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(Eds.)

Evoked Spinal Cord Potentials

An Illustrated Guide to Physiology, Pharmacology, and Recording Techniques

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With 130 Figures

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Dedicated to Our Parents
and Teachers

Preface

The technique of using evoked spinal cord potentials (SCPs) has become an important clinical tool for monitoring spinal cord surgery and diagnosing spinal cord diseases. The technique is a result both of the technical development of recording evoked SCPs from the epidural space without perforation of the dura mater and of the development of medical electronics. Its use as a monitoring tool is based on continuous epidural analgesia with an epidural catheter. Since the first development of epidural recording of evoked SCPs in 1971, the technique has been applied in various institutes, particularly for monitoring during spine or spinal cord surgery and cardiovascular surgery, and recently for diagnosis of spinal cord diseases.

Although the results of studies on monitoring during surgery have proved useful, more detailed neurophysiological mechanisms in the origin of each component of evoked SCPs remain to be explained in the area of diagnosis of spinal or central nervous system diseases. Further neurophysiological and neuropharmacological studies of the human spinal cord may contribute to the clinical application of recording evoked SCPs for diagnosis of spinal cord diseases.

The aim of this book is to furnish a survey of the neurophysiological and neuropharmacological bases of evoked SCPs with reference to animal studies and the techniques of recording the potentials mainly from the spinal epidural space. The authors have been involved in the field from the beginning of the 1970s. Many illustrations are presented for better understanding the neurophysiological and neuropharmacological backgrounds of monitoring spinal cord functions. Case studies also are presented and discussed to provide more insight into the monitoring and diagnosis of spinal cord dysfunctions and spinal cord diseases.

This book is thus appropriate even for students or those new to the fields of clinical neurophysiology, neurosurgery, neurology, orthopedics, and neuroanesthesia who are interested in monitoring spinal cord function during surgery or diagnosing spinal cord diseases. A diverse range of terminology has been used in the literature to date, sometimes leading to misinterpretation of each component in the field of evoked SCPs. To avoid such misinterpretation and to provide readers with an accurate understanding, terminology referring to basic animal studies is used, and lucid explanations are included in this volume.

K. Shimoji and W.D. Willis, Jr.
Editors

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Chapter 1
Neuroanatomical Considerations

William D. Willis, Jr.

1.1 Gross Anatomy of the Human Spinal Cord

The central nervous system includes the spinal cord and the brain. The spinal cord is an elongated, roughly cylindrical structure that is found within the vertebral canal (Fig. 1.1A,C). It joins the medulla oblongata at the level of the foramen magnum of the skull (Fig. 1.1A), and in adults it terminates caudally at the interspace between the first and second lumbar vertebrae (Fig. 1.1C). The spinal cord of the adult human is about 42–45 cm long and 1 cm in diameter at its widest extent, and it weighs about 35 g (Nolte, 2002).

The spinal cord develops in relation to the body segments (somites) that it innervates. This gives the spinal cord a segmented structure. The segments are best recognized by reference to pairs of dorsal and ventral roots[1] that enter or emerge from the spinal cord at each segmental level (Figs. 1.1C, 1.2, 1.3). Each dorsal and ventral root breaks up into a series of rootlets that extend the length of the corresponding spinal cord segment; the number of rootlets varies with the segment (see Fig. 1.2). Therefore, a segment of spinal cord can be demarcated by locating the entry or exit points of the most rostral and most caudal of the rootlets of the appropriate root.

The dorsal roots contain axons from sensory neurons whose cell bodies are in the dorsal root ganglia (Figs. 1.2 and 1.3), which form swellings located at the intervertebral foramina. Sensory axons passing to the periphery from the dorsal root ganglion cells intermingle with ventral root axons in the spinal nerves, which are just distal to the dorsal root ganglia (Fig. 1.3A). The ventral roots are composed of axons from alpha and gamma motor neurons and, at the appropriate segmental levels (T1–L2; S1–S3), of autonomic preganglionic neurons. Sympathetic white and gray communicating rami contain axons that connect the spinal nerves with sympathetic paravertebral ganglia (Fig. 1.3A). Sacral parasympathetic preganglionic axons distribute through the pelvic nerves and terminate on parasympathetic postganglionic neurons in ganglia close to or in the walls of the pelvic viscera.

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[1]Dorsal and ventral are terms that apply best to quadrupeds. Posterior and anterior are more appropriate for humans. However, common usage equates dorsal with posterior and ventral with anterior with respect to human spinal cord structures.

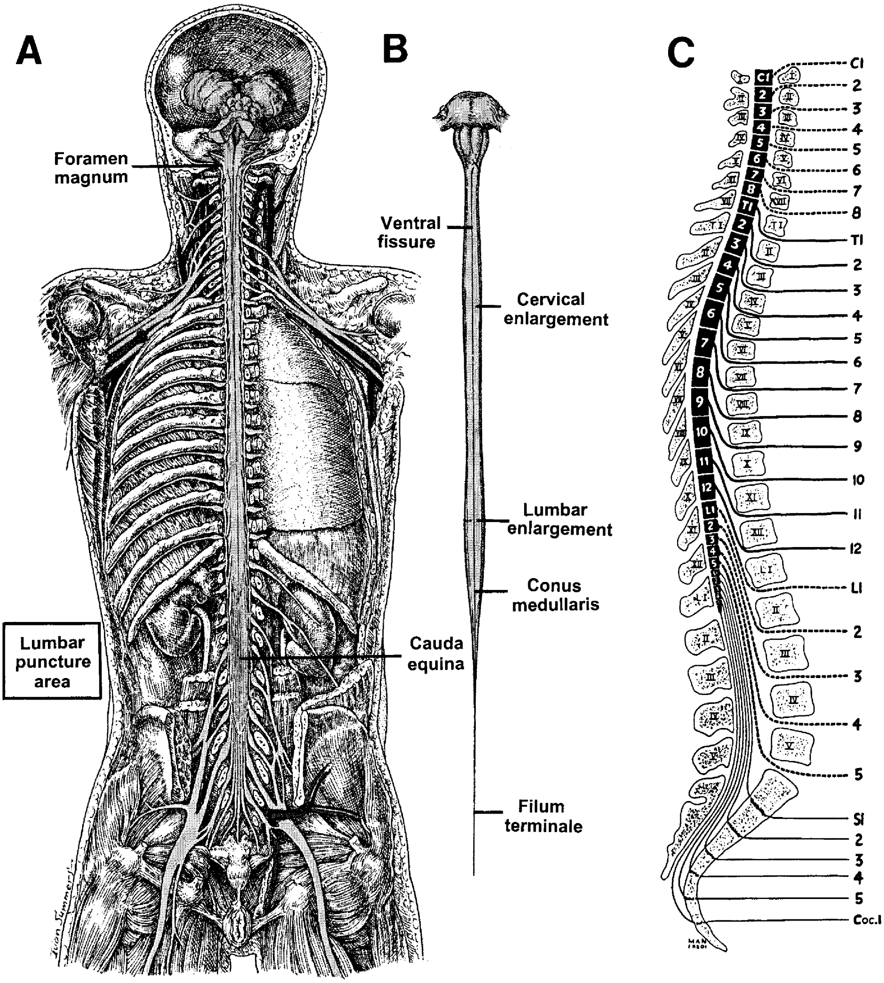

FIG. 1.1A–C. The shape of the spinal cord and its relationship to the vertebral column. **A** Gross dissection of the back in a human cadaver. A complete laminectomy was done and the dura opened, exposing the dorsal aspect of the spinal cord. The brachial and the lumbosacral plexuses are also shown. The spinal cord terminates at the L1–L2 interspace. The remainder of the dural sac contains the cauda equina. The filum terminale penetrates the dura and is attached to the coccyx. **B** Ventral view of the isolated spinal cord. The ventral fissure separates the two halves of the cord (**A** and **B** from Mettler, 1948). **C** Relationship of the spinal cord segments and spinal nerves to the vertebral column (from Crosby et al., 1962)

There are a total of 31 segments (8 cervical, 12 thoracic, 5 lumbar, 5 sacral, and 1 coccygeal) in the human spinal cord (Figs. 1.1 and 1.2). Other mammals may have slightly different numbers of segments. There are seven cervical vertebrae, and so there is one more cervical spinal cord segment than cervical vertebrae. The ventral roots of the first cervical segment emerge rostral to the first cervical vertebra (there are generally no first cervical dorsal roots; Fig. 1.2), and the eighth cervical dorsal and

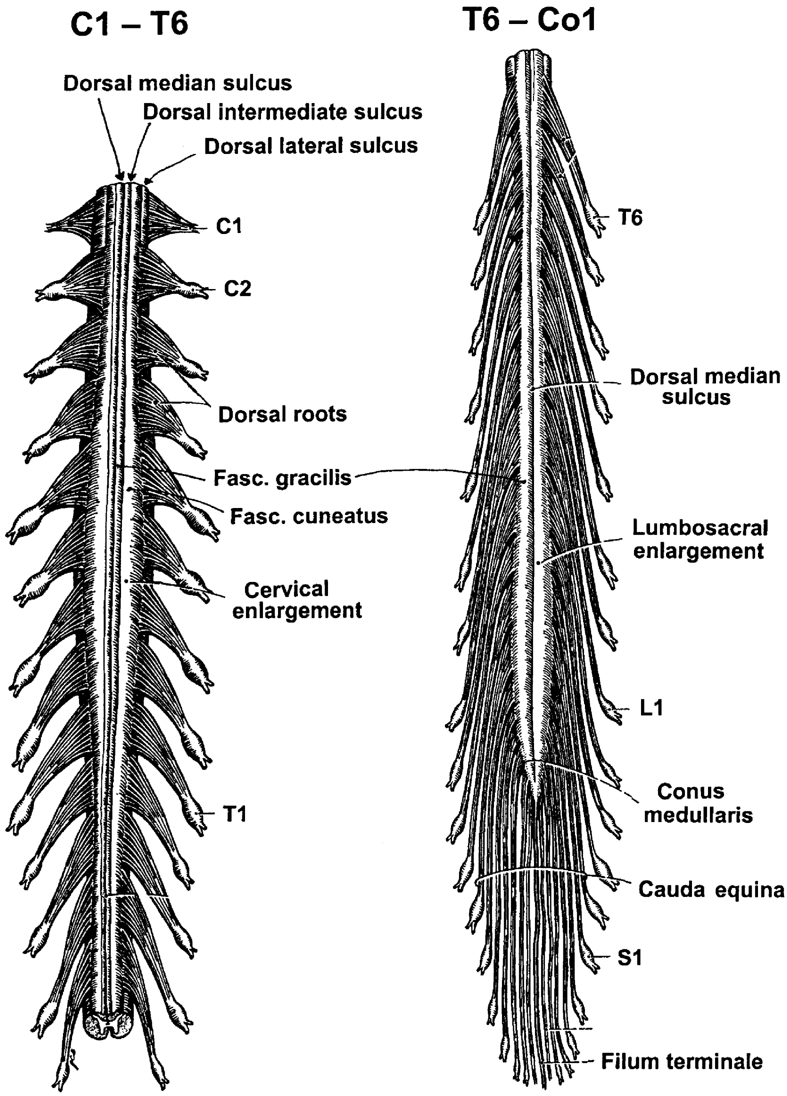

FIG. 1.2. Drawing of the dorsal surface of the spinal cord, dorsal roots and dorsal root ganglia. The spinal cord was transected between the T5 and T6 segments. The cervical and upper thoracic cord are shown at the *left* (including the cervical enlargement) and the lower thoracic and lumbosacral cord are shown at the *right* (including the lumbosacral enlargement). Note that at C1, only the ventral roots are seen because of the absence of C1 dorsal roots. The dorsal median sulcus is present throughout the length of the spinal cord, as is the dorsal lateral sulcus, which is the groove through which the dorsal roots pass to enter the spinal cord. However, there is a dorsal intermediate sulcus at T6 and more rostrally. This separates the fasciculus gracilis from the more laterally situated fasciculus cuneatus. Below T6, only the fasciculus gracilis is found. Caudal to the termination of the conus medullaris are seen the cauda equina and the filum terminale (from Crosby et al., 1962)

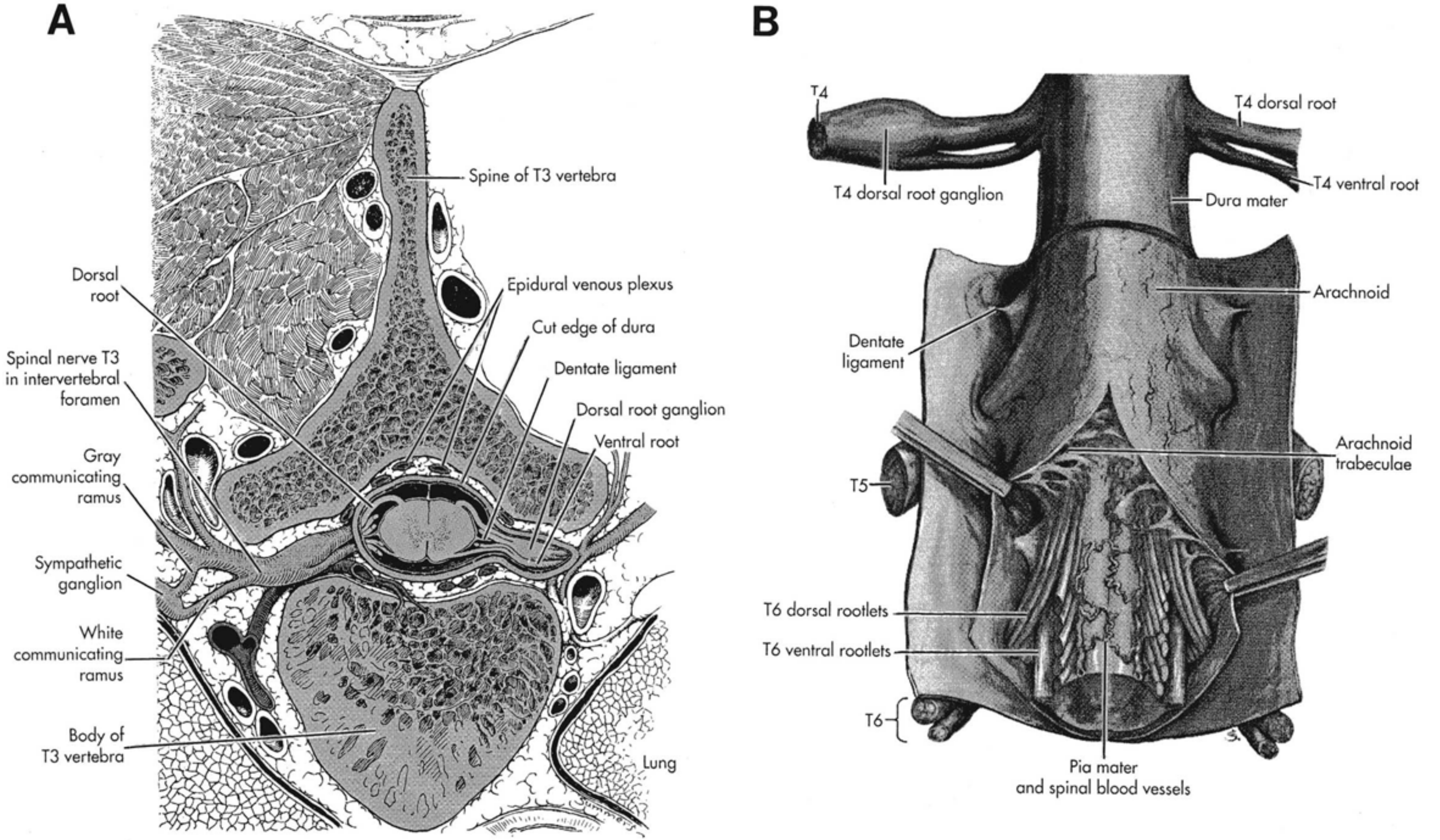

Fig. 1.3A,B. Spinal cord, associated components of the peripheral nervous system, and supportive bony and connective tissue structures. **A** Transverse section of the third thoracic vertebra, the spinal cord, T3 spinal roots, T3 dorsal root ganglia, T3 spinal nerves and meninges. Note the connections of the white and gray communicating rami with the T3 prevertebral sympathetic ganglion. Also note the epidural fat and venous plexus. **B** Dorsal view of the T4–6 levels of the spinal cord, showing the meningeal coverings, including the dura mater, arachnoid, and pia mater. Note the attachment points between the dentate ligament and the dura, as well as the arachnoid trabeculae (from Mettler, 1948)

ventral roots leave the vertebral canal just caudal to the seventh cervical vertebra (Fig. 1.1C). The roots of the remaining spinal segments exit from the vertebral canal below the vertebra of the same number.

The reason that the first cervical segment lacks dorsal roots is that it participates in trigeminal rather than in spinal cord sensory functions. Correlated with this lack of C1 dorsal roots is the absence of a C1 dermatome (see standard dermatome maps used for neurological examinations). The C1 segment receives input from descending branches of primary afferents belonging to the trigeminal nerve. Nociceptive, thermoreceptive, and tactile afferents with cell bodies in the trigeminal ganglion enter the brain stem at the level of the mid-pons through the trigeminal nerve and give off collaterals that project caudally through the spinal tract of the trigeminal nerve, which terminates in the spinal nucleus of the trigeminal nerve. This nucleus extends from the level of the pons to the upper cervical spinal cord. The subnucleus caudalis of the trigeminal complex, which is in the lower medulla and upper cervical spinal cord, resembles the dorsal horn of the spinal cord and is often referred to as the "medullary dorsal horn." Neurons in this nucleus give rise to a part of the trigeminothalamic tract that has equivalent sensory functions for the head to the spinothalamic tract for the extremities and trunk (pain, temperature and crude touch).

In the upper cervical spinal cord, the spinal roots leave the spinal cord and pass directly laterally to the appropriate intervertebral foramen. However, since the adult spinal cord does not extend beyond the L1–2 intervertebral space, roots below L2 must travel progressively more caudally to reach the appropriate intervertebral foramen (Fig. 1.1C). The collection of spinal roots below L2 is called the cauda equina from its fancied resemblance to a horse's tail (Figs. 1.1A and 1.2). At levels between the upper cervical spinal cord and L2, the roots angle progressively more. This leads to a discrepancy between vertebral level and spinal cord segmental level that can amount to a difference of 2 or more segments, depending on the level (Fig. 1.1C).

The diameter of the spinal cord is larger at the levels of the brachial (C5–T1) and lumbosacral (L2–S3) plexuses than at other levels (Figs. 1.1A,B and 1.2). The cervical and lumbosacral enlargements are produced by increases in the numbers of neurons and their connections at these levels, as required for the sensory and motor innervation of the upper and lower extremities.

The surface of the spinal cord is indented longitudinally by several sulci (shallow grooves) and a fissure (deep groove). These grooves define the boundaries between areas of the spinal cord white matter called funiculi (large bundles of axons) and between two fasciculi (smaller bundles of axons). At the dorsal midline is the dorsal median sulcus. This separates the left and right sides of the spinal cord (Fig. 1.2). The dorsal lateral sulcus is a groove that corresponds to the dorsal root entry zone. The dorsal funiculus extends from the dorsal median sulcus to the dorsal lateral sulcus. At some segmental levels (C1–T6), there is a dorsal intermediate sulcus, which separates the fasciculus gracilis from the more laterally placed fasciculus cuneatus (Fig. 1.2, left). Caudal to T6, there is no dorsal intermediate sulcus and there is only a fasciculus gracilis (Fig. 1.2, right). The ventral lateral sulcus is not well defined but marks the ventral root exit zone. The lateral funiculus extends from the dorsal lateral to the ventral lateral sulcus. At the midline ventrally is the ventral median fissure (Fig. 1.1B). The ventral funiculus lies between the ventral lateral sulcus and the ventral median fissure. Contained within the ventral median fissure is the ventral spinal artery.

1.2 Spinal Meninges

The spinal cord, like the brain, is enclosed within and protected by connective tissue sheaths called the meninges (Fig. 1.3A,B). The meninges include the dura mater, the arachnoid, and the pia mater. The dura mater is a thick connective tissue membrane that is continuous rostrally to the foramen magnum with the inner layer of the cranial dura mater. There is an epidural space between the spinal dura mater and the periosteum of the vertebral canal. This space contains epidural fat and a venous plexus (Fig. 1.3A). The dura mater extends caudally as far as the level of the S2 vertebra.

Beneath the dura mater is a thinner membrane, the arachnoid (Fig. 1.3B). The arachnoid bridges over surface features of the spinal cord, such as the sulci and the anterior median fissure. Tight junctions between cells of the arachnoid give this membrane a barrier function. The subarachnoid space contains cerebrospinal fluid, which is confined to this space by the barrier properties of the arachnoid. The cerebrospinal fluid originates largely from the choroid plexuses in the cerebral ventricles. The lumbar cistern, which is the subarachnoid space around the cauda equina, serves as a convenient reservoir from which to remove cerebrospinal fluid by lumbar puncture (Fig. 1.1A).

The innermost of the meninges is the pia mater (Fig. 1.3B). This thin membrane adheres tightly to the surface of the spinal cord and thus follows its contours closely. It fuses with astrocytic end-feet, forming a pia-glial membrane. Arachnoid trabeculi are connective tissue attachments between the arachnoid and pia. A thickening of the pia mater on each side of the spinal cord is called the dentate (or denticulate) ligament (Fig. 1.3B). Passing through the arachnoid, the dentate ligament makes a series of 20–22 firm attachments to the dura along the length of the spinal cord (Fig. 1.3B). The caudal end of the spinal cord is connected to the coccyx by the filum terminale (Fig. 1.1A,B). This is another thickening of the pia mater that penetrates the arachnoid and fuses with the dura. The dentate ligaments and filum terminale permit some movement of the dura without allowing much movement of the spinal cord (Romanes, 1981).

(Standard references that describe the anatomy of the spinal cord include Mettler, 1948; Crosby et al., 1962; Carpenter and Sutin, 1983; Nolte, 2002; Paxinos and Mai, 2004).

1.3 Cross-Sectional Anatomy of the Spinal Cord

A transverse section of the spinal cord reveals the basic arrangement of the spinal cord white and gray matter. The white matter is located around the periphery of the spinal cord, and the gray matter forms a butterfly-shaped region deep to the white matter (Fig. 1.4). The grooves at the surface of the spinal cord allow the subdivision of the white matter into dorsal, lateral and ventral funiculi, and, in the cervical and upper thoracic spinal cord, the further subdivision of the dorsal funiculus into the fasciculi gracilis and cuneatus (Fig. 1.4A,B). At lower thoracic levels and caudally, the dorsal fasciculus consists of just the fasciculus gracilis (Fig. 1.4C). Just deep to

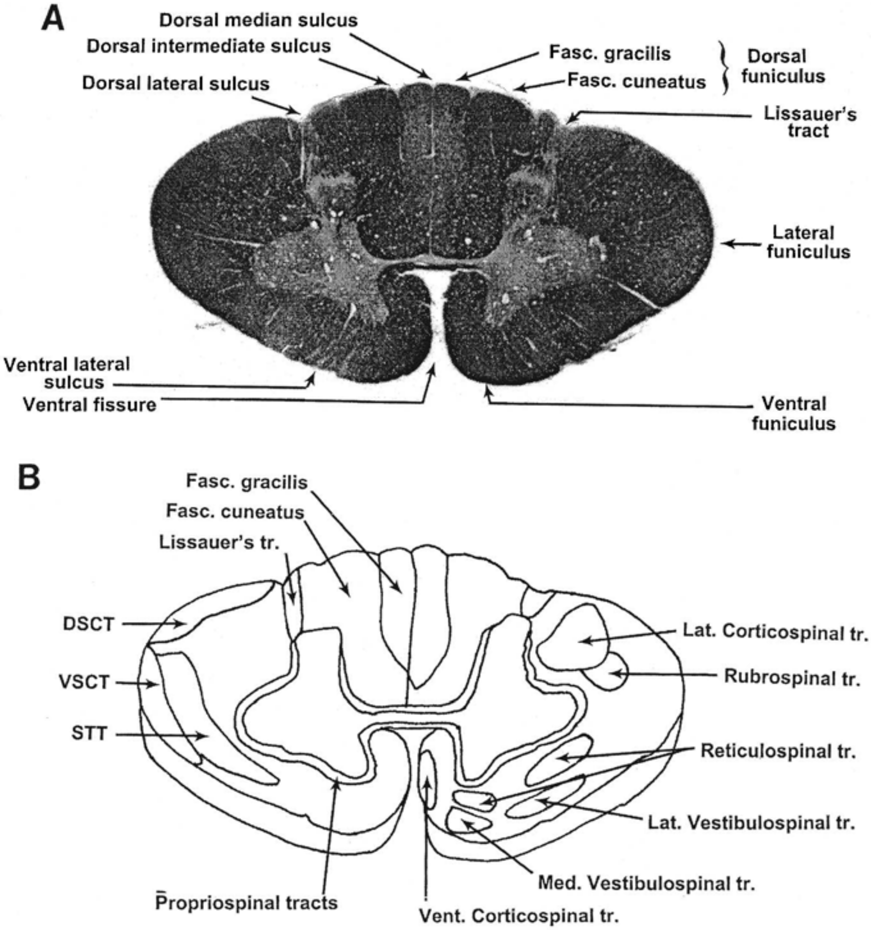

Fig. 1.4A–C. Transverse sections of the spinal cord. **A** Myelin-stained section of cervical enlargement of human spinal cord, emphasizing the different parts of the white matter. The dorsal median and dorsal lateral sulci demarcate the dorsal funiculus. Within the dorsal funiculus, the fasciculus gracilis is separated from the fasciculus cuneatus by the dorsal intermediate sulcus. Lissauer's tract is shown deep to the dorsal lateral sulcus. Between the dorsal lateral and the ventral lateral sulci is the lateral funiculus. The ventral lateral sulcus and the ventral median fissure are the boundaries of the ventral funiculus. **B** Drawing of a section through the cervical enlargement and showing the approximate locations of ascending (*left side of section*) and descending (*right side of section*) tracts. Propriospinal tracts surrounding the gray matter are also indicated. **C** Lumbar enlargement, emphasizing the main parts of the gray matter, including the dorsal horn, intermediate region, ventral horn and central gray. The dorsal funiculus includes only the fasciculus gracilis. The substantia gelatinosa is a special part of the gray matter that is lightly stained because of the relative lack of myelin in this region. These different parts of the gray matter are present throughout the length of the spinal cord

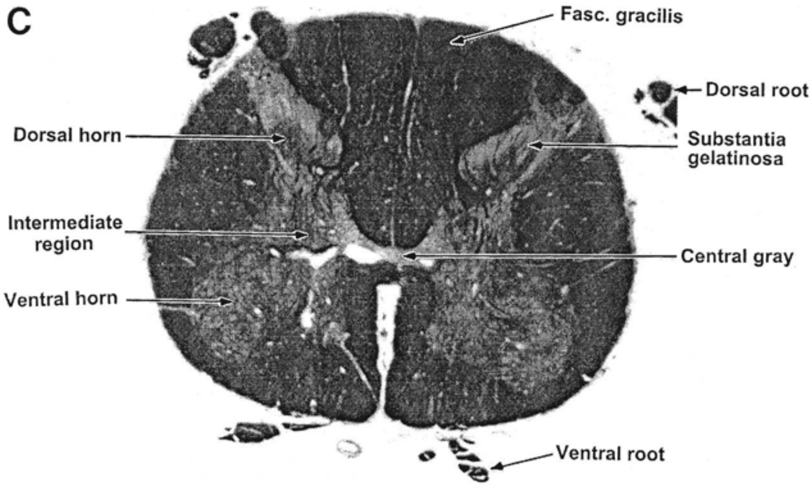

Fig. 1.4A–C. *Continued*

the dorsal root entry zone is a bundle of lightly myelinated and unmyelinated axons called Lissauer's tract (Fig. 1.4A,B; Lissauer, 1886).

The dorsal funiculus includes important ascending sensory pathways, the dorsal column pathway, and the postsynaptic dorsal column pathway (see below), and the lateral and ventral funiculi contain several ascending and descending tracts. These long pathways transmit information from the spinal cord to the brain or from the brain to the spinal cord (Fig. 1.4B). The names of these tracts often indicate the origin and destination of these pathways. For example, the dorsal and ventral spinocerebellar tracts (DSCT and VSCT) originate from neurons in the spinal cord and project to the cerebellum, and the lateral and ventral corticospinal tracts originate in the cerebral cortex and project to the spinal cord. Another ascending pathway is the spinothalamic tract (STT), and additional descending tracts include the pontine and medullary reticulospinal tracts, the lateral and medial vestibulospinal tracts, and the rubrospinal tract. The spinal cord white matter also contains propriospinal tracts, some of which are located just outside the gray matter and which interconnect different segmental levels of the spinal cord.

The gray matter of the spinal cord can be subdivided into the dorsal horn, intermediate region, ventral horn, and central gray (Fig. 1.4C). These extend longitudinally throughout the length of the spinal cord. A part of the dorsal horn called the substantia gelatinosa is prominent in myelin-stained sections because of the relative lack of myelin in this region (Fig. 1.4C; also Fig. 1.5A,B, left side of the sections). The substantia gelatinosa also extends the length of the spinal cord.

The cellular composition of the spinal cord gray matter is best revealed when the sections are stained by the Nissl method. In Nissl-stained sections, the substantia gelatinosa is seen to contain many small, densely packed neurons (Fig. 1.5A,B, right side of the sections). In the ventral horn are the motor nuclei, which contain numerous large alpha motor neurons, as well as smaller gamma motor neurons. An indi-

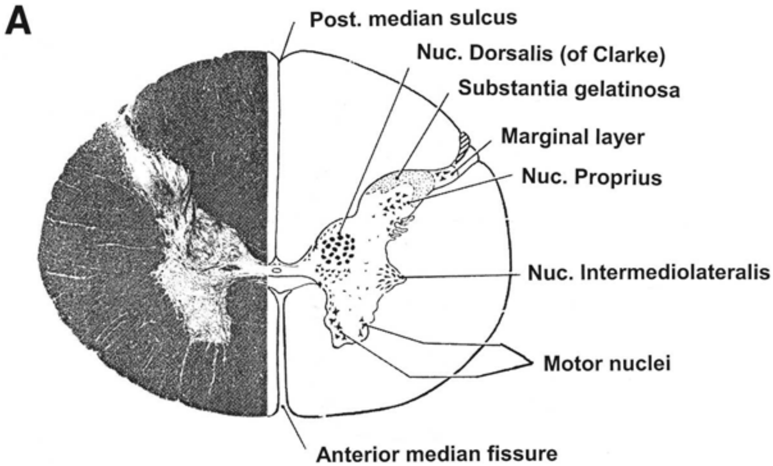

Fig. 1.5A–C. Transverse sections of the human thoracic and sacral spinal cord. The *left sides* of the sections in **A** and **B** are stained for myelin. The *right sides* of these sections are drawings of the locations of neuronal cell bodies stained with the Nissl technique. **A** Section through spinal cord segment T12 showing the locations of neurons in the marginal layer, substantia gelatinosa, nucleus proprius, Clarke's column (or nucleus dorsalis), the intermediolateral cell column, and motor nuclei. **B** Section through the S3 segment showing the locations of neurons in the marginal layer, substantia gelatinosa, nucleus proprius, sacral parasympathetic nucleus and motor nuclei (modified from Carpenter and Sutin, 1983). **C** Section through the lumbar enlargement showing the cell body, dendrites, and axon of an alpha motor neuron that had been injected intracellularly with horseradish peroxidase (from Nolte, 2002)

vidual alpha motor neuron labeled intracellularly with horseradish peroxidase is shown in Fig. 1.5C to have dendrites that are widely distributed throughout much of the ventral horn. In the enlargements, the gray matter of the spinal cord is expanded compared with that in the thoracic, upper lumbar and sacral levels (cf. sections through enlargements in Fig. 1.4 with sections through the thoracic and sacral spinal cord in Fig. 1.5A,B). This is especially evident for the ventral horn, which contains several columns of motor neurons. A given motor neuron column innervates a particular muscle and may extend longitudinally for several segments. The motor nuclei have a somatotopic arrangement. Motor neurons that supply distal muscles are located dorsolaterally, those that supply proximal muscles are placed more ventromedially, and motor neurons that innervate axial muscles are located medially in the ventral horn (Figs. 1.5B and 1.6).

At certain levels of the spinal cord, there are additional components of the gray matter. In the thoracic and upper lumbar spinal cord, there is a lateral horn, which contains a column of sympathetic preganglionic neurons called the intermediolateral cell column (Fig. 1.5A). At the same segmental levels, the intermediate region also contains the nucleus dorsalis (or Clarke's column); this nucleus projects to the cerebellum through the dorsal spinocerebellar tract (Fig. 1.5A). In the sacral spinal cord, the sacral parasympathetic nucleus (Fig. 1.5B) is located in a position similar to that of the sympathetic intermediolateral cell column and is composed of parasympathetic

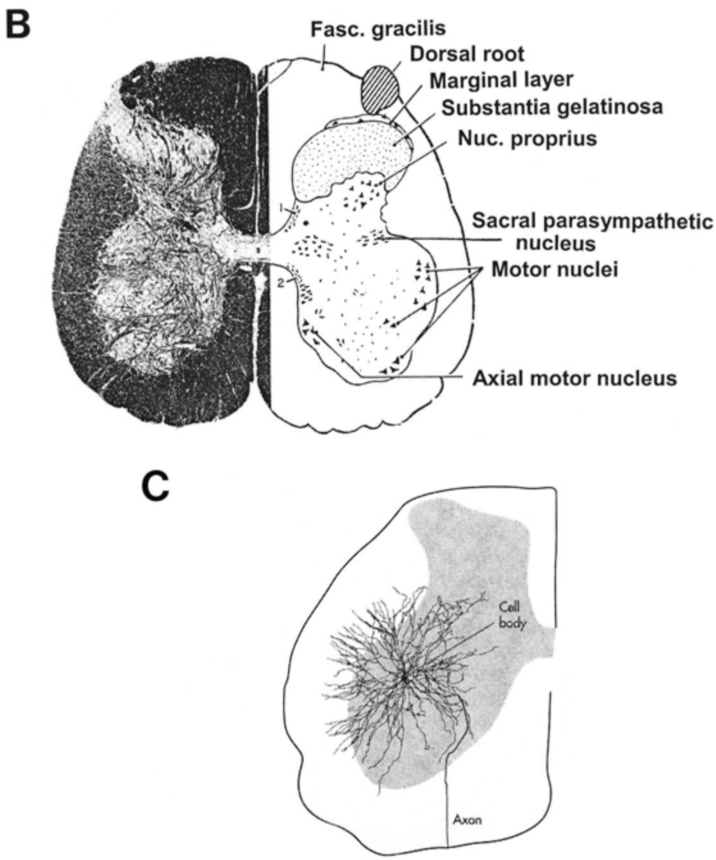

Fig. 1.5A–C. *Continued*

preganglionic neurons (Nadelhaft et al., 1983). The sacral parasympathetic nucleus extends through segments S1–S3. Visceral afferents reaching the spinal cord through the pelvic nerve enter Lissauer's tract and synapse on interneurons in the vicinity of the sacral parasympathetic nucleus. The neural circuits that are formed contribute to visceral reflexes.

A Swedish neuroanatomist named Rexed was able to show in Nissl-stained material that the spinal cord gray matter of cats is layered (Fig. 1.6A; Rexed, 1952, 1954). He subdivided the gray matter into 10 layers (Rexed's laminae). In the enlargements, the dorsal horn includes laminae I–VI (the substantia gelatinosa is equivalent to lamina II). The intermediate region is the dorsal part of lamina VII. The medial ventral horn is lamina VIII, and the motor nuclei collectively form lamina IX (which includes several separate motor neuron columns). The gray matter around the central canal (central gray) is lamina X. In the thoracic and upper lumbar cord, the intermediolat-