5
Anatomy and Physiology of Sensory Systems

INTRODUCTION

The receptors and the nervous system of our five sensory systems report events that occur outside the body to the brain as well as events that occur inside the body. Some of these events create conscious awareness while others do not. Some of the activation of sensory systems produces conscious awareness, whereas other sensory activation occurs without producing any awareness. Sensory information from the body itself is known as unconscious proprioception, and this kind of sensory activation occurs in the somatosensory system. A second type of sensory activation, exteroception, is concerned with events from outside the body such as touch, vibration, heat, and cold. Hearing, vision, taste, and olfaction are also senses of events from outside the body, thus, they too are included as sensations of exteroception. When the stimuli for these senses exceed the threshold for activation, they almost always cause awareness. Proprioception, such as that which occurs in the somatosensory system, can take place without creating any awareness, or it can cause awareness, for example, of the position of a limb. Conscious proprioception provides information about orientation of the body, movements of limbs, etc. The unconscious proprioception provides feedback to the motor

From: *Intraoperative Neurophysiological Monitoring: Third Edition*,
By A.R. Møller, DOI 10.1007/978-1-4419-7436-5_5,

system from receptors in muscles, tendons, and joints. This part of the somatosensory system is essential for controlling movements, and the loss of such feedback causes serious movement faults. Unconscious proprioception might be regarded as a part of the motor system rather than a part of the somatosensory system. The somatosensory system is, therefore, closely associated with the motor system.

Monitoring the sensory system is an important part of intraoperative monitoring. Knowing the anatomy and physiology of sensory systems is essential for being able to deliver high-quality intraoperative monitoring. Of our five sensory systems, the somatosensory system is probably the most important from a monitoring point of view because of its association with the motor system. It is monitored in many kinds of operations on the spine and the spinal cord. It is also monitored in aneurysm surgery associated with the middle cerebral artery. The reason that hearing is monitored is often for reducing the risk of injury to the auditory nerve, but it also plays a role for monitoring the general condition of the brainstem. Monitoring of the visual system is performed only in a few operations, such as those to resect pituitary tumors. Intraoperative monitoring of taste and olfaction has not been described.

THE SOMATOSENSORY SYSTEM

Intraoperative monitoring of somatosensory evoked potentials (SSEP) has mainly been employed in operations on the spine and the spinal cord such as operations that include fixation with instrumentation after trauma, corrective operations (for instance, scoliosis), and other operations on the spine where the spinal cord may be at risk due to surgical manipulation. Monitoring of SSEP is also essential in operations on the spinal cord, such as resection of spinal tumors, tethered cord syndrome (tissue attachment of the cord), and for syringomyelia (a cyst in the spinal cord). The spinal cord can also be at risk of being damaged in operations that affect its blood supply, which pose risks to the spinal cord from ischemia, such as in operations for aorta aneurysms. Compromised blood supply to the part of the spinal cord that generates the SSEP (mainly the dorsal part) can be detected by monitoring SSEP. Ischemia to parts of the brain that is involved in the generation of SSEP can also be detected by monitoring SSEP.

The somatosensory system includes the sense of touch, vibration, heat, cold, and pain, and not to forget, unconscious and conscious proprioception from muscles, tendons, and joints. This part of the somatosensory system is essential for normal motor function, which depends on proper feedback provided by the proprioceptive system.

This part of this chapter describes the anatomy and physiology of the somatosensory system that is important as a basis for intraoperative recordings of SSEP for monitoring the integrity of the somatosensory nervous system.

Sensory Receptors

The normal input to the somatosensory system is mechanical stimulation of receptors in the skin, muscles, tendons, and joints. This means that the somatosensory system has input from receptors that sense both external (exteroception) and internal events (proprioception). Exteroception that the somatosensory system receives is mediated by receptors in the skin that are sensitive to touch, vibration, and warm and cool temperatures.

The different types of receptors that provide the input to the somatosensory system respond to different forms of mechanical stimulation. Receptors in the skin respond to touch, vibration, and temperature (warmth and cold), and nociceptors respond to painful stimuli including hot and cold. Receptors in muscles provide unconscious proprioception and respond to the length of the muscles. Receptors in tendons measure the stretch of tendons, and receptors in joints are sensitive to pressure. Receptors in internal organs, such as the intestines, are sensitive to stretching and chemicals such as those associated with ischemia.

The particular aspects of the receptors that provide the input to the somatosensory system are of minor importance for intraoperative monitoring where electrical stimulation of sensory nerves is the common way of stimulation. For a detailed description of sensory receptors, see for example Møller 2003, (*1*).

Ascending Somatosensory Pathways

The peripheral nerve fibers that receive input from sensory receptors of the body enter the dorsal horn of the spinal cord as dorsal roots (**Fig. 5.1**) and ascend in the dorsal column of the spinal cord on the ipsilateral side to terminate in cells in the dorsal column nuclei

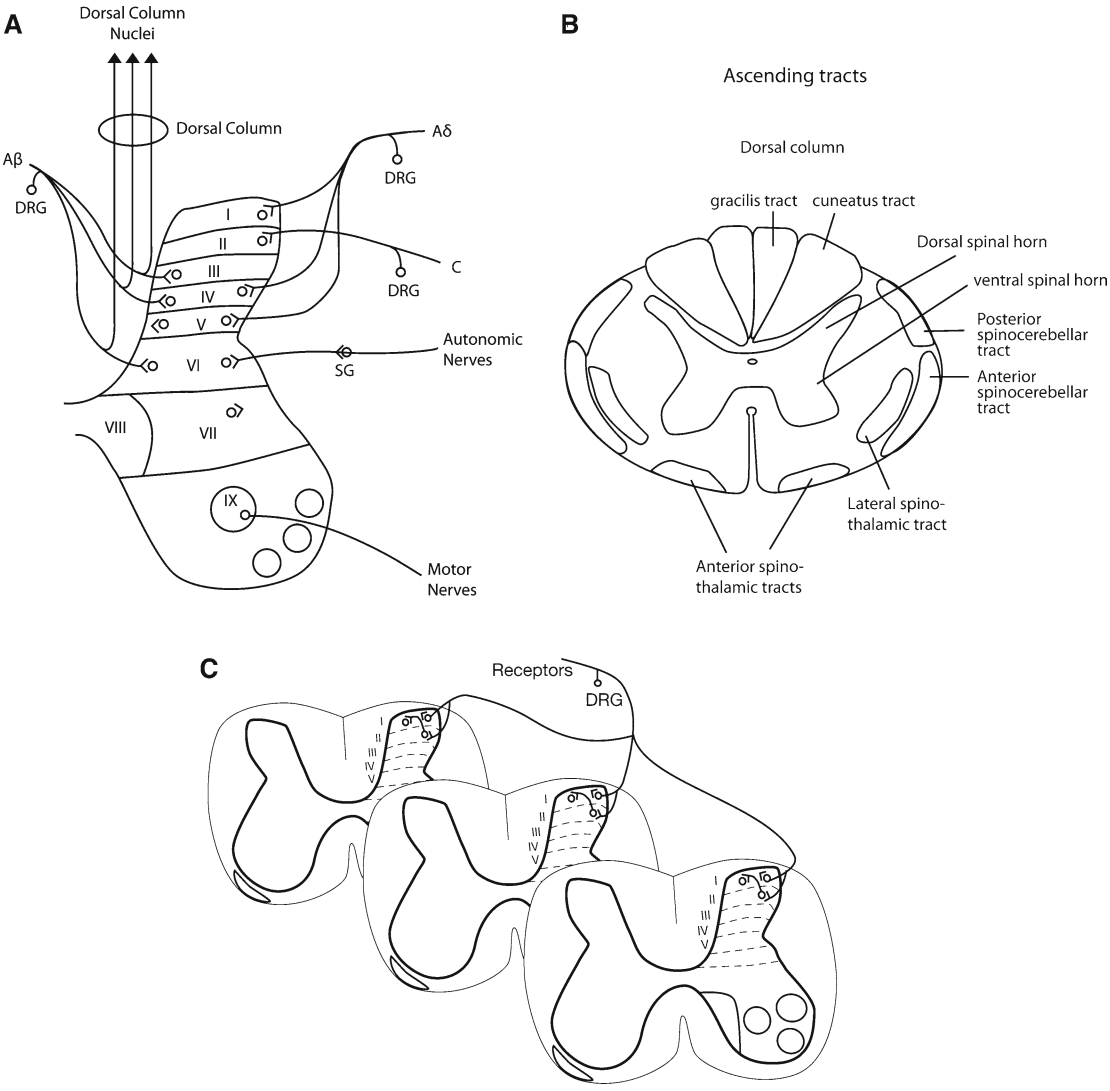


Figure 5.1: (**A**) Different types of sensory nerve fibers terminating on cells in the different lamina of the horn of the spinal cord (Rexed's classification (*2*)). (**B**) Anatomical localization of ascending tracts in the spinal cord. Based on Brodal 2004 (*74*). (**C**) Illustration of how dorsal root sensory fibers send ascending and descending branches to two adjacent segments of the spinal cord.

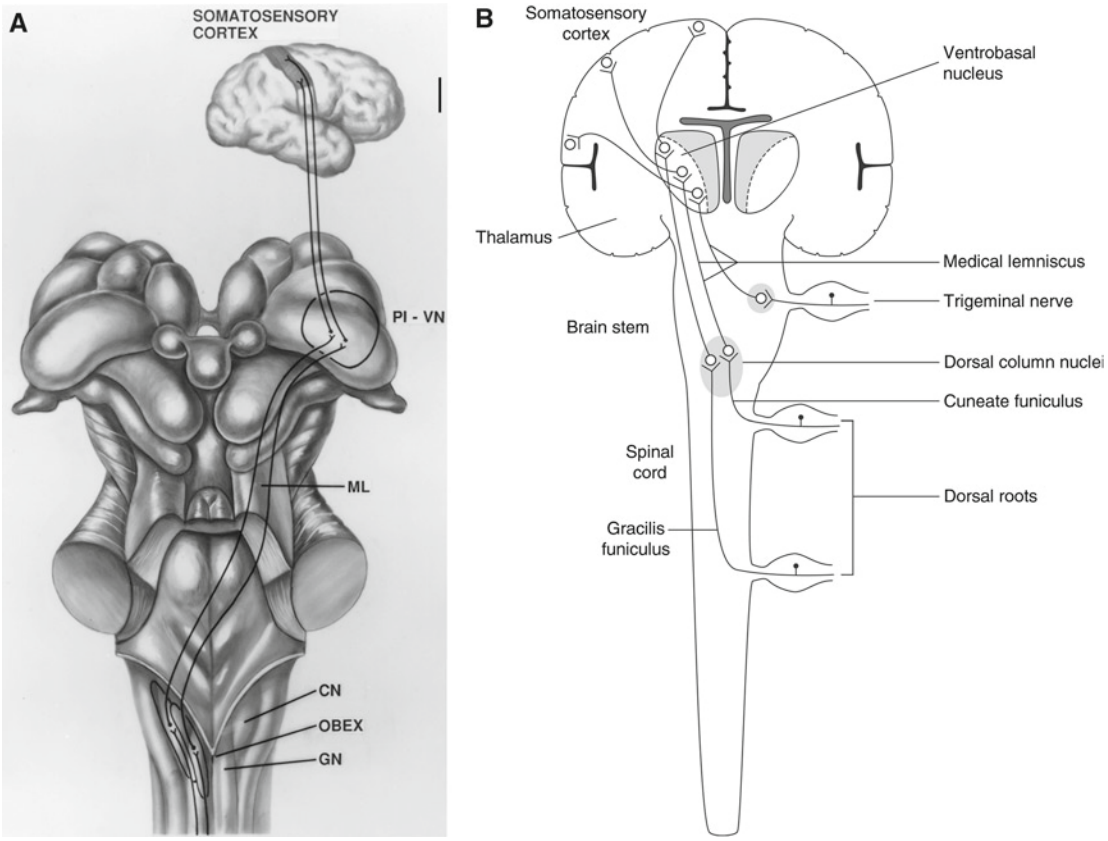


Figure 5.2: (**A**) Schematic diagram showing the neural pathway of the portion of the somatosensory system that travels in the dorsal column. *GN* gracilis nucleus, *CN* cuneate nucleus, *Pl-VN* Posteriolateral ventral nucleus of the thalamus, *ML* middle lemniscus. (Reprinted from (*75*)). (**B**) Schematic diagram showing the anatomical locations of the main components of the ascending somatosensory pathways (Reprinted from (*1*) with permission from Elsevier).

(**Fig. 5.2**). The cell bodies of these fibers are located in the dorsal root ganglia (DRG). (Sensory receptors of the head are innervated by cranial nerves.)

Several types of nerve fibers mediate sensory information to the spinal cord. Low threshold cutaneous receptors are innervated by Aβ fibers (6–12 μm diameter) with conduction velocities between 30 and 70 m/s. Proprioceptive fibers from muscle spindles, tendon organs, and receptors monitoring joint movements are large (Aα) fibers, but pain fibers are the smallest myelinated fibers (Aδ). Unmyelinated fibers (C fibers) also mediate pain.

The spinal horn has been divided into laminae (*2*). The dorsal roots of sensory nerve fibers enter the spinal cord, and some make synaptic contact with cells in different laminae of the dorsal horn of the spinal cord (**Fig. 5.2A**), whereas other fibers that travel in the dorsal column reach the dorsal column nuclei located in the lower medulla. The dorsal roots that enter the spinal cord branch several times, and the different branches make synaptic contact with cells in different parts of the dorsal horn of the segment on which they enter as well as on several adjacent segments. Some branches ascend uninterrupted on the same side of the spinal

cord as they entered to form the dorsal column, and these axons make synaptic contact with cells in the dorsal column nuclei (**Fig. 5.1**). Some small, myelinated fibers that mediate pain (Aδ fibers) terminate on cells in lamina I and IV of the dorsal horn, and the axons of these cells cross the midline and ascend on the opposite side of the spinal cord as the spinothalamic tracts to reach the thalamus (**Fig. 5.1B**).

Dorsal Root Fiber Collaterals. The sensory nerve fibers that enter a segment of the spinal cord send collateral fibers to several adjacent segments (**Fig. 5.1C**), where they can activate cells in the dorsal horns of these segments. **Fig. 5.1C** only shows three adjacent segments of the spinal cord, one above and one below the segment, where the dorsal root enters, but there is anatomical evidence that these branches continue up and down the spinal cord to several more segments (*3*).

The efficacy of the synapses that connect these fibers to cells decreases with the distance from the segment where the nerve fibers enter the spinal cord, but the efficacy can change as a result of the activation of neural plasticity. The branches that terminate on cells in the first few of the neighboring segments can normally activate cells in the dorsal horn, while the branches that terminate on cells in segments that are more distant cannot normally activate cells because of insufficient synaptic efficacy. The efficacy of the synapses that connect these collaterals to cells in the dorsal horns gradually decreases with the distance from the segment where the dorsal root enters.

The synapses that normally are "dormant" can be "unmasked" when neural plasticity is activated. This may occur when the dorsal root that enters a segment is severed or when the input is otherwise reduced. Such increased synaptic efficacy caused by injury and subsequent lack of input to the segment to which the dorsal root was damaged occurs as a result of the activation of neural plasticity (*4*).

This means that injury to a sensory nerve can have widespread effect on the excitability of dorsal horn neurons and cause an abnormal spread of sensory activity to more segments of the spinal cord than what normally occurs. This is one reason for the complex reactions that often occur from damage of a single dorsal root or a peripheral nerve.

Dorsal Column System. The dorsal column is entirely an anatomical structure with many kinds of nerve fibers, not a single tract. The majority of fibers are primary afferents and collaterals of primary afferents from sensory receptors. These first-order nerve fibers that receive input from receptors in the skin and muscles enter the dorsal horn of the spinal cord and ascend in the dorsal column (posterior funiculus consisting of the cuneate and gracilis funiculi) of the spinal cord on the ipsilateral side to terminate in cells in the dorsal column nuclei (**Fig. 5.3**).

The dorsal column has two parts, the funiculus cuneatus and the funiculus gracilis. The fibers of these two parts terminate on cells in the cuneate and gracilis nuclei, respectively. In addition, the dorsal column contains ascending fibers that originate in cell bodies of the dorsal horn of the spinal cord. These constitute what is known as the second order dorsal column pathway.

The fibers of the dorsal column that originate in the upper portion of the body (thoracic and cervical segments) terminate in the neurons of the cuneate nucleus, while some of the nerve fibers that innervate receptors of the lower body terminate in the gracilis nucleus of the dorsal column nuclei.

The fibers of the second order dorsal column pathway mainly originate from cells in lamina IV of the spinal horn in the cervical enlargement of the spinal cord and from cells in lamina V and VI in the lumbosacral cord. Many of the fibers in the second order pathways are activated by receptors in joint and muscle receptors (*5*).

The primary afferents of the dorsal column system mediate fine touch (from skin receptors) and unconscious proprioception (from muscle spindles and tendon organs) from the upper and lower limbs, respectively. The cuneate nucleus also relays impulses from

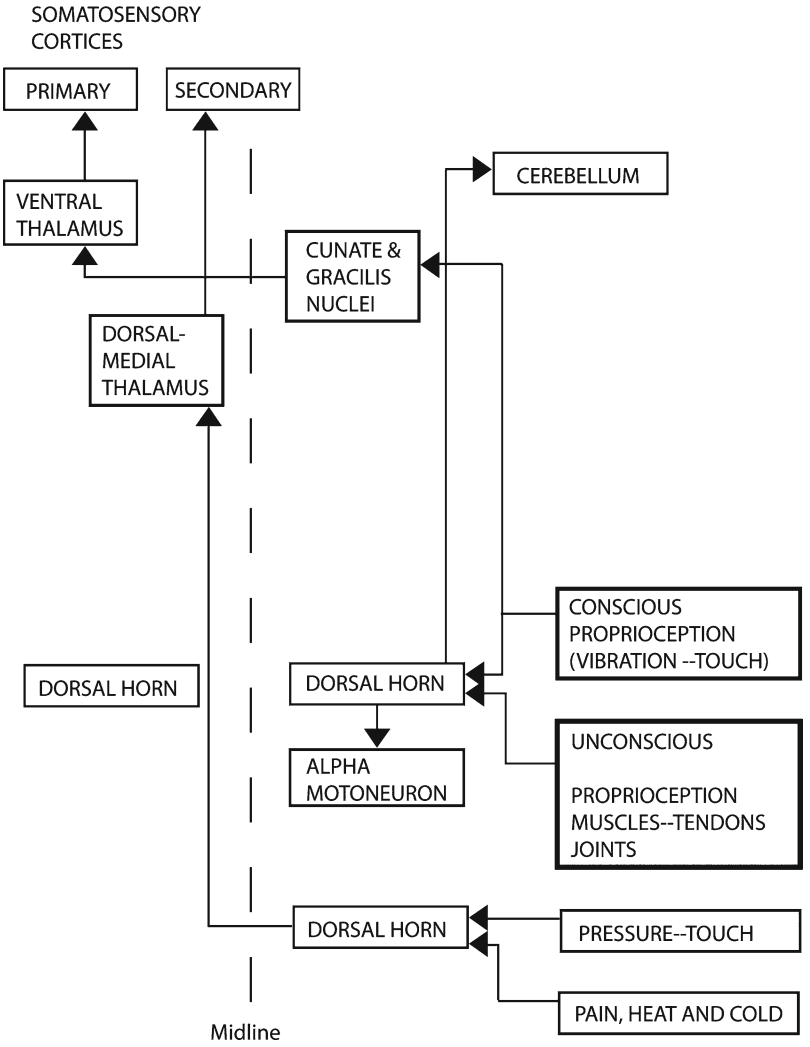


Figure 5.3: Simplified diagram of the most important ascending pathways of the somatosensory system.

slowly adapting receptors in muscles also from the lower body, and there are indications that damage to the dorsal column system may impair movement control.

The nucleus cuneatus and the nucleus gracilis, together known as the dorsal column nuclei, are located in the caudal portion of the medulla. The nucleus Z is located slightly rostral and medial to the dorsal column nuclei. Nucleus Z receives proprioceptive fibers from the lower body and low threshold skin receptors (*6*). It is assumed to be mainly involved in unconscious proprioception.

Fibers that leave the dorsal column nuclei and the nucleus Z cross over to the other side of the medulla and ascend to form the medial lemniscus. The medial lemniscus ascends in the brainstem, first near the midline and later, more laterally, to terminate in the somatosensory nuclei (the ventral posterior lateral (VPL) nucleus, also known as the ventrobasal (VB) thalamus comprising the VPL and ventral

posterior medial (VPM) nuclei, **Fig. 5.2**) of the thalamus, which is the second main relay nucleus of the somatosensory system. It is mainly the dorsal column that is monitored when using SSEP; (see Chap. 6).

This difference between the ascending pathways of the somatosensory system of the lower and upper body has important implications for the interpretation of the SSEP recorded in response to electrical stimulation of peripheral nerves of the lower limbs (peroneal or posterior tibial nerves) as well as when dermatomal stimulation is used, as we shall discuss later in this chapter. (When dermatomes of the lower body are stimulated electrically to elicit SSEP, it is probably mainly skin receptors that are activated, and such neural activity probably mainly travels in the dorsal column system; (see Chap. 6)).

Some of the fibers of the second order pathway terminate in the dorsal column nuclei and some terminate in nucleus Z in the cat and the external cuneate nucleus of the monkey. These fibers mediate proprioception that does not cause awareness such as information from muscle spindles and joint receptors (proprioception) in the lower body. These fibers travel ipsilaterally in the lateral fasciculi of the spinal cord and terminate in the nucleus Z, which is located more medially and rostral to the nucleus gracilis (6). Fibers that leave nucleus Z cross the midline and join the medial lemniscus. Nucleus Z of the cat medulla has been shown to act as a relay between the spinal cord and the ventral lateral (VL) nucleus of the motor thalamus (6). In one study, the authors presented evidence that group I muscle afferents from the hind limbs in the cat enter the dorsal lateral fasciculi at the L_3 level and terminate in nucleus Z (7). Tracey (1982) (5) showed that in the cat and the monkey, the fast-conducting group I muscle afferents from the lower limbs are likely to transverse the posterolateral funiculus.

Organization of the Somatosensory Cortex. The primary somatosensory cortex receives its input from the VPL nuclei of the thalamus as third-order neurons. These neurons travel in the posterior limb of the internal capsule and disburse over the somatosensory cortex (postcentral gyrus of the parietal cortex) in a somatotopic fashion, with the legs represented closest to the midline, followed in the lateral direction by the representation of the trunk, forearm, and hand (**Fig. 5.4**). Neurons in the primary cortex send axons to the secondary somatosensory cortex and to association cortices. Secondary somatosensory cortices occupy large parts of the somatosensory cortical areas (for details see (*1*)).

The primary somatosensory cortex also receives unconscious proprioceptive input, and evoked potentials have been recorded in response to electrical stimulation of deep tissue such as joints. Single cell recordings have confirmed that tracts that carry unconscious proprioception indeed project to cells in areas of the primary somatosensory cortex that are different from

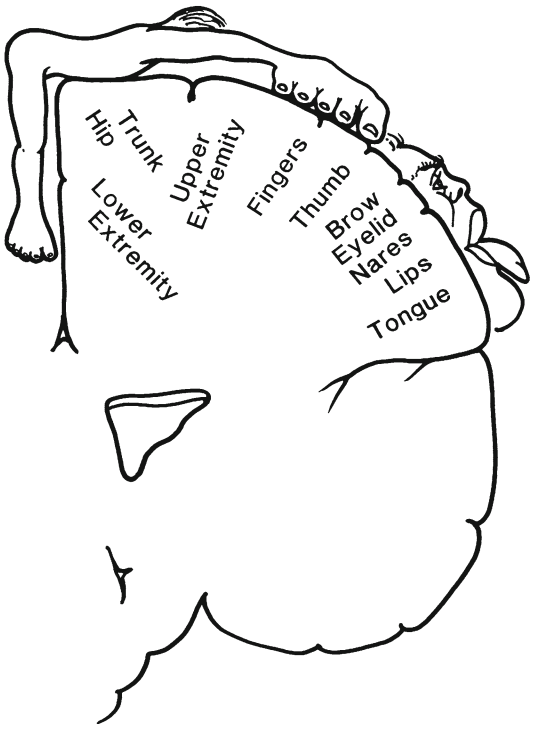


Figure 5.4: Somatotopic organization (homunculus) of the body surface on the somatosensory cortex by Penfield and coworkers (Reprinted from (*76*)).

those that receive conscious somatosensory input, such as from cutaneous receptors (*8*). In primates, it is area 2 (Brodmann's area, see Appendix A) of the primary somatosensory cortex that receives proprioceptive input (*9*). Humans may be assumed to have a similar organization.

The secondary cortex has been the target of attempts to modulate pain and tinnitus, and its connections may, therefore, become directly important for intraoperative monitoring where proper localization of the placement of recording electrodes may be facilitated by intraoperative recordings. Neurons in the S2 cortical region receive input from S1 and bilateral input from the thalamus. S2 neurons are topographically organized with the homunculus of the body surface similar to S1. These neurons also receive input from cells in the VB nuclei of the thalamus. There are also connections from S1 and S2 to the insular cortex.

Neurons in area 5, located in proximity to area 2, receive input from proprioceptors, such as muscle spindles and joint receptors, through input from the lateral posterior nucleus and the anterior nucleus of the pulvinar of the thalamus and corticocortical input from area 3a (*5*). Neurons in S2 also receive input from the anterior lateral system (thus pain information, see below) (**Fig. 5.5**).

Anterior Lateral System. Temperature and pain information travel in the anterior lateral system consisting of the spinothalamic tract, the spinomesencephalic tract, and the spinoreticular tract. The spinothalamic tract is the largest and probably the most important of these tracts. The anterior lateral system is concerned with less localized and more general tactile sensation in contrast to the dorsal column system, which communicates fine touch and has an almost 1:1 synaptic ratio, which provides for much more precise localization and discrimination.

The lateral and anterior spinothalamic tracts terminate on cells in the dorsal and medial thalamic (VPL) nuclei. The axons of these cells terminate in the secondary somatosensory cortex and association cortices (*1*). The anterior lateral system has great clinical importance, but intraoperative monitoring of this system has not been described (**Fig. 5.6**).

Anterior and Posterior Spinocerebellar System. The third ascending system consists of the anterior and the posterior spinocerebellar tracts (**Figs. 5.2** and **5.3**). This system furnishes unconscious proprioception and provides important feedback to the motor system, but it is not monitored intraoperatively either. The spinocerebellar tract may be regarded as belonging more to the motor system than to

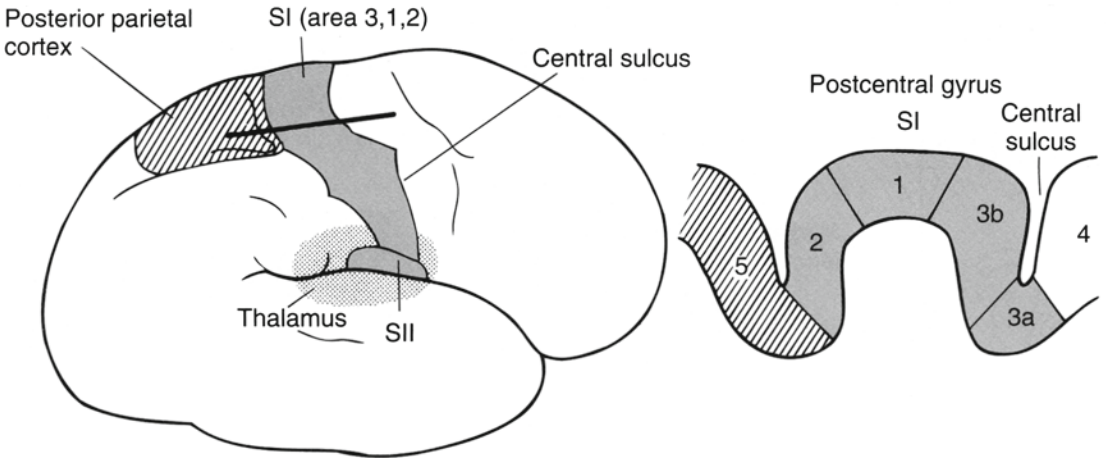


Figure 5.5: Somatosensory cortices, SI and SII (Reprinted from (*74*) with permission from Oxford University Press).

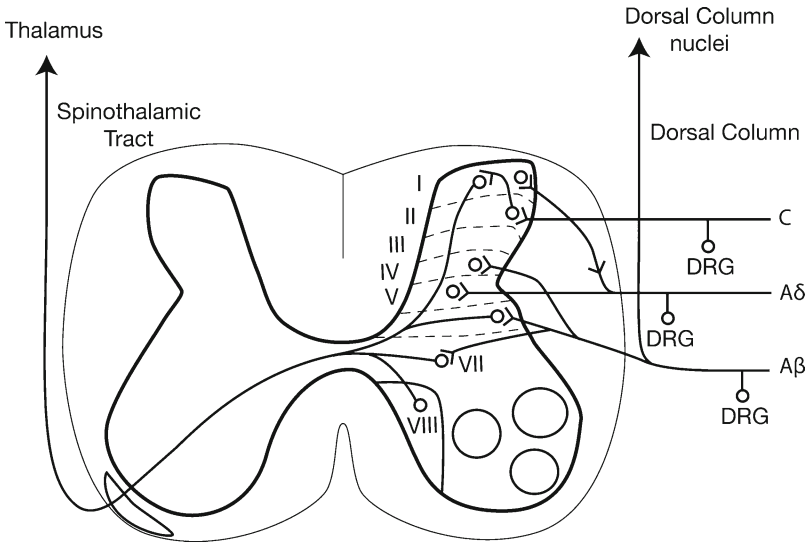


Figure 5.6: Illustration of the termination of the Aβ, Aδ fibers, and C fibers in the dorsal horn and their ascending connections that carry innocuous information to the dorsal column nuclei and pain pathways (spinothalamic tract). *DRG* Dorsal root ganglion. Lamina II is also known as substantia gelantinosa.

sensory systems. Both the anterior and posterior spinoreticular tracts receive their input not only from receptors in muscles (muscle spindles), tendons, and joints, but also from skin receptors. The fibers travel in peripheral nerves and enter the spinal cord as dorsal root fibers that terminate on cells in the central part of the spinal horn. The axons of these cells travel on both sides of the spinal cord and reach cells in the cerebellum without interruption. Collateral from the fibers in this tract reach nucleus Z of Brodal and Pompeiano (*7*) and terminate on its cells. These cells send axons to the thalamus where they terminate in the VPL.

The Trigeminal System. Tactile information from the face is mediated by the trigeminal system. The cell bodies of the trigeminal nerve (fifth cranial nerve) are located in the trigeminal ganglion (ganglion of Gasser or semilunar ganglion) where the trigeminal nerve central branches enter the sensory trigeminal nucleus that extends from the midbrain to the upper part of the spinal cord (**Fig. 5.7**). The ascending fibers from that nucleus join the medial lemniscus on the contralateral side and extend to the thalamic nucleus (medial portion of the ventral posterior nucleus, VPN). The fibers from the VPN project to the somatosensory cortex (postcentral gyrus) lateral to the homunculus projection of the hand (**Fig. 5.4**). The rostral portion of the trigeminal nucleus is concerned with touch, warmth, and cool sensations, while the most caudal portion, the spinal nucleus of the trigeminal nerve, is mainly concerned with pain and cold and hot sensations. This part of the nucleus is involved in the generation of pain in patients with trigeminal neuralgia. Treatment may involve operations that involve microvascular decompression of the trigeminal nerve or operations where a small cut is made in the nerve. In such operations, it may be useful to map the trigeminal nerve using intraoperative neurophysiology (see Chap. 14).

Electrical Potentials Generated by the Somatosensory Nervous System

Recordings of evoked potentials from the somatosensory system play an important role in intraoperative monitoring of the spinal cord

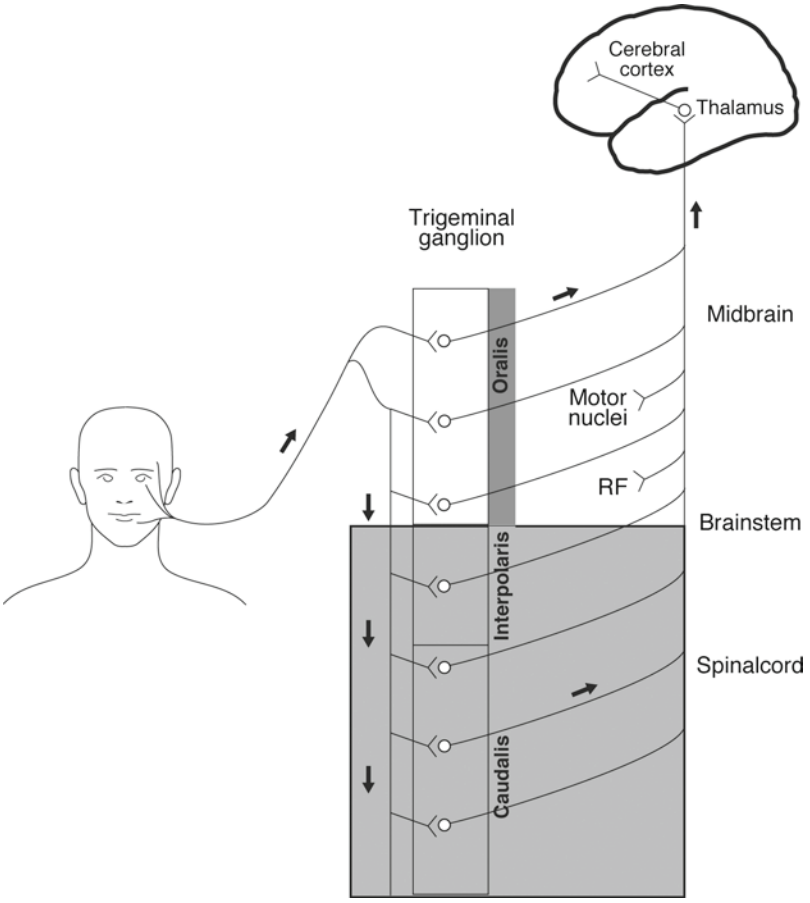


Figure 5.7: Schematic drawings of the pathways through the trigeminal sensory nucleus. The *upper part* is the sensory part and the *lower* (*shaded*) *part* is mainly involved in processing noxious stimuli (pain processing). *RF* Reticular formation. (Adapted from (*77*)).

and the brain, and both near-field and far-field potentials are used in various kinds of monitoring of SSEP.

In somatosensory system monitoring, peripheral nerves are often stimulated electrically while evoked potentials are recorded from electrodes placed on the scalp. There is a distinction between upper limb SSEP recorded in response to stimulation of the nerves at the wrist and lower limb SSEP stimulation performed at the knee or the foot. Responses from electrodes placed on the skin (dermatomes) are also used in intraoperative monitoring. Practical aspects regarding the monitoring of SSEP are detailed in Chap. 6.

Near-Field Evoked Potentials. Typical recordings made directly from the surface of the dorsal column nuclei in response to stimulation of the median nerve at the wrist are shown in **Fig. 5.8** compared with far-field SSEP recorded from electrodes placed on the vertex and the upper neck in a patient undergoing an operation where the dorsal column nuclei were exposed. It is seen that electrical stimulation of the median nerve gives a large response from the dorsal column nuclei (the cuneate nucleus) with a waveform that is typical for responses from a nucleus with an initial positive–negative potential followed by a broad negative potential (see Chap. 3).

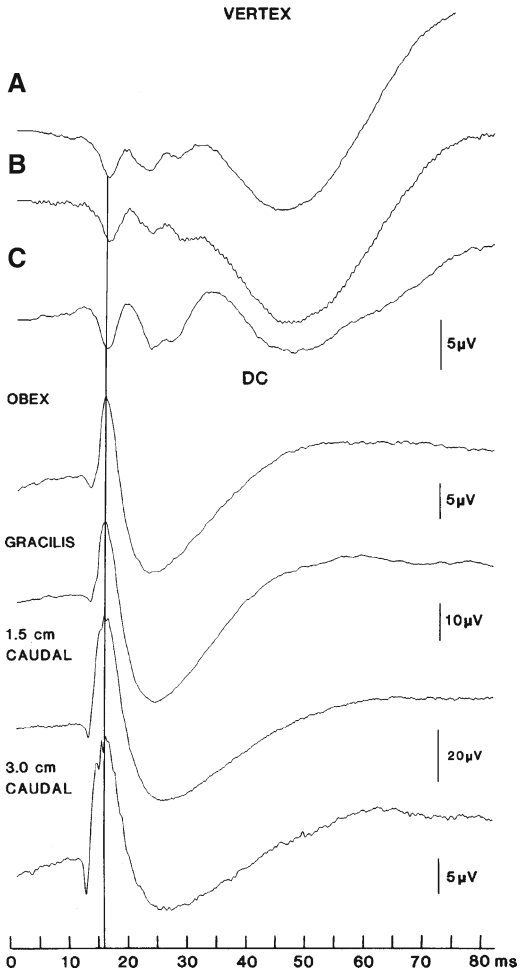


Figure 5.8: Responses to electrical stimulation by an electrode placed over the median nerve at the wrist. *Upper curves*: Far-field recordings (vertex-inion) obtained after the patient was anesthetized, but before the operation began (**A**), during direct recording (**B**), and during closure (**C**). *Middle curves*: Recordings from the surface of the cuneate nucleus using the opposite earlobe as a reference (DC). (Reprinted from (*20*) with permission from Wolters Kluwer Lippincott Williams & Wilkins).

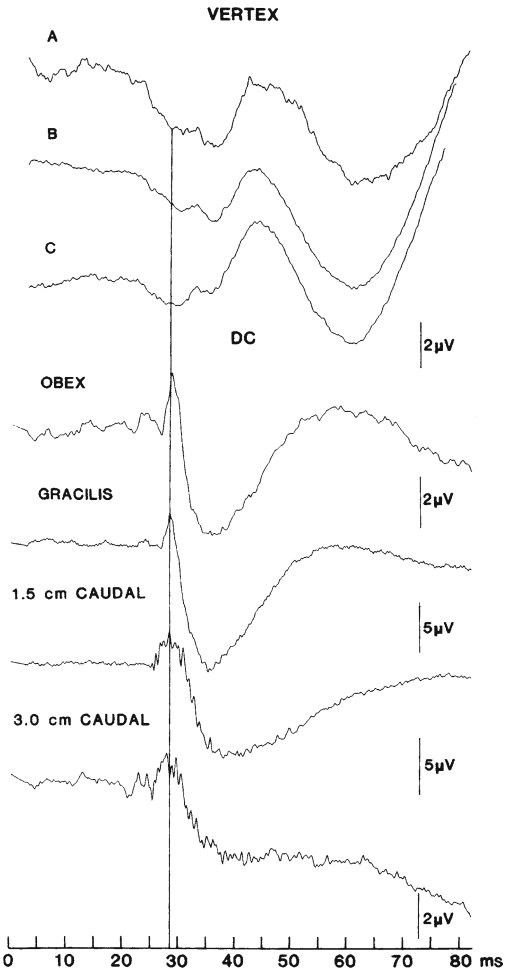


Figure 5.9: Recordings are similar to those in **Fig. 5.8**, but were obtained from the gracilis nucleus in response to electrical stimulation of the peroneal nerve at the knee. As in **Fig. 5.8**, the *top tracings* were obtained by recording from electrodes placed on the scalp (vertex-inion) before the operation began. (Reprinted from (*20*) with permission from Wolters Kluwer Lippincott Williams & Wilkins).

The response from the gracilis nucleus to stimulation of the peroneal nerve has a similar waveform, but with longer latencies containing a series of wavelets (**Fig. 5.9**) that indicate that the neural pathway that is activated is longer than that involved in the response from stimulation of the median nerve, and that there is a larger variation in fiber diameter. Therefore, the neural activity that arrives at the level of the upper spinal cord is dispersed in time.

The stimuli used to evoke the responses shown in **Fig. 5.8** and **5.9** were presented at a rate of 20 pps

and the recording filters were set at 3–3,000 Hz. Sampling intervals were 160 μs, and each recording had 512 data points. Negativity is shown as an upward deflection. The results were obtained in a patient undergoing microvascular decompression to relieve spasmodic torticollis.

Far-Field Evoked Potentials. When peripheral nerves, such as the median nerve of the upper limb or the posterior tibial nerves and peroneal nerves of the lower limb, are electrically stimulated for the purpose of recording SSEP, both the dorsal column system and the anterior lateral system are most likely activated, but it is generally assumed that the anterior lateral system is not represented to any noticeable degree in the responses that are recorded, nor is the spinocerebellar tract contributing noticeably to the far-field potentials.

Upper Limb SSEP. SSEP recorded from electrodes placed on the scalp in response to electrical stimulation of the median nerve at the wrist have a series of peaks and troughs. In recordings of such responses, the negative peaks are labeled with an "N" followed by the normal latency in milliseconds. The positive peaks (or valleys) of the SSEP are usually labeled with a "P" followed by a number that is the normal latency of that peak.

The SSEP recorded from electrodes placed on the scalp on the side contralateral to the stimulation, in an awake or lightly anesthetized person, are dominated by potentials that originate in the primary somatosensory cortex. These potentials are communicated through the dorsal column system and have a latency of ~20 ms (N_{20}), but potentials with shorter latencies can also be identified (**Fig. 5.10**). The waveform as well as the amplitude of the recorded potentials depends on the placement of the recording electrodes. A negative peak with latency of 18 ms

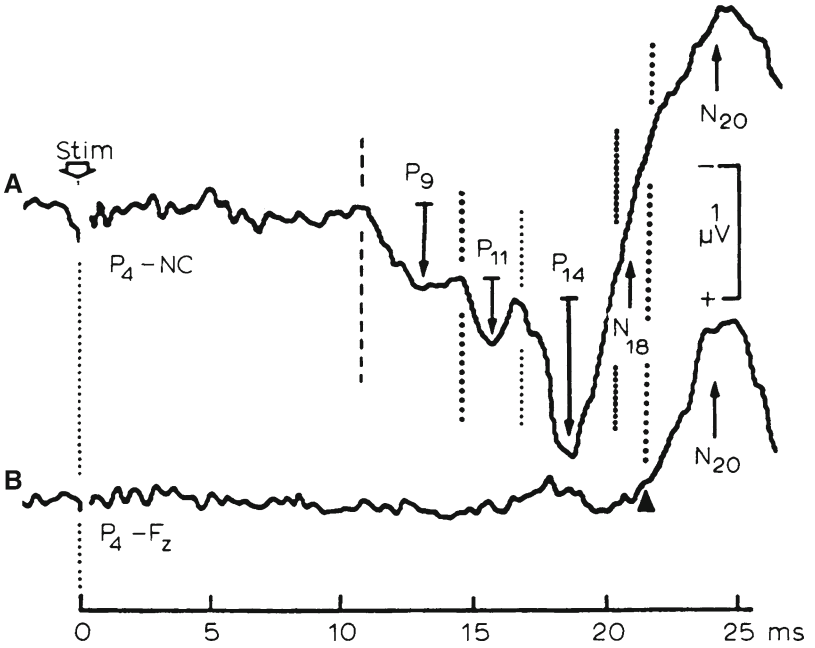


Figure 5.10: SSEP recorded in response to stimulation of the median nerve at the wrist. (**A**) Noncephalic reference. (**B**) Frontal references. *NC* Noncephalic; P4 and Fz (see 10–20 system, **Fig. 6.1**). (Reprinted from (*12*) with the permission from Elsevier).

(N_{18}) can be recorded from large areas of the scalp on both sides. These negative peaks are preceded by a series of positive peaks (P_9, P_{11}, P_{14}, P_{16}) which are best recorded from electrodes that are placed on the neck with a noncephalic reference (for instance, placed on the shoulder), but they can also be recorded from electrodes placed over the parietal region of the scalp and the upper neck (**Fig. 5.10**). Such electrode placement (contralateral–parietal to the upper dorsal neck) is practical for intraoperative monitoring and yields a clear representation of the $P_{13–16}$ peaks as well as the N_{18} and N_{20} peaks (see also Chaps. 6 and 17 for discussions of various recording techniques).

The two main negative peaks – N_{18} and N_{20} – are followed by a positive deflection (P_{22}), a large negative peak (N_{30}), and another positive deflection (P_{45}) that is broader than the P_{22} peak (not seen in **Fig. 5.10**). The N_{20}, P_{22}, and P_{45} peaks are localized to the contralateral parietal region (3 cm behind C_3 or C_4), while the N_{18} and $P_{14–16}$ components can be recorded from large regions of the scalp, including that of the contralateral side (**Fig. 5.10**). Subtracting the recordings from the ipsilateral and the contralateral sides yields more clearly identifiable N_{20}, P_{22}, and P_{45} peaks.

Evoked potentials that are generated by the brachial plexus in response to electrical stimulation of the median nerve may be recorded by placing an electrode at Erb's point (Erb's point is found just above the mid-portion of clavicle). These potentials are indicators of the degree of activation of the brachial plexus and are valuable in intraoperative monitoring of SSEP because their presence confirms that the electrical stimulation excites the median nerve.

Measuring the difference between the latencies of the different peaks in the SSEP and those of the potentials recorded from Erb's point eliminates the effect of changes in the conduction time of the median nerve in the arm (due, e.g., to changes in temperature). If the absolute value of the latencies of the various peaks in the SSEP is used, a prolongation in the conduction time of the central portion of the somatosensory pathway cannot be distinguished from a prolongation in the conduction time of the median nerve. Another measure that eliminates the influence of neural conduction in the peripheral (median) nerve, as well as that in the dorsal column, is the frequently used central conduction time (CCT), which is the interval between the $P_{14–16}$ and the N_{20} peaks (*10*) (**Fig. 5.11**). (Further details on this subject are discussed in Chap. 6).

Lower Limb SSEP. The latencies of the individual components of the lower limb SSEP depend on the height of the individual in whom they are recorded to a much greater extent than what is the case for upper limb SSEP. Large differences in these latencies are seen in children (*11*).

The SSEP elicited by stimulation of the posterior tibial or the peroneal nerves at the knee do not exhibit SSEP peaks as distinct and early as those elicited by median nerve stimulation. Because the nerve tracts involved in lower limb stimulation are much longer than those involved in median nerve stimulation, the latencies of the peaks in the lower limb SSEP are much longer than those of the peaks in the upper limb SSEP. The individual variability of these responses is much greater than the upper limb SSEP, and they are more affected by peripheral nerve neuropathy such as seen with age and diseases such as diabetes.

Recording of cortical responses elicited by lower limb stimulation may be performed using electrodes placed on the midline scalp (at C_z) level, or better yet, 3–4 cm posterior to C_z using F_{pz} or the ipsilateral mastoid as reference (**Fig. 5.12**). An electrode location 3–4 cm posterior to C_z with a noncephalic reference placed on the upper neck is also often used.

When recording potentials that are generated in the upper spinal cord and lower medulla, it may be advantageous to place the reference electrode on the upper neck, similar to that described for recording upper limb SSEP. However, the amplitudes of such early components are small and individually variable. From experience it is known that the earliest peaks in the lower limb SSEP (P_{17} and P_{24}) can only be recorded reliably from an electrode placed on the lower portion of the body, over the T_{12}

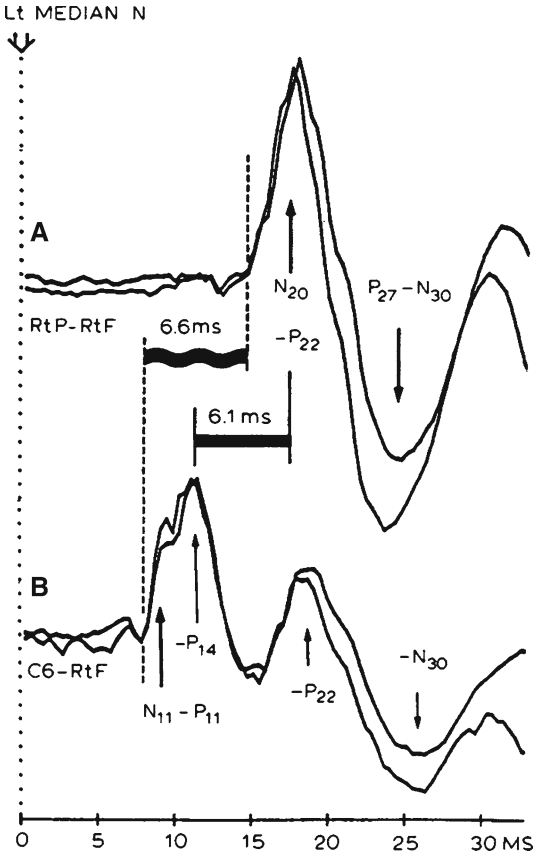


Figure 5.11: Illustration of how the CCT is determined based on recordings of the SSEP with two different electrode placements. The onset of the CCT is defined as the time of the earliest response from the spinal entry of the neural activity; the end is the beginning of the N_{20} component. (**A**) Recordings from a contralateral parietal location (behind C_3 or C_4) using a frontal reference. (**B**) Recording from a noncephalic (spinal C_6) location using the same frontal reference as in (**A**). (Modified from (*22*) with permission from Elsevier).

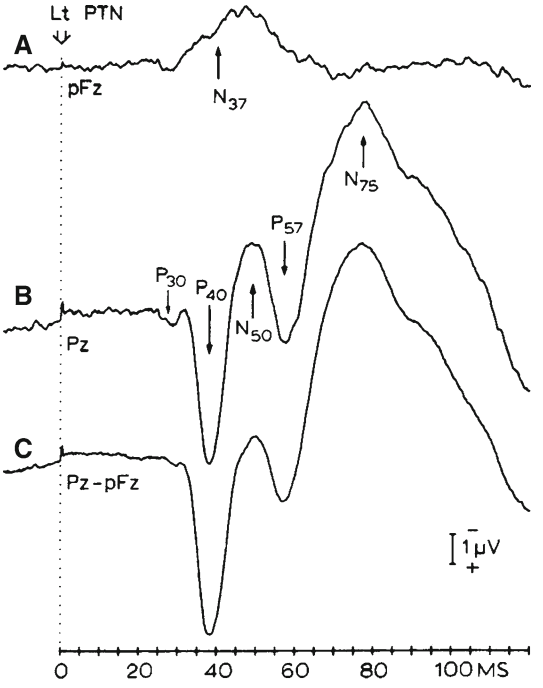


Figure 5.12: SSEP in response to stimulation of the left posterior tibial nerve using various locations for the recording electrodes (**A**) Recordings from a frontal location, F_{pz}. (**B**) Recording from a midline position, P_z. A noncephalic reference (on *left shoulder*) was used in both recordings. (**C**) The difference between the recording in (**A**) and the one in (**B**), mimicking a differential recording between F_{pz} and P_z. (Reprinted from (*22*) with the permission from Elsevier).

vertebra or below the hip (e.g., on a lower limb). Such an arrangement may be difficult to use for intraoperative monitoring because it often results in noisy recordings from electrical interference (*11*).

The response from the popliteal fossa (at the knee) to stimulation of the posterior tibial nerve shows the activation of the peripheral nerve that is being stimulated, similar to that which is noted in recordings from Erb's point in upper limb SSEP. These responses indicate that proper stimulation has been applied to the respective (posterior tibial) nerve.

Neural Generators of the SSEP

The SSEP elicited by stimulation of the median nerve (upper limbs) and the peroneal or posterior tibial nerves (lower limbs) are fundamentally different, and the neural generators of these two types of SSEP are discussed separately.

Upper Limb SSEP. Studies of the neural generators of the SSEP confirm that the major contributions to the SSEP recorded from electrodes placed on the scalp originate in the dorsal column system.

The short latency evoked potentials, in response to electrical stimulation of the median nerve, are generated by the peripheral nerves, the spinal cord (the dorsal column fibers) and possibly by the medial lemniscus (*12–15*) while the dorsal column nuclei seems to produce very small far-field potentials (*16*).

Recordings from different locations along the spine have shown that the P_9 peak dominates at the spinal C_7 level, and it has been concluded that P_9 of the scalp-recorded SSEP represents the neural volley that enters the spinal cord from the brachial plexus. Evidence has been presented that the P_{11} peak is generated in the dorsal horn by neural structures that are not parts of the ascending somatosensory pathway. This is important to consider when the recordings of SSEP are used in intraoperative monitoring; it means that the P_{11} peak may be preserved, despite the compromise of ascending somatosensory tracts at the level of the foramen magnum.

The introduction of the use of a noncephalic reference for recording upper limb SSEP (13, 17) was a major breakthrough in studies of the neural generators of the SSEP studies because it made it possible to identify the early components of the SSEP and enabled investigators to study the origin of these potentials in more detail (12, 13). Some of these studies compared recordings from the scalp with recordings from the ventral side of the spinal cord using a recording electrode that was placed in the esophagus.

The origin of the $P_{14–16}$ peaks is not entirely clear. Some investigators (18) assumed that P_{14} was generated in the medial lemniscus. These results are supported by work by other investigators, such as Allison and coworkers (19), while yet other investigators have arrived at different interpretations of the origins of these early components. These authors described the peaks as $P_{13–16}$ peaks, thus assuming that the first of these occurred 1 ms earlier than other investigators. Some investigators (14) found evidence that P_{13} was generated more peripherally, namely, where the dorsal column passes through the foramen magnum and that P_{11} was generated by the dorsal root at the spinal C_2 level. It has been suggested that what these investigators Lueders et al. (14) identified as P_{13} was, in fact, the same peak as identified by the other investigators (the Desmedt group) and labeled P_{14}. The confusion between which peaks were P_{13} and which were P_{14} could have been a result of slightly different electrode placements and a small difference in the ways in which recordings were filtered by these two separate groups of investigators.

Studies comparing the responses from the exposed surface of the dorsal column nuclei evoked by electrical stimulation of the median nerve in patients undergoing neurosurgical operations, with those recorded from the scalp (SSEP) (20) (Fig. 5.8) recorded simultaneously with the intracranial recordings, indicate that P_{14} is most likely generated by the fiber tract that terminates in the cuneate nucleus.

Studies in the monkey (16) where the dorsal column nuclei were stimulated electrically and the elicited antidromic activity in the median nerve was recorded have provided accurate determinations of the neural conduction time in the median nerve. These studies indicated that the initial components of the potentials that are recorded from the surface of the dorsal column nuclei reflect ascending activity in the dorsal column (16) and support the assumption that the P_{14} peak in humans is generated by the termination of the dorsal column fibers on the cells of the cuneate nucleus.

Most studies, however, agree that the dorsal column nuclei themselves contribute little to the far-field potentials possibly because the organization of these nuclei is such that they produce a closed, or nearly closed, electrical field (*21*) (see Chap. 3). This is similar to the conclusions regarding the neural generators of the auditory brainstem responses (ABR), where the nucleus of the inferior colliculus was found to produce only a weak far-field response (see page 84).

The N_{18} peak that can be recorded over large regions of the scalp has a different origin than the N_{20} peak. The N_{18} is generated by bilateral brainstem structures while the somatosensory cortex generates N_{20}, which is specifically localized contralaterally to the side that is stimulated. The N_{18} peak is assumed to be the result of excitatory postsynaptic potentials in several nuclei that receive input from the medial lemniscus, such as the superior colliculus (*22, 23*). (It is important to keep in mind that fibers that constitute tracts such as the fibers of the medial lemniscus have many collaterals that connect to neurons in different parts of the CNS).

The N_{20} peak can only be recorded from a small area of the contralateral parietal scalp, and it is assumed to be generated by the primary somatosensory cortex, where it represents the early response of the input from the thalamus (*22*). The generators of the components (positive and negative peaks) that follow N_{20} (P_{22}, N_{30}, and P_{45}) are not known in detail, but the generators of these components are assumed to be higher brain structures that receive input from the primary somatosensory cortex, such as the secondary cortices and perhaps association cortices. There is considerable neural processing in the primary somatosensory cortex, and the result of that processing may contribute to some of the components in the SSEP that have latencies longer than 20 ms. These peaks are more individually variable, and they are more sensitive to anesthesia than earlier peaks, a sign that more synapses are involved.

Lower Limb SSEP. The generators of the lower limb SSEP (elicited by stimulation of the posterior tibial or the common peroneal nerves) have been studied much less comprehensively than the upper limb SSEP (elicited by stimulation of the median nerve). Likewise, the origins of the components of the lower limb SSEP are incompletely known. The N_{17} peak that can be seen in some recordings is assumed to be generated near the hip joint, and the P_{24} peak is assumed to be generated at the level of the twelfth thoracic vertebra. The P_{31} peak is probably generated where the spinal cord passes through the foramen magnum, and together with the P_{34} peak, these potentials may correspond to the $P_{14–16}$ complex of the upper limb SSEP. The P_{34} peak is thus, assumed to be generated by structures in the brainstem (medial lemniscus), but this peak could also be analogous to the N_{18} peak of the upper limb SSEP (*24*) (see **Figs. 5.12** and **5.13**). The negative deflection (N_{34}) following these positive peaks may be generated in brainstem structures or in the thalamus. The lower limb response elicited by electrical stimulation of the posterior tibial nerve has a main positive peak with a latency of ~40 ms (P_{40}) followed by a large negative peak at a latency of 45 ms (N_{45}). (The exact latency of these peaks depends on the height of the person in question, but there are other causes for the considerable variations seen in lower limb SSEP.) This negative peak is generally assumed to be generated by cortical structures, and it is best recorded with an active electrode at the midline, 3–4 cm behind the C_z (*22*). A frontal reference is usually used for such recordings. However, as discussed in Chap. 6, this is not an optimal electrode placement for intraoperative monitoring.

One reason that interpretation of the neural generators of the different components of the lower limb SSEP is less certain than for those of the upper limb SSEP is that anatomical structures of the ascending somatosensory pathway from the lower portion of the body are more complex and diverse compared to structures in the upper portion of the body (page 69). The early peaks in the SSEP evoked by lower limb stimulation are less distinct than those evoked by upper limb stimulation because of the greater temporal dispersion of the neural activity that arrives at the brain from the lower portion of the body due to the longer pathway than those of the upper limb SSEP. When nerve fibers have different conduction velocities, the temporal coherence of neural activity decreases along such nerves. Long nerves, therefore, tend to deliver less temporally coherent neural activity to central neural structures than shorter pathways. Since the amplitudes of the various peaks in the far-field response depend on the degree of temporal coherence of the neural activity, such temporal dispersion results in the

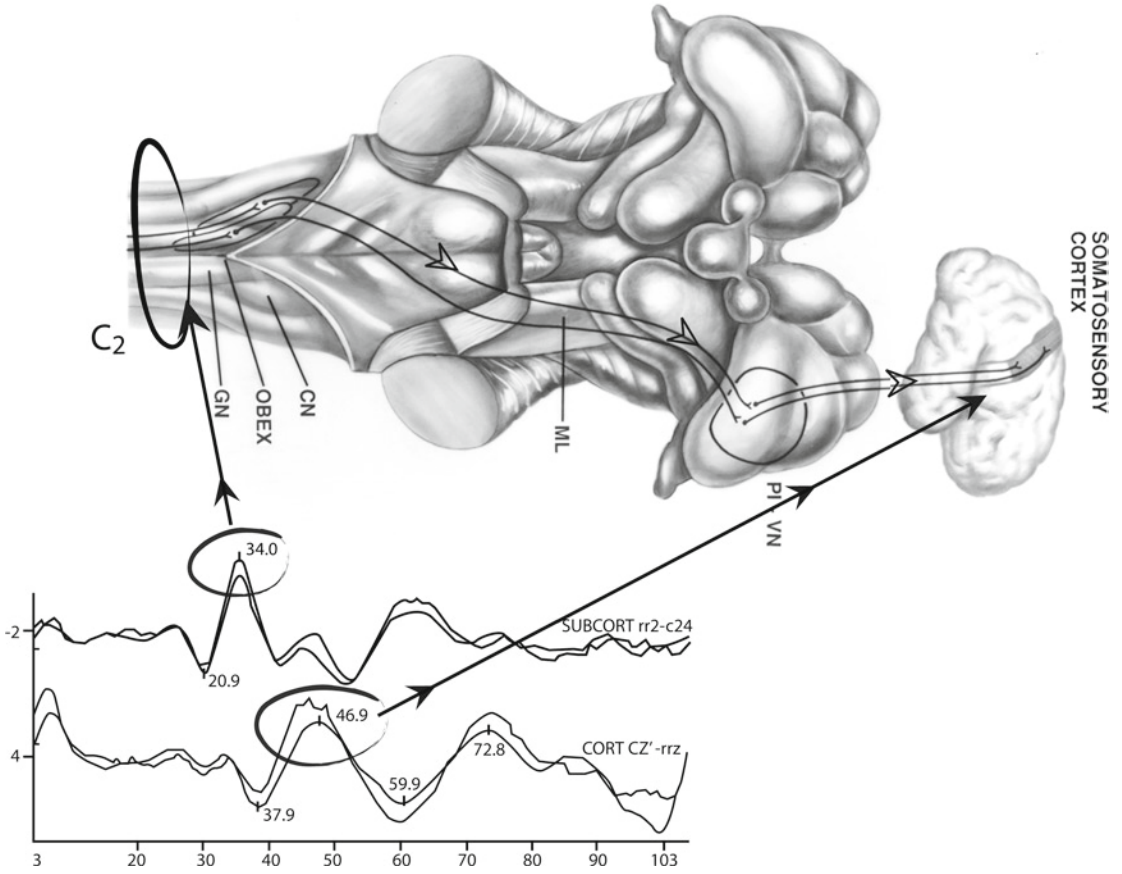


Figure 5.13: Response from stimulation of the posterior tibial nerve. *Upper trace*: Subcortical recording, Fpz-C_2S. *Lower trace*: Cortical response, recorded from Cz-Fpz.

peaks becoming broader and of smaller amplitudes compared to similar peaks in systems that have shorter pathways – such as the upper limb SSEP (see also discussion about the effect of temporal dispersion in Chap. 6, **Fig. 6.4**).

THE AUDITORY SYSTEM

Knowledge about the anatomy and physiology of the auditory system is a prerequisite for understanding not only the normal function of the auditory system, but also for understanding that changes in function may result from surgical manipulations of the auditory nerve and other, more central, structures of the auditory nervous system.

This section of this chapter describes the anatomy and physiology of the auditory system as applicable to intraoperative monitoring of different kinds of auditory evoked potentials (AEP). Generation of far-field auditory evoked potentials, auditory brainstem responses (ABR), near-field AEP, and compound action potentials (CAP) from the auditory nerve and cochlear nucleus are discussed. The practical aspects of hearing preservation in various types of operations and far-field/near-field recordings of ABR are discussed in detail in Chap. 7.

The Ear

The ear consists of the outer ear, the middle ear, and the inner ear (cochlea) where the first processing of sounds occurs and where the sensory receptors are located (**Fig. 5.14**).

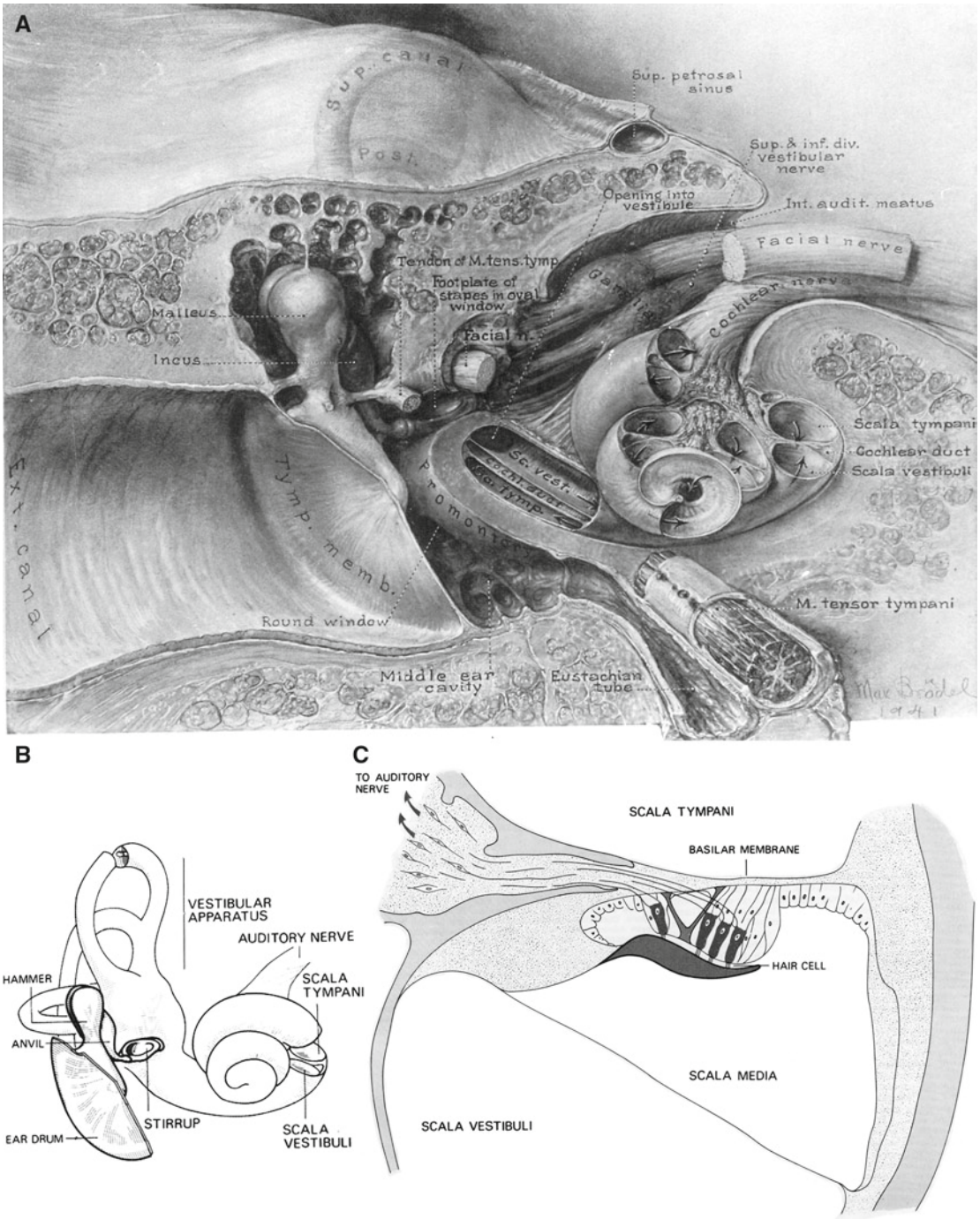


Figure 5.14: Anatomy of the ear. (**A**) Cross-section of the human ear. (Reprinted from (*78*)). (**B**) Schematic drawing of the ear. (Reprinted from (*79*)). (**C**) Cross-sectional drawing of the cochlea illustrating the fluid-filled canals and the basilar membrane with hair cells. (Reprinted from (*79*) with the permission from the Royal Swedish Academy of Science).

Sound Conduction to the Cochlea. The middle ear functions as an impedance transformer that facilitates transmission of airborne sound into vibrations of the fluid in the cochlea. This transformer action is the result of a difference between the area of the tympanic membrane and the area of the stapes footplate. The stapes footplate, which is located in the oval window, performs a piston-like, in–out motion that sets the fluid in the cochlea into motion. The middle ear cavity is filled with air and acts as a cushion behind the tympanic membrane. The proper function of the middle ear depends on the air pressure in the middle ear cavity being equal to the ambient pressure (*25*). This pressure equalization is normally maintained by the opening and closing of the Eustachian tube (**Fig. 5.14A**), which occurs naturally by the swallowing action. Since anesthetized individuals do not swallow, a negative pressure may build up in the middle ear cavity during anesthesia and that can cause a reduction in sound transmission for low-frequency sounds. Although the effect of such a reduction on the results of intraoperative monitoring of auditory evoked potentials has been discussed, there is no substantial evidence of any noticeable effect on the results of monitoring click-evoked auditory potentials. The reason is likely that negative pressure in the middle ear cavity mainly affects the transmission of low frequencies, and AEP elicited by click sounds mainly depend on the high frequency components of the sounds.

The acoustic middle ear reflex that normally reduces the transmission of mainly low frequency sounds through the middle ear is inactivated by the commonly used anesthetics. (For more details about the anatomy and physiology of the middle ear and the acoustic middle ear reflex, refer to books on the physiology of the ear, for instance, (*25, 26*).)

The Cochlea

The cochlea is shaped like a snail shell and has three fluid-filled compartments (scalae), which are separated by the cochlear partition (or basilar membrane) and the Reissner's membrane (**Fig. 5.14c**). The cochlea separates sounds according to their spectra, and it transforms each sound into a neural code in the individual fibers of the auditory portion of CN VIII. Another important function of the cochlea is that it compresses the amplitude range of sounds.

Frequency Analysis in the Cochlea. The special micromechanical properties of the basilar membrane are the basis for the frequency analysis that takes place in the cochlea. The basilar membrane is set into vibration by the fluid in the cochlea, which in turn is set into motion by the in-and-out motion of the stapes footplate. The particular properties of the basilar membrane and its surrounding fluid create a motion of the basilar membrane like that of a traveling wave. This traveling wave starts at the base of the cochlea and progresses relatively slowly toward the apex of the cochlea, and at a certain point along the basilar membrane, its amplitude decreases abruptly. The distance that this wave travels before its amplitude decreases is a direct function of the frequency of the sound. A low-frequency sound travels a long distance before being extinguished, while a high-frequency sound gives rise to a wave that only travels a short distance before its amplitude decreases abruptly. Thus, a frequency scale can be topographically mapped along the basilar membrane, with low frequencies at the apex and high frequencies at the base of the cochlea.

Each point on the basilar membrane may be regarded as being "tuned" to a specific frequency (**Fig. 5.15**). The region of the basilar membrane nearest the base is tuned to the highest frequencies, and the frequency to which the membrane is tuned decreases toward the top (apex) of the cochlea. The highest audible frequencies produce maximal vibration amplitude of the basilar membrane near the base of the cochlea.

The frequency tuning of the basilar membrane depends on the intensity of the sounds that reach the ear (*27, 28*). The basilar membrane is more frequency-selective for low intensity sounds than high intensity sounds as revealed by measuring the vibration amplitude

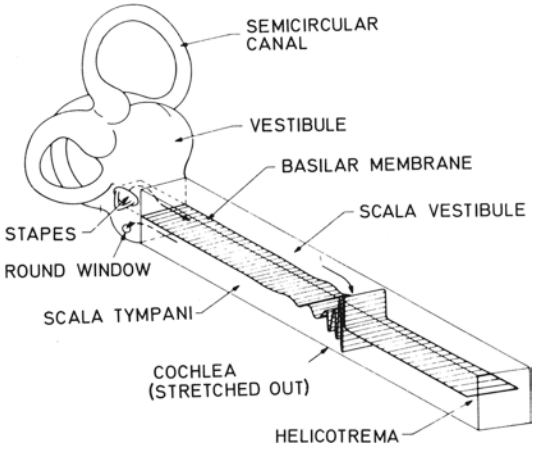


Figure 5.15: Schematic drawing of an ear with the cochlea uncoiled and shown as a straight tube to illustrate the traveling wave. (Reprinted from (*80*) with the permission of the American Institute of Physics).

of a single point of the basilar membrane when tones of different frequencies and different intensities are applied to the ear of an animal (guinea pig) (**Fig. 5.16**).

Sensory Transduction in the Cochlea. Sensory cells, known as hair cells (because of their hair-like stereocilia), are arranged in rows located along the basilar membrane. There are two types of hair cells – outer and inner – and they are arranged along the basilar membrane as one row of inner hair cells and three to five rows of outer hair cells (**Fig. 5.17**). The human cochlea has ~30,000 hair cells. The axons of the cochlear portion of CN VIII connect to the two types of hair cells in distinctly different ways: each inner hair cell connects with several axons, while several outer hair cells connect with one nerve fiber (*29*) (**Fig. 5.18**) (for details see (*25*)). About 95% of the nerve fibers of the cochlear nerve connect to inner hair cells, while about 5% of the nerve fibers connect to outer hair cells.

The motion of the basilar membrane deflects the hairs on the hair cells – deflection in one direction causes the intracellular potentials of the hair cells to become less negative (depolarization), while a deflection in the opposite direction causes hyperpolarization (more positive).

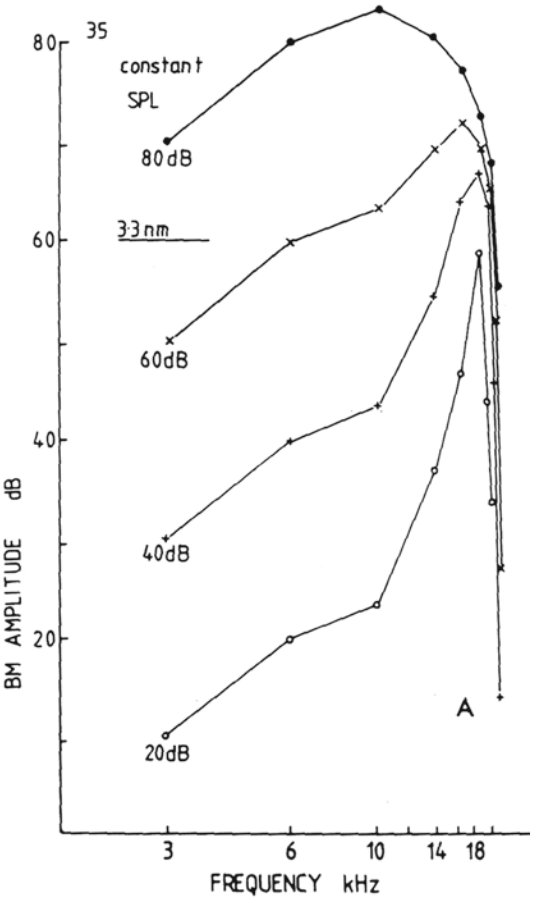


Figure 5.16: Frequency tuning of a point on the basilar membrane; the vibration amplitude of a point on the basilar membrane in a guinea pig is shown as a function of frequency. (Modified from (*81*), which was based on (*28*) with the permission of the American Institute of Physics).

The function of inner hair cells and that of outer hair cells is fundamentally different. Thus, while the inner hair cells function as transducers, which allow the motion of the basilar membrane to control the discharges of the individual auditory nerve fibers that connect to these hair cells, the outer hair cells function as "motors" that amplify the motion of the basilar membrane. Unlike the inner hair cells, outer hair

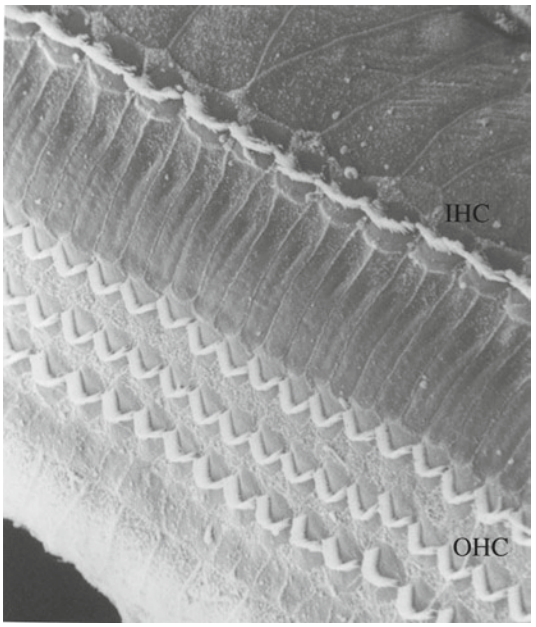


Figure 5.17: Scanning electron micrograph of hair cells along a small segment of the basilar membrane. *IH* inner hair cells, *OH* outer hair cells. (Courtesy of Dr. David Lim).

cells, as far as we know**,** do not participate in communicating information about the motion of the basilar membrane to higher auditory nervous centers. The active motion of the outer hair cells injects energy into the motion of the basilar membrane, and this injected energy compensates for the frictional losses in the basilar membrane that would have dampened the motion of the basilar membrane. Amplification by outer hair cells improves the sensitivity of the ear by about 50 dB, and it increases the frequency selectivity of the basilar membrane considerably, more so for weak sounds than for more intense sounds (see (*25*)).

Since low-frequency sounds give rise to the largest vibration amplitude of the apical portion of the basilar membrane, a low-frequency sound stimulates hair cells located in that region more than it stimulates hair cells in other regions. In a similar way, high-frequency sounds produce the largest vibration amplitude of more basal portions of the basilar membrane, thereby exciting the hair cells in that region to a greater extent than they do hair cells in other regions of the basilar membrane.

An otoacoustic emission is a sound generated by the cochlea as a result of the active function of the outer hair cells, and it can be measured in the ear canal. The otoacoustic emission is increasingly becoming a valuable clinical test, but it has not yet been found to be of specific use in intraoperative monitoring.

Electrical Potentials Generated in the Cochlea. Several different types of electrical potentials can be recorded from the cochlea or in its vicinity as a result of excitation of the hair cells. The cochlear microphonics (CM) potential follows the waveform of a sound closely (hence, its name), and the summating potential (SP) follows the envelope of a sound. Excitation of the auditory nerve is the source of the action potentials (AP), which can best be elicited in response to click sounds or the sharp onset of a tone burst. Although all of these potentials can be evoked by the same sounds, each type responds best to specific types of sounds. Thus, the AP is most prominent in response to transient sounds, while the CM is most prominent in response to a pure tone of low-to-medium high frequency. The SP is most prominent when elicited in response to high-frequency tone bursts. **Fig. 5.19** shows how the sharp onset of the tone burst elicits a prominent AP, and the CM from the sinusoidal wave of the tone is seen over the entire duration of the tone. The baseline shift seen during the tone burst is the SP (see (*25*)). Clinically, these potentials are recorded from the cochlear capsule or the ear canal near the tympanic membrane, and in the clinic they are known as electrocochleographic (ECoG) potentials (for details see (*30, 31*)). These evoked potentials have gained little use in intraoperative monitoring. Some investigators have suggested that recording ECoG potentials can monitor the function of the auditory nerve, but the most common source of intraoperative damage to the auditory nerve is found in its intracranial

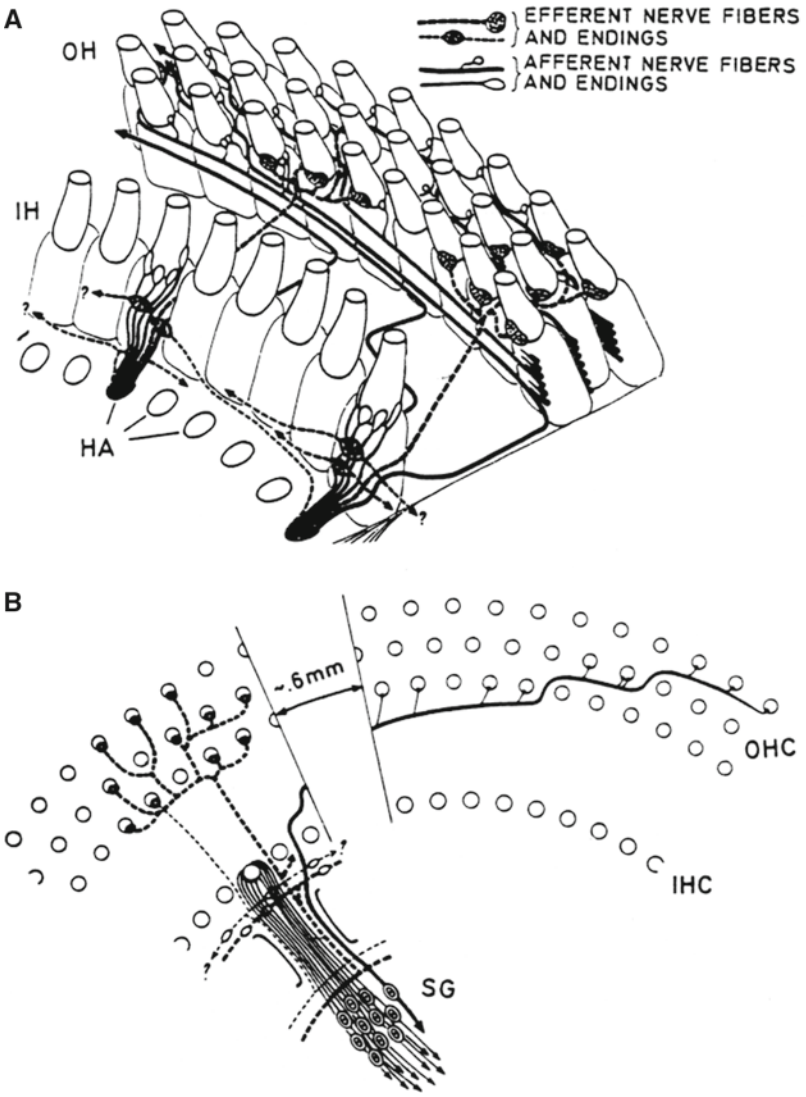


Figure 5.18: Schematic drawing of hair cells located along the basilar membrane with their connections to the ascending fibers of the auditory nerve (*solid lines*). Also shown are the efferent fibers (*dashed lines*). *OH* outer hair cells, *IH* inner hair cells, *HA* habenula perforate, *SG* spinal ganglion. (Reprinted from (*29*)).

course proximal to the generation of the ECoG (see Chap. 7).

Auditory Nervous System

The auditory nerve is longer in humans than in the small animals used for auditory research, which has had implications for the interpretation of human ABR (see page 79). The anatomy of the ascending auditory pathway is more complex than that of other sensory systems, such as the visual and somatosensory systems. There are two main, mostly parallel, ascending auditory pathways: the classical (or lemniscal pathways) and the nonclassical (or extralemniscal pathways). These two pathways are also known as the specific and the nonspecific or

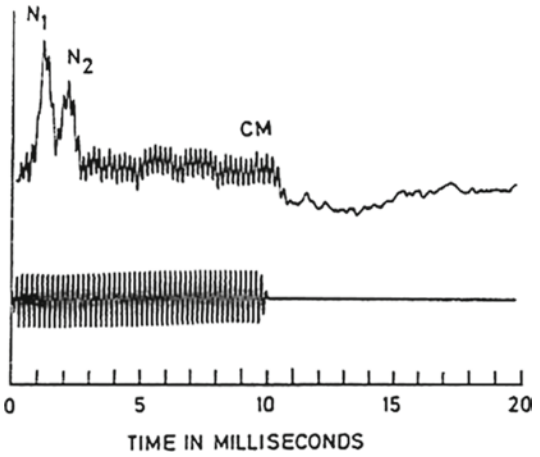


Figure 5.19: Different sound-elicited potentials that can be recorded from the round window of the cochlea. The recordings were obtained in a rat. The stimulus was a 5-kHz tone burst (10 ms). The cochlear microphonics appears as an oscillation with the frequency of the stimulus, the nerve action potentials appear as two upward peaks (N_1 and N_2), and the summating potential appears as the shift (*upward*) in the baseline recording that is seen during the time the stimulus was on. (From (*82*) with the permission from Elsevier).

polysensory pathways (*1, 25*). Much less is known about the anatomy and physiology of the nonclassical pathways than the classical pathways. In parallel to the ascending pathways are descending pathways.

Although the descending pathways are more abundant than the ascending pathways, much less is known about the descending pathways than the ascending pathways (*1, 25, 32*). The descending pathways may be regarded as reciprocal to the ascending pathways, and these two parts of the auditory pathways form loops in which information can circulate.

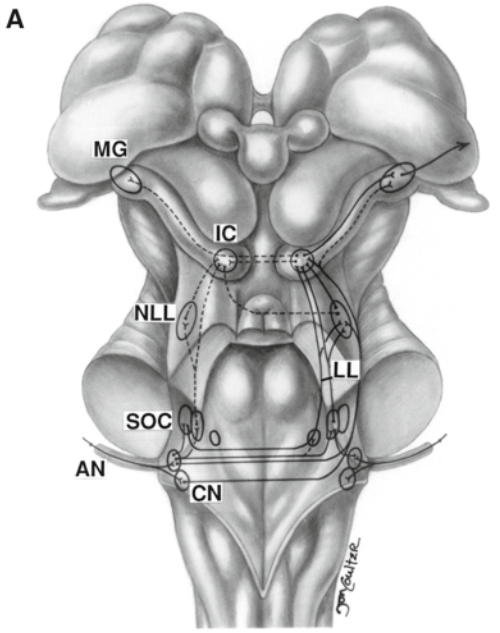
Anatomy

CLASSICAL (LEMNISCAL) PATHWAYS. The most important nuclei of the ascending auditory pathway and their connections are shown in **Fig. 5.20**. The first relay nucleus of the ascending auditory pathway is the cochlear nucleus. All fibers of the auditory nerve (AN) are interrupted in this nucleus, which has three main divisions: the dorsal cochlear nucleus (DCN), the posterior ventral cochlear nucleus (PVCN), and the anterior ventral cochlear nucleus (AVCN). Each fiber of the cochlear nerve bifurcates to terminate in the PVCN and the AVCN. The fibers that reach the PVCN send collateral fibers to the DCN. In that way, all auditory nerve fibers reach cells in all three divisions of cochlear nucleus.

Recordings from the surface of the cochlear nucleus are used for monitoring the function of the auditory nerve in operations where the nerve is at risk of being injured. Implantation of stimulating electrodes on the surface of the cochlear nucleus is used as auditory prostheses in individuals who have congenital malformations that make the auditory nerve nonfunctional and in individuals with damage to the auditory nerve bilaterally from, for example, the removal of bilateral vestibular schwannoma.

The neurons of cochlear nucleus connect to the central nucleus (ICC) of the IC via several fiber tracts that cross the midline: the dorsal acoustic stria (DAS), the ventral acoustic stria (VAS), and the trapezoidal body (TB). There are also connections from cochlear nucleus to the IC that do not cross the midline. Some of the crossed fibers that originate in the cochlear nucleus reach the ICC without any synaptic interruption while other connections from the cochlear nucleus are interrupted in the nuclei of the superior olivary complex (SOC) (medial superior olivary nucleus, or MSO, lateral olivary nucleus, or LSO) or the TB. The fibers from these nuclei as well as those from cochlear nucleus proceed to the ICC as the fiber tract of the lateral lemniscus (LL). Some of the fibers of the LL reach the dorsal or ventral nuclei of the LL. All fibers that reach the ICC are interrupted in the ICC. The output fibers of the ICC form the brachia of the ICC and connect to the thalamic auditory relay nucleus, namely, the medial geniculate body (MGB). The MGB furnishes auditory information to the primary auditory cortex (A1) (**Fig. 5.20A**). (For details, see (*1, 25, 32*).)

The lengths of the different tracts of the ascending auditory pathways in humans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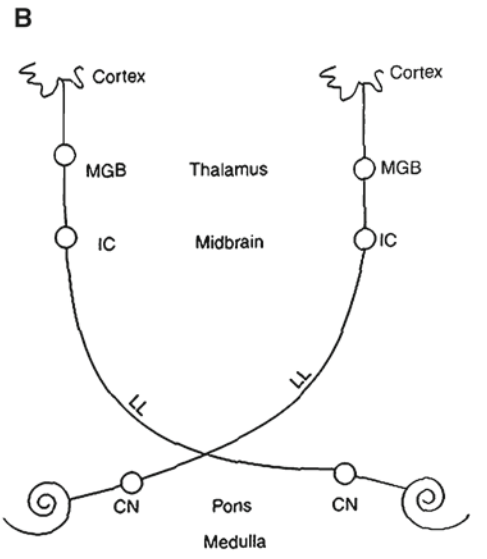
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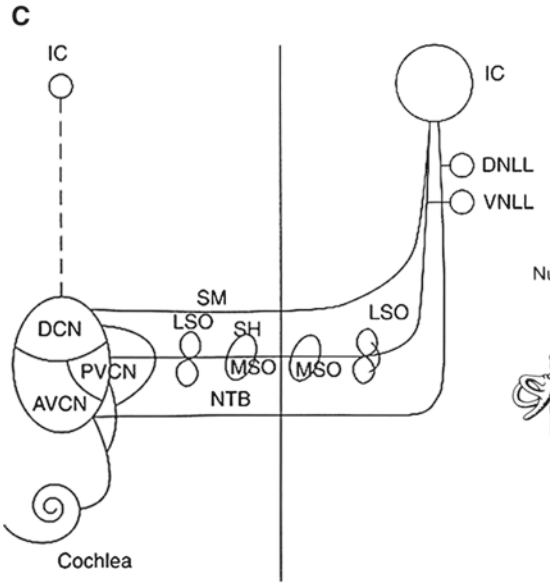
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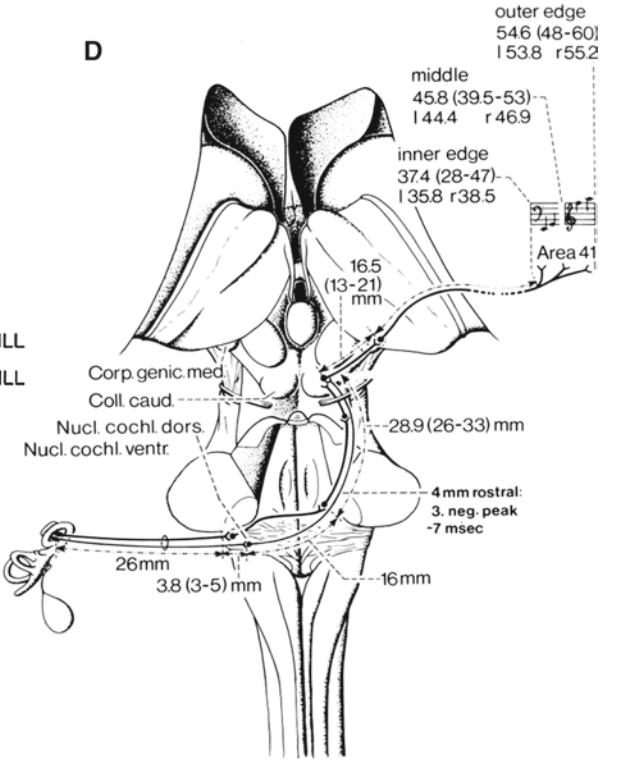
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-7 msec
26mm
3.8 (3-5) mm
16mm

(**Fig. 5.20D**) are longer than those in the animals that are commonly used for the studies of the auditory system. This means that the travel time throughout the ascending auditory pathways is longer in humans than in animals and results in longer latencies of the different components of the ABR in humans compared with that in animals.

Auditory Cortex. The auditory cortex in humans is located deep in Hechel's gyrus in the lateral fissure of the temporal lobe (Brodmann's area 41). The different areas of the auditory cortex are labeled primary cortex (A1), secondary cortex (A2), anterior auditory field (AAF), and posterior auditory field (PAF). The A1 area receives input from the ventral part of the auditory nucleus (MGB) of the thalamus and sends a large fiber tract back to the MGB (*33*). These descending connections from the cerebral cortex to the MGB are important in connection with recent developments where the auditory cortex is stimulated electrically to treat hyperactive auditory disorders, such as tinnitus and hyperacusis (*34*). The electrical stimulation that is applied to the cerebral cortex may have its effect by activating cells in the MGB via these descending pathways.

The connections from the MGB to the cortex and back again form a loop, the cortico-thalamic loop that may play an important role in creation of some forms of tinnitus (*35*).

Nonclassical (Extralemniscal) Pathways. Nonclassical pathways project to the secondary and association cortices, thus bypassing the primary auditory cortex. These pathways use the dorsal thalamus whereas the classical pathways use the ventral thalamic nuclei.

Many of the neurons in the nonclassical pathways respond to other sensory modalities, and other sensory modalities can modulate the response to sound. Intraoperative neurophysiological monitoring does not involve nonclassical pathways as far as is known (for details about the nonclassical pathways, (*1, 25, 36*)).

Physiology. The physiology of the auditory system is covered only briefly here; more detailed descriptions can be found in Møller 2006 (*25*) and Møller 2003 (*1*).

Frequency Tuning. Frequency or spectral selectivity is a prominent feature of the response from single auditory nerve fibers. Since each nerve fiber is tuned to a specific frequency, nerve cells in the nuclei of the ascending auditory pathway are tuned to a specific frequency as well. Complex processing of information takes place in the various nuclei of the ascending auditory pathway; the nature of the processing is not completely understood, but for the most part, processing seems to enhance changes in amplitude and frequency of sounds.

Figure 5.20: Anatomy of the ascending auditory pathway. (**A**) Illustration of how the main nuclei and fiber tracts are located in the brain. *AN* auditory nerve, *CN* cochlear nucleus, *SOC* superior olivary complex, *LL* lateral lemniscus, *IC* inferior colliculus, *MG* medial geniculate body. (From (*75*)). (**B**) Schematic drawing of the ascending auditory pathway. The crossed pathways are shown. *VCN* ventral cochlear nucleus, *DCN* dorsal cochlear nucleus, *IC* inferior colliculus, *MGB* medial geniculate body. (**C**) Schematic drawing of the pathways from the cochlear nucleus to the inferior colliculus. *DCN* Dorsal cochlear nucleus, *PVCN* Posterior ventral cochlear nucleus, *AVCN* Anterior ventral cochlear nucleus, *LSO* lateral superior olive, *NTB* nucleus of the trapezoidal body (NTB), *MSO* medial superior olive, *SH* stria of Held (intermediate stria), *SM* stria of Monakow (dorsal stria), *LL* lateral lemniscus, *DNLL* dorsal nucleus of the lateral lemniscus, *VNLL* ventral nucleus of the lateral lemniscus, *IC* inferior colliculus (Reprinted from (*25*) with permission from Elsevier). (**D**) Schematic drawing of the ascending auditory pathway showing the length of the auditory nerve and the various fiber tracts. Results from 30 specimens (Modified from (*55*) with the permission from Elsevier).

The temporal pattern of a sound is coded in the timing of the discharges of single auditory nerve fibers. Temporal coding of sounds provides information about the spectrum of a sound, as does the place code that is represented by the tuning of various neural elements. Both place and temporal coding of auditory information are important for the discrimination of complex sounds, such as speech and music, but either one alone can provide speech discrimination. It is evidenced from the efficacy of cochlear implants that place coding alone is sufficient for speech discrimination (*37, 38*), but temporal coding alone has been shown to suffice for speech discrimination also (*37*). Under normal circumstances, both temporal and place coding is used, and the fact that either one is sufficient for speech discrimination is an indication of redundancy in the auditory system.

Tonotopic Organization. Nerve fibers of the auditory nerve as well as those of nerve cells of the nuclei of the ascending auditory pathway are arranged anatomically in accordance with the frequency at which their threshold is lowest (tonotopic organization). Thus, all neural structures of the classical ascending auditory pathway can be mapped to the frequency to which the neurons of these neural structures respond best (for details see (*25*)).

Descending Auditory Nervous System

Descending auditory pathways are abundant, and while the anatomy is relatively well understood, the function of these systems is not understood to any great detail (*32, 39*). As mentioned above, the descending pathways may be regarded as reciprocal to the ascending pathways, and together these two pathways form loops where information may circulate.

Anatomy. Efferent pathways extend from the auditory cerebral cortex to the hair cells in the cochlea (*32*). These pathways have been regarded as several separate systems, but it may be more appropriate to regard the descending systems as reciprocal to the ascending pathways. The best-known parts of these descending pathways are the peripheral parts. Thus, the auditory nerve contains efferent nerve fibers that originate in the SOC and terminate mainly at the outer hair cells. These efferent fibers, also known as the olivocochlear bundle, consist of both crossed and uncrossed fibers. The efferent nerve fibers travel in the vestibular portion of the eighth cranial nerve (CN VIII) from the brainstem to Ort's anastomosis located deep in the internal auditory meatus, where they shift over to the cochlear portion of the CN VIII (for more details see (*1, 25*)).

Physiology. The function of the descending pathways is poorly understood. The abundant descending system from the primary auditory cortex to the thalamus may function to change the way the thalamus processes sounds. Electrical stimulation of the primary auditory cortex may therefore affect the thalamus, which is important to consider when such stimulation is used to control tinnitus (*40*). The olivocochlear bundles seem to influence outer hair cells, which are involved in "otoacoustic" emission. Therefore, measurements of otoacoustic emission can be used to investigate the function of this part of the efferent system.

Electrical Potentials from the Auditory Nervous System

For intraoperative monitoring, it is most important to know how the various nuclei of the ascending auditory pathways are connected, and how these nuclei, together with the fiber tracts that connect them, produce electrical activity when the ear is stimulated with transient sounds.

Factors that are important for interpreting the responses used in intraoperative monitoring include the design of the auditory nervous system in parallel pathways and the architecture of various auditory nuclei that contribute to far-field potentials, which are recorded from electrodes placed on the scalp.

The function of the descending system, as well as matters regarding coding of complex sounds in the nuclei of the ascending auditory nervous system, are described in textbooks on

hearing (*25*) but are probably of relatively little importance to the understanding of how neural activity in these structures contributes to the electrical activity that is recorded from electrodes placed on the scalp (ABR). The sounds commonly used to elicit such responses are simple sounds, such as tone bursts and click sounds, and the complex processing that occurs in the auditory system of sounds, such as speech and music, probably does not affect the response to such simple sounds to any noticeable degree.

Auditory Brainstem Responses. ABR (also known as brainstem auditory evoked potentials, BAEP) are generated by the activity in structures of the ascending auditory pathways that occurs during the first 8–10 ms after a transient sound, such as a click sound, has been applied to the ear.

Traditionally, the ABR are recorded between electrodes placed at the vertex. When the ABR is recorded in the traditional way with one electrode placed on the vertex and another one placed on the earlobe or mastoid and each connected to the input of a differential amplifier, both of these electrodes are active (record sound-evoked potentials). The potentials that are recorded by each one of these two electrodes contribute to the recorded ABR. The standard way of displaying evoked potentials is to show negativity at the active electrode as an upward deflection. Since both electrodes are active, the ABR can be displayed in two different ways. A negative potential at the vertex electrode produces an upward deflection (as shown in the bottom tracing in **Fig. 5.21**) if the vertex electrode is connected to the inverting input (G_2) of the amplifier (see Chap. 18). If the vertex electrode is connected to the noninverting input (G_1), then a positive potential at the electrode placed at the vertex results in an upward deflection (**Fig. 5.21**, top tracing).

Obtained that way, in a person with normal hearing, the waveform is characterized by five or six (vertex-positive) peaks. These peaks are traditionally numbered consecutively using Roman numerals from I to VI (*41*) (**Fig. 5.21**).

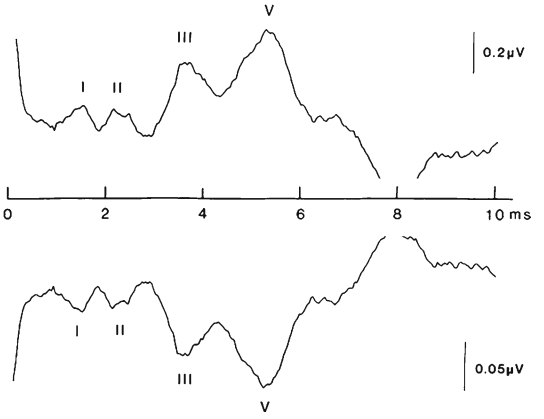

Figure 5.21: Typical recording of ABR obtained in a person with normal hearing. The recording is the summation of 4,096 responses to rarefaction clicks recorded differentially between the forehead and the ipsilateral mastoid with a band-pass of 10–3,000 Hz. The top recording is shown with vertex-positivity as an upward deflection, and the bottom curve is the same recording, but with vertex-positivity shown as a downward deflection. Reprinted from (*75*).

The earlobe electrode contributes mainly to the first two (or three) peaks of the ABR while the vertex electrode makes the greatest contribution to peak V.

The waveform of the ABR depends on three key factors: the electrode placement used for recording ABR (the much used vertex-earlobe, or mastoid placement is not ideal), the stimuli used to elicit the responses, and how the recorded potentials are processed (filtered). (Discussed in Chaps. 7 and 18).

There is a certain distinct individual variation in the wave shape of the ABR – even in individuals with normal hearing. Pathologies that affect the auditory system (*42*) may result in abnormalities in the ABR that are specific for different pathologies. Hearing loss of various kinds may affect ABR in a complex way.

The fact that only the vertex-positive peaks in ABR are labeled (with Roman numerals) could imply that only vertex-positive peaks are important. This choice of labeling was, however,

not based on any experimental evidence showing that the vertex-positive peaks of ABR are more important in diagnostics than the negative valleys, nor was this choice in labeling related to the neural generators of these peaks. This arbitrary choice of labeling only the vertex-positive peaks of ABR is unfortunate because it focuses only on vertex-positive peaks while the vertex negative peaks may be just as important for detecting functional abnormalities of the auditory system both in the clinic and in the operating room. (Studies of the neural generators of ABR have supported the assumption that vertex-negative peaks (or valleys) are indeed important (*42*)).

Only a few studies have made use of the traditional way of labeling the different components of the ABR using "N" for negative peaks, followed by the normal value of the latency of the peak; conversely, positive peaks are labeled with a "P" followed by a number that is the peak's normal latency.

Since the convention of labeling the vertex-positive peaks of the ABR with Roman numerals has been in use for a long time, this book uses this method for labeling ABR peaks.

Neural Generators of the ABR. Because of the (mainly) sequential activation of neural structures of the auditory pathways, ABR consist of a series of components that are separated in time. The peaks and valleys that form the ABR generally appear with different latencies in accordance with the anatomical location of their respective neural generators. **Fig. 5.22** shows a schematic and simplified picture of the present concept of the neural generators of the human ABR. This depiction is a simplified description of the relationship between the different components of the ABR and the anatomy of the ascending auditory pathway. It can only serve as a first approximation because of the complexity of the ascending auditory pathway with its extensive parallel systems of neural pathways. Neural activation of some nuclei may, therefore occur simultaneously, and the electrical activity of different nuclei and fiber tracts that is elicited by a transient sound may, therefore overlap in time.

Comparisons between ABR made directly from the capsule of the cochlea in humans (ECoG) have shown evidence that peak I in the ABR is generated by the auditory nerve (distal portion). The finding that the negative peak of the CAP recorded from the exposed intracranial portion of the auditory nerve in humans has a latency close to that of peak II in the ABR (*43–45*) indicates that wave II is generated by the proximal portion of the auditory nerve, and this finding has been supported by later studies (*46–48*). This means that the auditory nerve in humans is the generator of both peaks I and II of the ABR and that no other neural structure contributes to either of these two peaks. These are the only components of the ABR that are generated from a single anatomical structure.

Peak II may be generated because neural activity propagates in the auditory nerve, where the electrical conductivity of the surrounding medium changes (*14, 49*) or when the propagation of neural activity stops (as it does when it reaches the cochlear nucleus). The importance of the electrical conductivity of the medium that surrounds the auditory nerve intracranially has been shown in studies of patients undergoing operations in the cerebella pontine angle (CPA) (*50*).

> The auditory nerve in animals commonly used in experimental research only generates one peak in the ABR (peak I). Peak II in such animals is generated by the cochlear nucleus (see, e.g. (51–54)). This difference between humans and animals commonly used in auditory research is due to the fact that the auditory nerve is much longer in humans (~26 mm (55, 56); Fig. 5.20D) than it is in many research animals, 8 mm in the cat (57), and similarly in monkeys (54).

The average diameter of axons in the auditory nerve in children is 2.5 µm with a narrow distribution in young individuals. With increasing age, the diameter increases and the variation becomes larger – 0.5–7 µm by the age of 40–50 years ((*58*) **Fig. 5.23**). Because the diameters of the fibers of the auditory nerve are relatively small, the conduction velocity in the

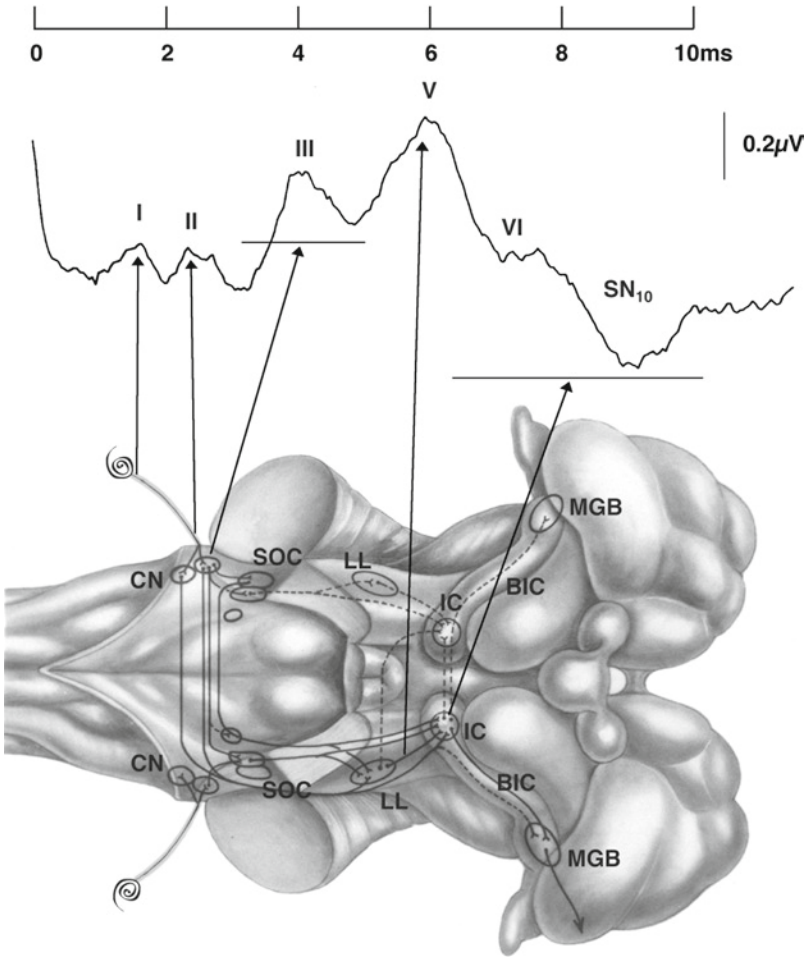

Figure 5.22: Schematic illustration of the neural generators of the ABR recorded in the traditional way and displayed with vertex positive potentials as an upward deflection. Reprinted from (*25*), by permission from Elsevier.

auditory nerve is only about 20 m/s (*59*). The time it takes for neural activity in the human auditory nerve to travel a distance of 2.6 cm from the ear to the brainstem is, therefore a little more than 1 ms. The fact that the amplitude of ABR decreases with age in humans may be explained by the greater variations in the diameter of the axons and thus, larger variations in conduction velocity and consequently, larger temporal dispersion of the nerve impulses that arrive at the cochlear nucleus.

The generators of the vertex positive peaks of the ABR with latencies that are longer than that of peak II are more complex, and these peaks most likely have multiple sources. The high degree of parallel processing in the auditory nervous system may result in different structures being activated simultaneously, and this may cause an individual component of the ABR, for example, peak IV, to receive contributions from fundamentally different structures of the ascending auditory pathway.

Intracranial recordings in patients undergoing neurosurgical operations have shown evidence that the earliest component in the ABR that originates in brainstem nuclei is peak III (*25*).

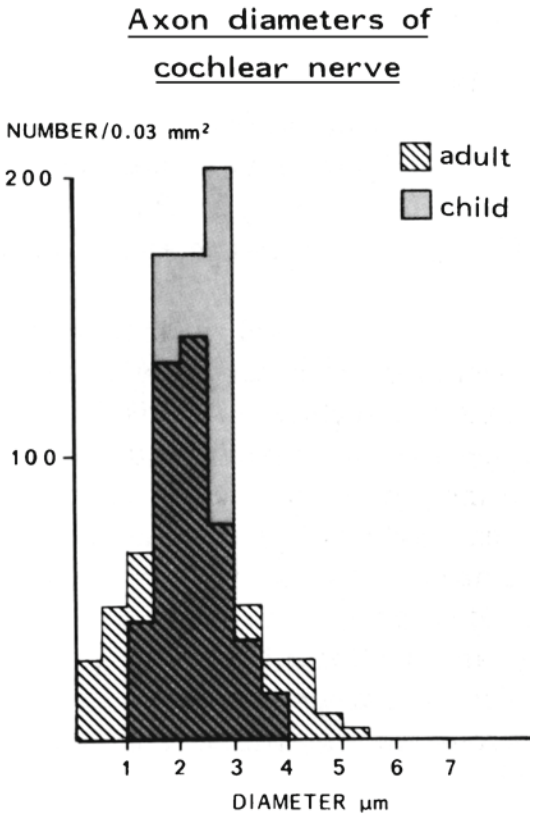

Figure 5.23: Distribution of the diameters of the axons of auditory nerve fibers for a child and an adult. (Reprinted from (*58*) by permission from Elsevier).

While the cochlear nucleus is most likely the main generator of that peak (*60*), there is evidence that the vertex-negative component between peaks III and IV also receive contributions from the cochlear nucleus (*42, 60*). Peak IV is not always visible, and the vertex negative component between peak III and peal IV is not always a prominent valley. The contralateral cochlear nucleus may contribute to the ABR (*42, 61*) through connections between the cochlear nuclei on the two sides.

Less is known about the source of peak IV than the sources of peaks I–III and peak V of the ABR. Peaks I, II, and III receive input from only the ipsilateral side (see **Fig. 5.23**) (*42*), while peak IV is likely to be the earliest positive peak of the ABR that receives contributions from contralateral structures of the ascending auditory pathway (see also (*25*)). Thus, peak IV may thus receive contributions from both sides of the brainstem. There is evidence that the anatomical location of the source of peak IV is deep in the brainstem (near the midline), maybe in the pons (the SOC) (*42, 62*). Most likely, other structures contribute to peak IV, such as the cochlear nucleus and the distal parts of the lateral lemniscus.

Comparisons between the latencies of the different components of responses recorded intracranially and the vertex-positive and vertex-negative peaks of the ABR (*42, 63*) also emphasize that it is not only the vertex-positive peaks of the ABR that have anatomically distinct neural generators, but also the vertex-negative valleys in the ABR recorded in the conventional way. In fact, the vertex-negative components may be just as important as indicators of pathologies.

Some studies (*42*) show that the response recorded from the dorsal acoustic stria, on the floor of the fourth ventricle, generates a peak that is slightly shorter than that of peak V. This indicates that if the lateral lemniscus is interrupted along its more rostral course (by surgically induced injury or by disease processes), the lateral lemniscus, and maybe even the DAS itself, may generate a peak in the ABR that is indistinguishable from the normal peak V of the ABR (except for a slightly shorter latency than the normal peak V).

Peak V of the ABR in humans has a complex origin. There is evidence that the sharp tip of peak V is generated by the lateral lemniscus, where it terminates in the inferior colliculus (*64*). There is also evidence from animal experiments that the inferior colliculus itself generates only a very small far-field response, even though a large evoked potential can be recorded from its surface (*54*). The reason for this phenomenon may be found in the anatomical organization of the inferior colliculus, where its dendrites may point in many directions so that the nucleus generates a “closed field” (*21*). The slow negative potential in the ABR in humans that occurs with a latency of ~10 ms (SN_{10}) (*65*)

most likely represents postsynaptic potentials generated by the dendrites of the cells of the inferior colliculus. The amplitude of this component varies widely from individual-to-individual, but the filters used in the recordings of ABR often attenuate it.

Studies in patients undergoing neurosurgical operations that included comparisons among the ABR and intracranial potentials recorded from different locations along the lateral side of the brainstem have confirmed that peaks I–III receive contributions mainly from ipsilateral structures of the ascending auditory pathway, while peak V receives its major contributions from contralateral structures (*42*).

Little is known about the generators of peaks VI and VII, but these components of the ABR may be generated by neural firing in cells of the inferior colliculus (somaspikes) (*48, 64, 66*).

THE VISUAL SYSTEM

Visual evoked potentials (VEP) have been used in connection with intraoperative monitoring during operations in which the optic nerve or optic tract is involved, such as those to remove pituitary tumors, tumors of the cavernous sinus, and aneurysms in this area (*67*). However, intraoperative monitoring of the visual system plays a much smaller role than monitoring of the auditory and somatosensory systems because of technical difficulties in presenting adequate stimuli to the eye of anesthetized individuals (*68, 69*). The adequate stimulus for the visual system is a pattern that changes in contrast (for details see (*1*)), such as a reversing checkerboard pattern. The use of such a stimulus requires that the pattern be focused on the retina, which is not possible in an anesthetized patient. Therefore, flash stimulation is the only form of stimulation that can be used in an anesthetized patient, and that is not an appropriate stimulus for evoking VEP for the purpose of detecting changes in the function of the visual nervous system (see Chap. 8).

The Eye

Before it reaches the retina, light passes through the conductive apparatus of the eye consisting of the cornea, the lens, and the pupil. The optic apparatus of the eye projects a sharp image on the retina, where the light-sensitive receptors are located together with a complex neural network that enhances the contrast between areas with different degrees of illumination. Much of the neural processing of visual stimuli takes place in the neural network in the retina of the eye itself. This processing is also the basis for the representation of differences in illumination over the visual field, and there are optic nerve fibers that have small excitatory fields that are surrounded by inhibitory areas, while others have inhibitory center areas that are surrounded by excitatory areas. The position of the eye is controlled by six extraocular eye muscles that are innervated by three cranial nerves (CN III, CN IV, and CN VI) (see Chap. 11 and Appendix B).

Receptors. There are two kinds of sensory cells, cones and rods, in the human retina. The outer segments of cones and rods contain light sensitive substances (photo pigment) (*1*). The three different kinds of photo pigment in the cones, one for each of the three principal colors, blue, green, and red, provide the eye's color sensitivity (photopic vision). Rods are more sensitive than cones and provide vision in low light (scotopic vision).

Adaptation of the photoreceptors plays an important role for the processing of information in the visual system, as it does in other sensory organs. Adaptation of the eye is a form of automatic gain control that adapts the sensitivity of the eye to the ambient illumination. The adaptation of photoreceptors provides most of the eye's automatic gain control. The pupil also provides some automatic gain control, the range of which varies among species.

Adaptation of the eye is often referred to as dark adaptation, which refers to the recovery of sensitivity that occurs after the exposure to bright light. The first part of the dark-adaptation curve is steeper than the following segment

and represents the dark-adaptation of cones; the second segment is related to the function of rods. Light adaptation (the opposite of dark adaptation) is caused by the exposure to bright light causing reduced sensitivity of the eye.

Ascending Visual Pathways

Two different afferent pathways have been identified, the classical and the nonclassical pathways, which are similar to that of the auditory and the somatic sensory systems (*1*). In this book, only the classical pathway, known as the retino-geniculo-cortical pathway, is described. This pathway involves the lateral geniculate nucleus (LGN) of the thalamus and the primary visual cortex (striate cortex, V1) (**Fig. 5.24**).

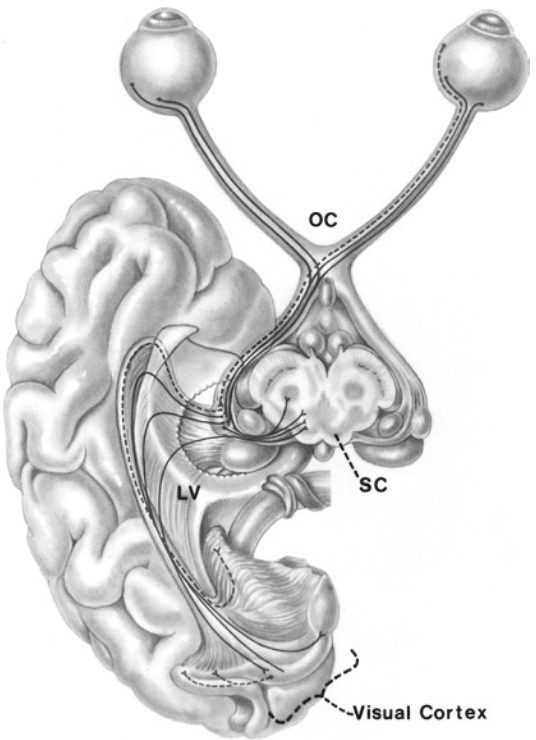

Figure 5.24: Schematic drawing of the major visual pathways. OC, optic chiasm; SC, superior colliculus; LV, lateral ventricle. (Reprinted from (*75*)).

After processing in the neural network in the retina, all visual information travels in the optic nerve (CN II) that enters the optic chiasm, where the fibers of the optic nerve reorganize. From the optic chiasm, the information travels in the optic tracts to the LGN in the thalamus, from which there are connections to the visual cortex (V1), which is located in the posterior portion of the brain.

The organization of the part of the optic nerve that belongs to the classical visual pathways is best illustrated by the effect on vision from visual defects that are caused by lesions of the optic nerve and the optic tract at different locations. If the optic nerve from one eye is severed, no visual information from that eye will reach the LGN. If the optic tract is severed on one side between the optic chiasm and the LGN in animals with forward pointed eyes, the result is homonymous hemianopsia. Visual information from the nasal field on the same side and the temporal field of the opposite eye does not reach the LGN, but visual information from the temporal field on the same side and the nasal field of the opposite eye is unaffected. Midline sectioning of the optic chiasm causes loss of vision in the temporal field in both eyes (the crossed pathways) causing "tunnel vision."

Lesions at more central locations of the visual pathways, such as the LGN or the visual cortex, can cause complex visual defects such as scotoma that manifest by blind (black) spots in the visual fields.

Visual Evoked Potentials

VEP show large individual variations and depend on the stimuli used to elicit the responses and the placement of recording electrodes. A positive peak with a latency of 75–100 ms (P100) usually dominates the VEP recorded from electrodes placed on the scalp (*70*), and sometimes a small peak with a latency of 45–50 ms and a negative peak with a latency of ~70 ms (N70) can be recognized (**Fig. 5.25**).

Neural Generators of the VEP. Years of intensive research on coding in the visual system have resulted in the accumulation of wealth of

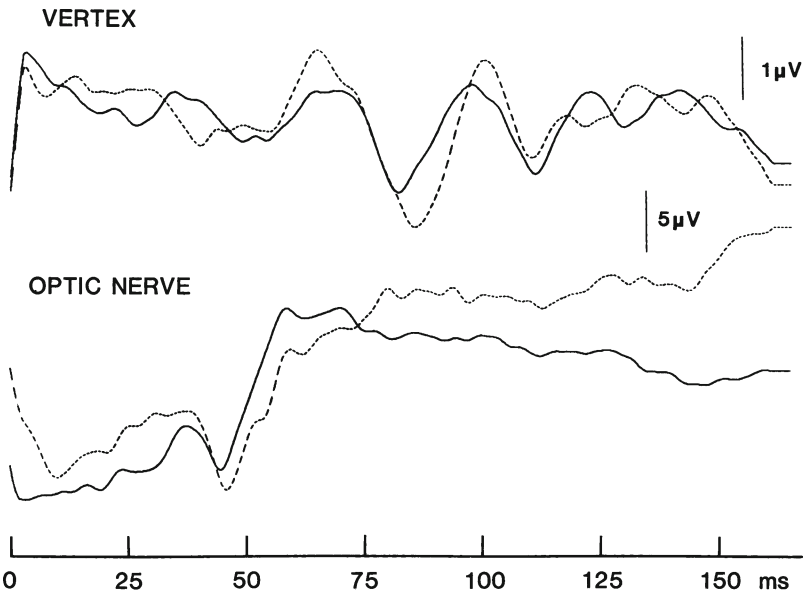

Figure 5.25: Recordings from an electrode placed directly on the optic nerve and from an electrode placed on the scalp at a location approximately overlying the visual cortex in response to stimulation with flashes of light delivered by light-emitting diodes (LED) attached to a contact lens (Reprinted from (*72*) with the permission from Futura Publishing Co.).

knowledge about the responses from single nerve cells in the visual cortex and the LGN as well as from the neural network in the retina. Unfortunately, the information about the generators of the evoked response from the optic nerve and LGN is sparse, and the relationship between the different components of the VEP and the potentials that can be recorded directly from the different parts of the visual system (near-field potentials) is poorly understood.

It is assumed that the N70 and P100 peaks are somehow generated in the visual cortex (striate cortex, Broadman's area 17, see Appendix A) (*1, 71*), but little is known about how these potentials relate to the normal functioning of the visual system. The exact anatomical location of the generators of early components of the VEP is poorly understood. Intraoperative recordings from the optic nerve show an early positive deflection with a latency of 75 ms followed by a broad negative potential with a latency of ~55 ms, in response to short light flashes (*72*) (**Fig. 5.25**). These potentials do not seem to have any corresponding components in the scalp recorded far-field potentials.

The reason that the optic nerve produces such a small far-field potential may be that the medium surrounding the optic nerve and the optic tract is relatively homogeneous with regard to electrical conductivity. The abrupt change in conductivity of the medium around the nerve, which is regarded to be a prerequisite for a nerve to generate stationary far-field peaks (*14, 49, 73*), does not seem to exist for the optic nerve.

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