR TRANSMISSION OF SOMATIC SIGNALS INTO THE CENTRAL NERVOUS SYSTEM

Almost all sensory information from the somatic segments of the body enters the spinal cord through the dorsal roots of the spinal nerves (with the exception of a few very small fibers of questionable importance that enter the ventral roots). However, from the entry point of the cord and then to the brain the sensory signals are carried through one of two alternate sensory pathways: (1) the *dorsal column–lemniscal system;* and (2) the *anterolateral system.* These two systems again come together partially at the level of the thalamus.

The dorsal column–lemniscal system, as its name implies, carries signals mainly in the *dorsal columns* of the cord and then, after crossing to the opposite side in the medulla, upward through the brain stem to the thalamus by way of the *medial lemniscus.* On the other hand, signals of the anterolateral system, after originating in the dorsal horns of the spinal gray matter, cross to the opposite side of the cord and ascend through the anterior and lateral white columns to terminate at all levels of the brain stem and also in the thalamus.

The dorsal column–lemniscal system is composed of large, myelinated nerve fibers that transmit signals to the brain at velocities of 30 to 110 m/sec, whereas the anterolateral system is composed of much smaller myelinated fibers (averaging 4 μm in diameter) that transmit signals at velocities ranging from a few meters per second up to 40 m/sec.

Another difference between the two systems is that the dorsal column–lemniscal system has a very high degree of spatial orientation of the nerve fibers with respect to their origin on the surface of the body, whereas the anterolateral system has a much smaller degree of spatial orientation.

These differences immediately characterize the types of sensory information that can be transmitted by the two systems. That is, sensory information that must be transmitted rapidly and with temporal and spatial fidelity is transmitted in the dorsal column–lemniscal system, while that which does not need to be transmitted rapidly nor with great spatial fidelity is transmitted mainly in the anterolateral system. On the other hand, the anterolateral system has a special capability that the dorsal system does not have: the ability to transmit a broad spectrum of sensory modalities—pain, warmth, cold, and crude tactile sensations; the dorsal system is limited to the more discrete types of mechanoreceptive sensations alone.

With this differentiation in mind we can now list the types of sensations transmitted in the two systems:

THE DORSAL COLUMN–LEMNISCAL SYSTEM

1. Touch sensations requiring a high degree of localization of the stimulus.
2. Touch sensations requiring transmission of fine gradations of intensity.
3. Phasic sensations, such as vibratory sensations.
4. Sensations that signal movement against the skin.
5. Position sensations.
6. Pressure sensations having to do with fine degrees of judgment of pressure intensity.

Topical Diagnosis in Neurology

Anatomy · Physiology · Signs · Symptoms

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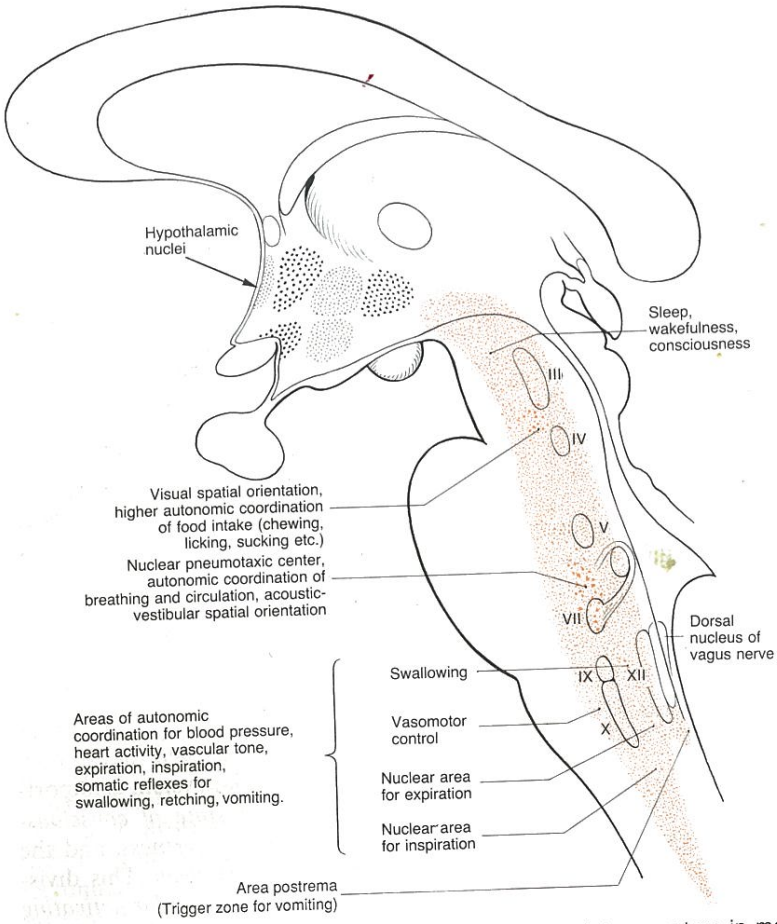

Fig. 3.**51 a** Reticular formation. Its most important regulatory centers in medulla oblongata, pons, and midbrain.

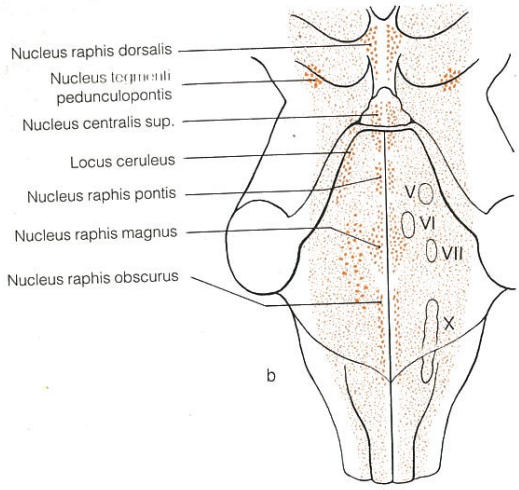

Fig. 3.**51 b** Reticular formation. View from dorsal showing the rapheal nuclei.