Chapter 1

Introduction

There are few difficult concepts in clinical medicine. Rocket science it definitely is not. But the bewildering profusion of nomenclature is undoubtedly a barrier to the understanding of many disciplines, clinical neurophysiology included.

Clinical neurophysiology is the application of electronic techniques to the nervous system and its connections for the purposes of diagnosis, monitoring and, occasionally, treatment. This book deals only with electromyography (EMG) and nerve conduction studies (NCS) as used in diagnosis and monitoring.

As with all diagnostic methods, be they purely clinical, or investigative or a combination, a number of general questions need to be addressed. These are listed here together with the issues specific to clinical neurophysiology:

- What is the location of the disorder? (Is it in muscle, nerve or the neuromuscular junction, and if in the nerve, is the condition local or widespread?)
- What is the pathology? (If muscle is affected, can it be defined? If nerve is implicated, is it degenerating, in which the nerve fibre itself is involved, or is it demyelinating, in which the insulating sheath around the nerve is damaged?)
- What is the severity and thus the prognosis? (What is the degree of change? And what is the likely clinical diagnosis and thus prognosis?)
- Having identified an abnormality, can it be monitored?

We start by defining the scope of the book. The first part deals with basic elements of anatomy, physiology and technical matters in an effort to provide some simple but sufficient background material. The second part then describes the principles of the examination methods and how they are used in clinical practice.

Peripheral nerves carry nerve impulses from the skin via the dorsal root ganglion to the spinal cord and thence to other parts of the central nervous system. These are sensory nerves. Nerve impulses to a muscle are sent from an anterior horn cell within the grey matter of the spinal cord to the neuromuscular junction from where they are transmitted to the muscle fibres. These are motor nerves. Both types are shown in Diagram 1.1.

Electromyography investigates disorders of neuromuscular transmission and also abnormalities within muscle arising from primary muscle disease or as a consequence of pathology within its nerve supply.

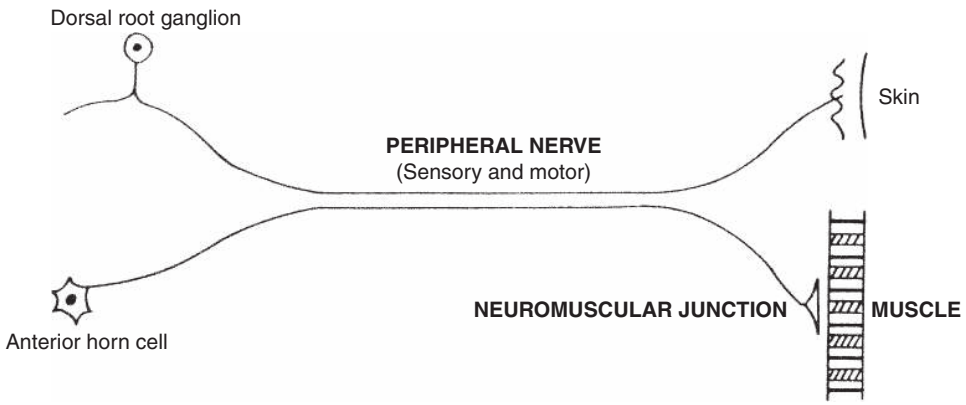

Diagram 1.1 An overview of the anatomical structures investigated by EMG and NCS. (Image included with permission from the Sheffield Teaching Hospitals NHS Foundation Trust.)

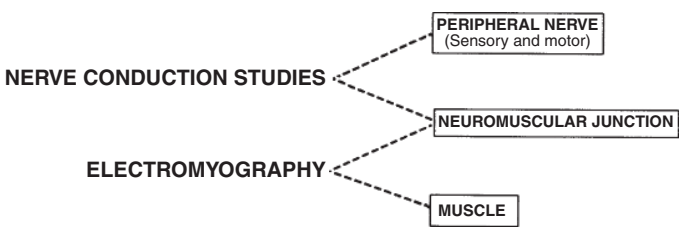

Diagram 1.2 An overview of the application of EMG and NCS to diagnosis. (Image included with permission from the Sheffield Teaching Hospitals NHS Foundation Trust.)

Nerve conduction studies are also used to investigate neuromuscular transmission. Their main function is to detect changes in peripheral nerves arising as a result of compression, or other forms of trauma, or systemic disease (Diagram 1.2).

The summary table, Table 1.1, outlines the plan of the text showing how these techniques are used in the clinic to try and answer the diagnostic questions posed earlier.

The completed table, Table 21.1, is given at the end of the book.

Table 1.1 A summary table outlines the plan of the book. The book concludes with its completion.

Anatomy	Pathology	Neurophysiology	
		EMG	*NCS*
Muscle	Myopathy		
Neuromuscular junction	MG		
	LEMS		
Peripheral nervous system		**D/M Neuropathy**	
	Compression lesions* GPN***		
		D/G Neuropathy	
	Peripheral nerve lesions* Plexus lesions** Radiculopathy** GPN***		
	AHC disease***		
	Key to abbreviations:		
	* Local changes ** Regional changes *** Widespread changes		
	MG Myasthenia gravis LEMS Lambert–Eaton myasthenic syndrome GPN Generalised peripheral neuropathy AHC disease		
	D/M Demyelinating D/G Degenerating		

Chapter 2

Basic Anatomy and a Little Physiology

The nervous system can be considered to consist of two parts: the central nervous system and the peripheral nervous system. A third component, the autonomic nervous system, features little if at all in the clinical application of electrophysiological testing. This and its complexity might permit us the notion that it should be enjoyed rather than understood.

The function of the individual elements, the neurons, of both parts of the nervous system is to transmit information from one site to another. Each neuron comprises a cell body, the soma, bearing an extrusion, the axon, which is usually of such impressive length that when referred to as a 'nerve' it is easy to overlook the fact that it is merely a conduit between the soma and its destination. Sensory neurons in the peripheral nervous system have two such axons and are therefore called bipolar cells.

The transmission of information may take place between sensory receptors and a neuron, between neurons or between a neuron and a muscle. The axon terminals from one neuron connect to the soma of another neuron at junctions called synapses. These are mainly located on dendrites, which are also extrusions of the soma but much shorter than the axon. A motor nerve connects to muscle fibres at the neuromuscular junction.

The brain and spinal cord comprise the central nervous system. Within this system, areas containing the cell bodies of nerves appear darker and are referred to as grey matter. At the base of the brain is a stalk-like structure, the brain stem, which forms a continuation of the spinal cord.

Grey matter in the brain is located over the surface, forming the cerebral cortex, or in clusters such as the thalamus and basal ganglia buried within the substance of the hemispheres. The grey matter in the spinal cord is deeply situated. It is roughly H-shaped having two ventral, or anterior, horns and two dorsal, or posterior, horns.

The interconnecting nerves between the cell bodies in the central nervous system are bundled into tracts known as white matter. They are sheathed in myelin which, containing lipids, imparts their lighter appearance. This insulates them from one another thus preventing unwanted 'cross-talk' between adjacent nerves. As we shall see in Chapter 4, 'Peripheral Nerve Function', the presence of myelin also increases the conduction velocity along the nerve.

Nerves supplying the limbs and trunk form the peripheral nervous system. The nerves to the head and neck have complex and individual anatomies and so rather than being thought of as a system, they are referred to by their individual cranial nerve names.

The majority of peripheral nerves are unmyelinated but in those that are, the myelin is applied in multiple, short segments.

Nerves carrying impulses into the central nervous system are called afferent or sensory nerves whilst those carrying impulses from the central nervous system to muscles are called

efferent or motor nerves. Most but not all peripheral nerves contain some of both types of nerve and are therefore called mixed nerves.

Motor System

The motor nerves which supply the limbs and trunk arise in the cerebral cortex and then run through the part of the brain stem known as the medulla and thence down into the spinal cord where they form a synaptic link with the anterior horn cells in the ventral grey matter. Most of these fibres cross to the other side as they pass through the region of the medulla known as the pyramids to form the pyramidal or lateral corticospinal tract. The remainder form the anterior corticospinal tract.

The spinal cord, although a continuous structure, can be thought of as a sequential series of segments. The motor outflow from a given segment supplies a series of muscles, the myotome. The anterior horn cell pool of motor neurones supplying the myotome receives connections from the pyramidal tract and from the anterior corticospinal tract after it has decussated (crossed sides) at that level.

The nerves issuing from the anterior horn cells destined for the limbs and trunk exit from the spinal cord via the ventral nerve roots and then negotiate plexuses where sensory and motor nerves arising from different segmental levels in the spinal cord combine. Each paraspinal muscle receives its nerve supply from the dorsal ramus which arises just distal to the point where the dorsal and ventral roots at that segmental level merge.

The anterior horn cell, its peripheral nerve and all the muscles fibres it innervates is called a motor unit. The size of the motor unit is proportional to the number of muscle fibres it contains.

Sensory System

Sensory neurons within the peripheral nervous system are located in the dorsal root ganglia just outside the spinal cord. They differ from motor neurons in having not one but two extruded nerve fibres, hence the name bipolar cells. The peripheral, distal fibre brings in impulses from the limbs or trunk. It also participates with the motor nerves in the formation of plexuses. The centrally projecting fibre from the dorsal root ganglion runs into the spinal cord via the dorsal root and then follows one of two main pathways.

Nerves carrying pain, temperature and deep touch sensations cross the midline and form synapses in the posterior horns of the spinal grey matter. From here the lateral spinothalamic tracts relay signals to the cerebral cortex after making further synaptic connections in the thalamus.

Nerves carrying light touch and proprioceptive sensations do not cross the midline at this stage. They enter tracts called the dorsal columns which synapse in the cuneate and gracile nuclei located in the medulla. They then cross the midline in the medial lemniscus tract to the thalamus. Here they also engage in further synaptic activity before their onward journey to the cerebral cortex.

There is an exception to this general trend of relays mediated via multiple synapses. Nerves from the intrafusal muscle spindles, which signal information about its length, form a monosynaptic link with the anterior horn cells supplying the force-producing extrafusal fibres of the same muscle. This will be discussed further when we consider the H-reflex in Chapter 17, ‘Other Techniques: F-waves and H-reflexes’. The intrafusal and extrafusal muscle fibres are discussed more fully in Chapter 6, ‘Muscle’.

Soma, Axon Hillock and Initial Segment

We are now in a position to consider how an impulse from the spinal cord begins its journey to a muscle.

As we have seen, the soma – in this case, the anterior horn cell – has numerous small projections called dendrites and a long, extruded portion, the axon, which forms the peripheral motor nerve fibre. The activity in the connections between the axon terminals from other nerves and these anterior horn cell dendrites determines the activity of the soma and hence its nerve.

Neurotransmitters cross the junctions between these connection, the synapses, and induce either an excitatory or inhibitory potential in the soma. These are known as excitatory post-synaptic potentials (EPSPs) or inhibitory post-synaptic potentials (IPSPs), respectively. A single EPSP is insufficient to generate a so-called action potential in the axon, that is to say, a potential that will be propagated down the nerve. Both EPSPs and IPSPs may be augmented by spatial and/or temporal summation. In spatial summation, the effects of activity in multiple dendrites are summed. In temporal summation, the effects of repeated activity at a single dendrite are summed. The algebraic summations of the EPSPs and IPSPs then determine if the soma has been sufficiently depolarised to generate an action potential. If so, the soma is said to fire. How is this achieved? The currents from these potentials are routed to a bulge in the soma called the axon hillock from which the axon itself arises. The axon hillock and the so-called initial segment of the axon leading from it are both especially sensitive to depolarisation as they contain very high concentrations of sodium channels which facilitate the entry of sodium ions.

In this way, the soma weighs the evidence of incoming signals in determining whether or not to fire. When it does decide to do so, the physiology of the peripheral nerve means that there is no going back in either sense of the term. This relates to something called the absolute refractory period which, together with further details of the depolarisation process, will be described in Chapter 4, 'Peripheral Nerve Function'.

Chapter 3

Peripheral Nerve Types

Peripheral Nerve Classification

Peripheral nerves were originally classified as A, B or C, in descending order of diameter. Nerve types A and B are myelinated; C is not. A more recent classification defines four subclasses of the A fibres, namely α, β, γ and δ, again in descending order of diameter. The Aα fibres are the efferents to the extrafusal muscle fibres; that is, fibres not within the muscle spindle. The Aγ fibres are the efferents to the muscle spindles. Afferent fibres within peripheral nerves now have a Roman numeral classification. The Ia fibres supply the annulospiral receptors of the muscle spindle; the Ib supply the Golgi tendon organ. Smaller diameter fibres, type II, supply the flower-spray endings in the muscle spindles and also the cutaneous mechanoreceptors. The smallest myelinated fibres within the group, type III, supply fast pain and cold receptors in the skin and also the free nerve endings subserving touch and pressure. Type IV fibres, the type C of the earlier classification, are unmyelinated fibres relaying sensations of pain and heat. These subtypes based on diameter/conduction velocity and function are helpful even though there is considerable overlap between the categories. Table 3.1 summarises the differences between them.

Nerves with the largest diameters, up to 20 microns (i.e. micrometres or μm), are found in the Ia, Ib and Aα categories. The smallest diameter fibres, of about 1 μm, belong to the unmyelinated type IV nerves.

Whilst it is important to have an appreciation of this classification, the message that needs to be kept in mind when performing nerve conduction studies is that peripheral nerves contain fibres of different diameters and these conduct at different speeds.

The detailed analysis of the behaviour of these different components of peripheral nerves falls within the remit of academic neurophysiology but a brief summary of the more pertinent aspects follows.

Sensory Nerves

Sensory nerves from the muscle spindles and tendons are designed to monitor muscle length and tension, respectively, and operate at the subconscious level. Sensory fibres supplying the muscle spindles, the Ia afferents, are the largest and fastest-conducting fibres in the peripheral nervous system. They provide information about muscle length and the rate of any change. They are relayed in the central nervous system to the cerebellum which co-ordinates movement. In the spinal cord, they also form a connection with the alpha motor neurons supplying the same muscle. If the muscle is stretched, they excite this alpha

Table 3.1 Peripheral nerve fibre types.

Fibre type	Myelination		Efferents	Afferents
Aα	Myelinated		Muscle extrafusal fibres	
Aγ	Myelinated		Muscle spindle	
		Unmyelinated		See IV
Ia	Myelinated			Muscle spindle annulospiral endings
Ib	Myelinated			Golgi tendon organs
II	Myelinated			Muscle spindle flower-spray endings and specialised receptors for touch, pressure and vibration
III	Myelinated			Mainly free nerve endings for fast pain and cold, and touch
IV		Unmyelinated		Mainly free nerve endings for slow pain, heat and cold

motor neuron to elicit a contraction thereby restoring muscle length. Because this reflex arc is based on one sensory neuron and one motor neuron it is called a monosynaptic reflex. And since this compensatory contraction would stretch antagonist muscles, the Ia afferents also form an inhibitory connection, via an interneuron, with the alpha motor neurons supplying them. The phenomenon is familiar as the tendon reflex of the knee-jerk. The tendons also contain receptors which signal muscle tension via the Ib afferents.

Other specialised cutaneous sensory receptors respond to specific stimuli such as pressure, vibration or light touch. Attempts to refine sensory nerve conduction studies by using modality-specific stimuli have not so far been clinically useful. Fortunately, there are abundant peripheral sensory nerves which can be easily stimulated to provide valuable diagnostic information.

Motor Nerves

The alpha motor neurons which arise in the ventral grey matter (also known as the anterior horn) of the spinal cord are responsible for muscle contraction. They are also fast-conducting nerves, only slightly less so than the Ia afferents.

More slowly conducting gamma motor neurons, which also arise in the ventral grey matter, supply the muscle spindles. They maintain tension on the spindle to match the desired length of the extrafusal muscle fibres. This is called alpha–gamma co-activation. Unintended departure from this state is signalled by the Ia afferents to the alpha motor neurons whose firing rates, which determine muscle tension, are correspondingly adjusted.

Chapter 4

Peripheral Nerve Function

We now need to consider in more detail the structure of a peripheral nerve and how this relates to its functioning. The peripheral nerve has a semipermeable membrane. Outside the nerve, there is a predominance of sodium ions. Within the nerve, potassium ions predominate. An active energy-dependent process, the sodium–potassium pump, pushes out three potassium ions for every two sodium ions that enter. This leads to a resting membrane potential in which the interior of the nerve is approximately –70 millivolts (mV) relative to the exterior. Given that there is an excess concentration of sodium ions outside the nerve within a positively charged environment, one has to ask why the concentration and/or electrical gradients fail to propel them into the cell. One reason, but not the most important, is that sodium ions are hydrated, making them larger and so less diffusible. The other and critical factor is that entry of sodium ions takes place at specialised sites incorporating voltage-gated channels. These are ion channels which only open in response to specific changes in membrane potential. In the case of sodium ions, this is when the membrane is depolarised, that is to say, when the interior becomes more positive and the exterior becomes more negative.

If a peripheral nerve is stimulated as, for example, in a nerve conduction study, and if the stimulus strength is very low, the membrane will be depolarised but not sufficiently to produce a potential that will be propagated along the nerve. By definition, this is a subthreshold stimulus. But if the stimulus strength is sufficiently great to exceed the threshold, about 15 to 20 mV, the potential will be transmitted along the nerve. This is called an action potential and the nerve is said to fire. Once the threshold has been breached, many more local sodium channels are opened and the ions pour into the nerve, reducing the membrane potential even further.

As we have seen in Chapter 2, 'Basic Anatomy and a Little Physiology; Soma, Axon Hillock and Initial Segment', the depolarisation of the anterior horn cell and initial segment of the axon as a result of the opening of these sodium channels is well above threshold to produce an action potential.

Before we address the issue of how the action potential is then propagated along the nerve, we need to reflect a moment on peripheral nerve structure. Some, but not most, of the peripheral nerves are myelinated and since these are the ones we study in the clinic, they are the ones we consider first.

Diagram 4.1 shows a myelinated nerve fibre at low-power magnification and, below it, cross-sectional and longitudinal sectional diagrams at higher magnification. In reality, myelin appears as concentric rings in a cross-sectional view, which the author hopes will justify the artistic licence in depicting it as such.