The purpose of the nervous system is to interact with the environment to promote survival and reproduction. Thus, the nervous system must receive sensory inputs, the central nervous system (CNS) must "process" these inputs as well as internal signals and must respond via appropriate outputs many of them related to muscle movement. CNS "processing" includes such complicated phenomena as consciousness, emotion, and memory. The complexity of the nervous system is immense, a fact demonstrated by the expanding population of scientists involved in its study. The annual meeting of the Society of Neuroscience, basic scientists involved in the study of the nervous system, regularly attracts over 30,000 attendees. More clinically oriented neurology research meetings attract thousands of neurologists, physicians who care for patients with diseases of the nervous system. Since the focus in this chapter is neurological disease, rather than normal neurological function, there is not much basic neuroscience here, but the basis of all neurology is neuroscience, and the distinction between the two fields is somewhat artificial.

The human nervous system, as well as that of nonhuman primates, is an aberration among animals in its size and extravagant energy expenditure. One of the differences in the nervous system of primates relative to that of other animals is its dependence on vision instead of smell; the visual system requires a large amount of brain, but provides significant survival advantages to primates.

While accounting for only 2% of body weight, the brain utilizes approximately 20% of the total energy expenditure.

1 Organization of the Nervous System

The nervous system is generally divided into the CNS, consisting of the brain, brain stem, cerebellum, and spinal cord, and the peripheral nervous system (PNS), consisting of the nerve roots, plexi, peripheral nerves, the neuromuscular junction, and the muscle. The flow of sensory information is from the periphery toward the brain, and the motor output is from the brain peripherally. This "brain outward" flow of motor output in the nervous system is also called "rostrocaudal" flow. A small minority of sensory inputs with motor responses, requiring great speed, can bypass the brain and are called reflexes.

1.1 Electrical Nature: Nerve Transmission and Neurotransmitters

The nervous system is electrical, and information is composed of electrical signals which are transmitted along nerve cells or across synapses. The first demonstration that the nervous system was electrical was by Luigi Galvani, an Italian physician,

in 1771 who demonstrated that an electrical impulse applied to a frog's leg made it kick. The electrical signal which passes along a nerve is called an action potential or nerve impulse and is a very fast, transient change in voltage across the nerve membrane mediated by specialized molecules in the membrane, voltage-gated ion channels. The speed of movement of the action potential averages about 50 m/s in the human or 110 miles/h. The membrane recovers very quickly and can generate many impulses per second. These electrical signals are transmitted by specialized cells called neurons. Communication between neurons is accomplished by synapses in which the arrival of an action potential results in the release of neurotransmitters, specialized molecules that can be quickly moved and processed, across the synapses leading to an action potential in the downstream neuron. The nervous system uses many different types of synapses which can be differentiated by location within the nervous system as well as by the type of neurotransmitter. There are many different types of neurons in the CNS, defined by their shape and their variety of synapses. One particularly striking and important type of neuron is the Purkinje cell, first described in 1837 by the Czech anatomist, Jan Purkinje, and localized to the cerebellum. This cell is a target in the disease paraneoplastic cerebellar degeneration (see Chap. 14).

The human nervous system utilizes a wide variety of neurotransmitters, which for any synapse can be considered excitatory or inhibitory in their effect on transmission of the impulse. The most well understood is acetylcholine, mentioned below, which is used both in the central and PNS. The most prevalent neurotransmitter is glutamate, which is usually excitatory, while gamma-amino butyric acid (GABA) is usually inhibitory. GABA is, in addition, an important neurotransmitter for the neuroimmunologist because GABA agonists, such as baclofen, are used in the treatment of spasticity caused by the most common neuroimmunological disease, multiple sclerosis (MS) (see Chap. 7). Monoamines, such as dopamine, epinephrine, and norepinephrine, are also important neurotransmitters; the adrenergic agonist tizanidine is also used in MS.

1.2 Cells of the Nervous System

A typical neuron possesses a cell body (often called soma), dendrites, and an axon (see Fig. 2.1), arranged in a variety of configurations. The axon is the main electrical cable and is highly specialized for action potential transmission, while the cell body provides the housekeeping functions for the whole cell, and the dendrites communicate with other neurons via synapses. Axons can be very long; in the human, axons traveling in the sciatic nerve, which have their cell bodies in the spine and extend to the feet, can be four feet in length, while many nerve cells in giraffes are much longer. Proteins from the cell body to distal parts of the axon are transported along axonal neurofilaments via a class of molecules called kinesins, considered to be "molecular motors." The axon of most neurons, but not the cell body, is covered by myelin, which provides insulation. This allows the electrical signal to be saltatory, or hopping, between specialized unmyelinated areas along the
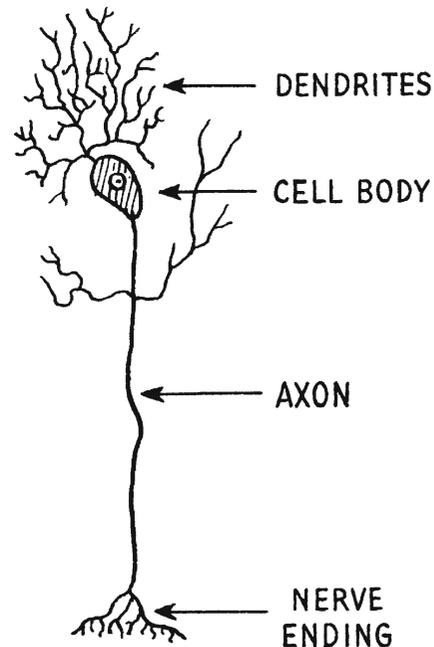

Fig. 2.1 Neurons. Nerve cells conduct impulses in a directed manner, from the dendrites through the axon to the nerve ending. The position of axons and dendrites relative to the cell body and to each other may vary (Wikimedia, public domain, at http://commons.wikimedia.org/wiki/File:Dendrite_%28PSF%29.png)

axon called nodes of Ranvier, which are present at intervals along the axon, discovered in 1878 by Louis-Antoine Ranvier. Myelin is mostly lipid in content, while the cell body is mostly proteinaceous, leading to a distinctive whiteness in CNS areas where myelinated axons are preponderant, and to grayness where cell bodies mostly occur. This distinction leads to the commonly used terms for the gross appearance of areas within the brain and spinal cord, "white matter," where there are myelinated axons, or "gray matter," for areas where there are mostly neurons. Myelin is not a component of the neurons themselves, but of specialized myelin-producing cells. In the CNS, myelin is produced by oligodendrocytes ("cells with few dendrites") and in the PNS, it is produced by Schwann cells first described by Theodor Schwann in the nineteenth century. Myelin, a complex mixture of lipid and proteins, is different biochemically in the CNS versus the PNS. Myelin is essential for efficient transmission of impulses, similar to the way insulation around a wire is essential to efficient transmission of electricity along the wire. Demyelination, the loss of myelin during diseases is a major feature of two common neuroimmunological diseases, multiple sclerosis (Chaps. 4–8) and Guillain–Barré syndrome (Chap. 9). Most of the protein in central myelin is proteolipid protein (PLP) which is abnormal in the genetic disease, Pelizaeus–Merzbacher disease (see Inset 2.1), while in peripheral myelin the major protein is myelin protein zero (MPZ). Both central and peripheral myelins contain myelin basic proteins (MBPs) and myelin-associated glycoprotein (MAG), two proteins which will be discussed in later chapters.

Inset 2.1 Pelizaeus–Merzbacher Disease: A Genetic Disease of Myelin [4]

At-risk population, cause, symptoms/signs. The disease as originally described in Germany in the late nineteenth century is a genetic X-linked disease, beginning in infancy, resulting in slow, progressive loss of motor control, ataxia, spasticity, and cognitive impairment, characterized pathologically by the loss of myelin and oligodendrocytes. The cause is a problem with the gene for PLP; these abnormalities range from missense mutations to the more common duplications of the entire *PLP* gene, which account for the majority of cases of Pelizaeus–Merbacher disease. The absence of a clear understanding of the role of PLP in healthy myelin function, and the wide variety of genetic alterations in this gene, have led to great difficulty in genotype–phenotype correlations.

Morbidity/mortality. The disease is fatal in its most severe form. However, many patients with abnormal PLP genetics can have relatively mild disease. One form is the slow development of spastic paraplegia, called spastic paraplegia 2 (SPG2), which can be quite mild.

Treatment. There is no effective treatment. Although gene replacement may help some patients, it will not help most, since the most common cause is gene duplication.

Prevention. Genetic counseling should be made available to the families of patients with PMD or SPG2.

Oligodendrocytes are members of a family of cells in the CNS called glia, Greek for "glue"; other glia are astrocytes and microglia. There are approximately equal numbers of glia and neurons in the human CNS, with the most common glial cell being the astrocyte. The microglia of the brain can be considered the brain macrophages and constitute about 20% of all brain cells. Microglia are derived from hematopoietic precursors, can multiply in response to an antigen stimulus, and are mobile within the CNS. They are extremely changeable, being able to accommodate quickly to changes in the microenvironment within the CNS. They can assume multiple morphologies depending on their level of activation. Astrocytes are not motile and have diverse functions, thought

to be mostly in support of neurons. They are able to communicate with each other using calcium waves through gap junctions; the role of this communication is unknown [1]. Astrocytes are the cells thought to be destroyed first in the neuroimmunological disease neuromyelitis optica (NMO) described in Chap. 6.

1.3   Structure of the Nervous System: CNS, PNS, Upper and Lower Motor Neurons

The CNS is divided structurally into three areas which have different functions: the brain, brainstem, and spinal cord (Fig. 2.2). The brain, consisting of the cerebrum and cerebellum, is the central processing center for sensory input and motor output, as well as the source of consciousness, memory, emotion, and thought. Just below the brain is the brainstem, the processing center for the cranial nerves, which account for critical functions related to vision, hearing, facial movement sensation, swallowing, and speech. The spinal cord is the local processing center for the

Fig. 2.2 Organization of the human brain, brainstem, and spinal cord in sagittal section, with brain stem highlighted (from Patrick Lynch http://commons.wikimedia.org/wiki/File:Brain_sagittal_section_stem_highlighted.svg)

functions of the arms and legs, as well as bowel and bladder function. The cerebrum is divided into specific lobes, frontal, temporal, parietal, and occipital lobes, each of which becomes specialized for certain brain functions, as the brain develops both in utero and after birth. The primary motor cortex, activated for the purpose of muscle movement, is in the frontal lobe, while the primary sensory cortex, the initial site of cortical processing of sensory information, is located in the parietal lobe. Language function is located in the temporal lobe, while the very large occipital lobes of the human are devoted to vision and its processing. Most motor fibers cross sides within the lower part of the brainstem, the medullary decussation, while sensory fibers cross within the spinal cord. Thus, a destructive lesion in the right parietal lobe will result in sensory loss on the left side of the body, while damage to the left frontal lobe, will result in weakness of the right side of the body. The speech centers of the brain are located in the left temporal lobe, and destructive lesions there will cause aphasia, loss of language function. The brain consists of two broadly different types of neurons, those involved in communication within the brain, called interneurons, which are by far the most common, and those involved in communication with caudal structures, called projection neurons.

The CNS is protected from trauma by bone. The brain and brainstem is surrounded by the skull, and the spinal cord by the vertebrae. The vertebral column, also called the spine, consists of 24 articulating vertebrae divided in sections called cervical, thoracic, and lumbar spine. There are nine fused vertebrae below the lumbar vertebrae in the sacrum and coccyx. To provide mobility to the spine, the vertebrae are connected to each other posteriorly through specialized joints and anteriorly are stacked one above the other, with cushions in between called disks. Sometimes disks can become damaged, herniate, and compress nerve roots or spinal cords (see Inset 6.1).

The PNS consists of all parts of the nervous system peripheral to the CNS and includes nerve roots, plexi of roots and nerves (especially the brachial and lumbar plexus), peripheral nerves, neuromuscular junctions, and muscle. Since each muscle is
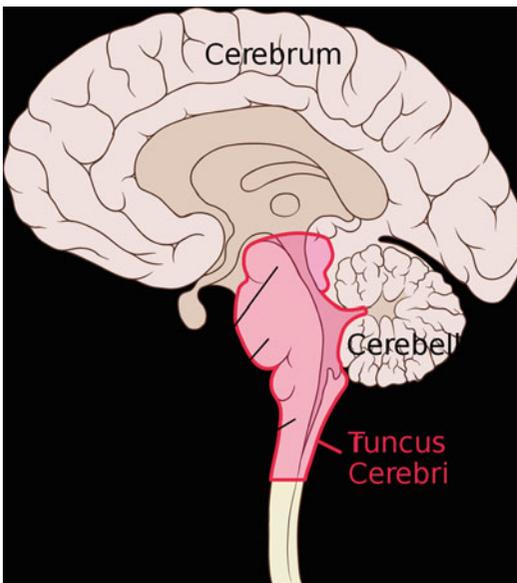
innervated by one nerve, injury to nerves can be detected by electrical testing of muscles, called electromyography (see Inset 2.2). The sensation of touch is also transmitted through nerves according to specific areas assigned to specific nerves, e.g., two major nerves lead to the hand, the median and the ulnar, both of which are relatively superficial and susceptible to injury (Inset 2.3). Transmission of signals from motor nerves to muscle is effected by a specialized synapse called the neuromuscular junction, in which the neurotransmitter is acetylcholine, and the receptor on muscle which captures and processes released acetylcholine, is the acetylcholine receptor (AChR). The AChR is a target of autoantibodies in the neuroimmunological disease myasthenia gravis (see Chap. 10).

Inset 2.2 Clinical Problem—Diabetic Neuropathy and the Modern Equivalent of the Galvani Experiment

At-risk population. Approximately 3% of the world's population suffers from diabetes, a large percentage of which has neuropathy, i.e., nerve damage causes numbness, weakness, and pain.

Cause. Diabetes mellitus is a disorder of insulin production or response, and, by mechanisms that are not understood, is associated with injury to neurons in the PNS but not in the CNS.

Symptoms and signs. Patients with diabetic neuropathy typically have symptoms in a "stocking-glove" distribution, usually consisting of pain, numbness, and tingling. As the disease worsens strength in the legs and then arms decreases, and walking can be impaired.

Patients with diabetic neuropathy can be diagnosed using electrical stimulation of tissue by electromyography/nerve conduction (EMG/NCV) studies, a commonly used neurological test which is a modern modification of Galvani's stimulation of the frog leg. *Morbidity/mortality*. The burden to society of this disease is substantial, because of its progressive nature and the large number of individuals affected.

Treatment. Generally ineffective. Various pain medications, including anticonvulsant type drugs, are used to give some symptomatic relief.

Prevention. It is generally believed, but not proven, that careful control of blood sugar can delay or prevent diabetic neuropathy.

Inset 2.3 Clinical Problem—The Hand: The Funny Bone and Carpal Tunnel Syndrome

At-risk population. The human hand is a wonder of biology, but the nerves innervating the hand are prone to injury.

Cause. The most common neuropathy is a transient one, caused by "hitting the funny bone," when the ulnar nerve is traumatized, as it travels through the elbow and passes very close to the skin at the medial epicondyle of the humerus. Chronic trauma can lead to permanent injury. Another common neuropathy is carpal tunnel syndrome, or CTS, in which the median nerve is traumatized by constant pressure against the tendons in the wrist.

Symptoms and signs. These two conditions lead to numbness and tingling in the hand, the particular area of which depends on the innervation associated with the nerve.

Morbidity/mortality. Each of these conditions, which are very common, can cause dysfunction of the hand and are common causes of disability in our society, where working with hands, especially keyboards, has become so important.

Treatment. Surgery can result in the protection of the nerve from future injury.

Prevention. Repetitive trauma to the arm can be hard to prevent but some simple measures such as using cushioned arm rests may be helpful.

Table 2.1 Clinical differences between UMN and LMN lesions

Characteristic	UMN	LMN
Location of injury	CNS	PNS (except for anterior horn cell in spinal cord)
Strength	Decreased	Decreased
Muscle tone	Increased	Decreased
Muscle bulk	Normal	Decreased
Deep tendon reflexes	Increased	Decreased
Sensory abnormalities	Variable	Variable

The motor system of the body can also be conceptually divided into upper motor neuron (UMN) and lower motor neuron (LMN) territories. UMNs are always in the CNS and project onto LMNs in the brain stem spinal cord. The anterior horns of the spinal cord contain the cell bodies of these LMNs which send axons that innervate muscles. Most diseases selectively target one location in the CNS and frequently have distinctive UMN or LMN clinical presentations (Table 2.1). One disease that has a combination of UMN and LMN findings is amyotrophic lateral sclerosis (ALS) which damages anterior horn cells and also UMN pathways within the spinal cord (see Inset 2.5). Stroke and multiple sclerosis which are CNS disorders manifest only UMN findings.

The dominant sensory input in humans is vision, a characteristic that distinguishes primates from most other animals. A large part of the human CNS is devoted to vision and its processing. The optic nerve, which carries signals from the retina to the brain, is actually not really a true nerve, but an extension of the CNS. The optic nerves, i.e., cranial nerves II, lead to the occipital lobe where visual images are processed; the occipital lobe is the only part of the brain devoted entirely to one function, vision. Inflammation of the optic nerve is common in neuroimmununological diseases, especially multiple sclerosis (see Chap. 4). Optic nerve inflammation is called optic neuritis and results in the loss of vision and eye pain. Smell is brought to the brain from the nose via cranial nerve I, the olfactory nerve; touch on the face via cranial

nerve V; and hearing via cranial nerve VIII. Touch, position, and vibration sense in the body come to the brain from peripheral nerves to the spinal cord and then via the spinothalamic tract to the brain. The sensory inputs come from specialized receptors called mechanoreceptors for touch and vibration, including Meissner's corpuscles, Pacinian corpuscles, and Merkel disk receptors, and nociceptors for pain. Position sense, identifying position in space with or without movement, is mediated by a group of specialized receptors in muscles, tendons, and joints.

The CNS is surrounded by a number of membranes. The one immediately overlying the CNS parenchyma is the thin and delicate pia mater, which accompanies blood vessels as they penetrate into the brain; the pia mater is a part of the neurovascular unit [2]. The neurovascular unit is a structure composed of components of both blood vessels and CNS cells that determines, among other things, the blood–brain barrier (BBB) and is further described in Chap. 3. The BBB and the blood–CSF barrier consist of cellular barriers between blood and CNS parenchyma that prevent the easy flow of large or highly charged molecules between the blood and the CNS. Between the pia and the next layer, the arachnoid mater, is a space called the subarachnoid space. Over the arachnoid is the thick dura mater, and the space under the dura is thus called the subdural space. The spaces defined by these membranes are used frequently in describing pathological problems, especially bleeding. Bleeding within the brain can either be localized to the brain parenchyma and not spread elsewhere, in which case it is considered an intracerebral hemorrhage (ICH), or it can be restricted to the subarachnoid space [subarachnoid hemorrhage (SAH)] or subdural space [subdural hemorrhage (SDH)].

The brain is suspended in a fluid, called cerebrospinal fluid (CSF). After being produced by ependymal cells, epithelial cells that line the ventricles, this clear, colorless fluid, circulates around the CNS in the subarachnoid space, i.e., between the arachnoid and pia maters, and eventually becomes resorbed by the arachnoid villi or drained into lymphatics. In many diseases of

Table 2.2 Some examples of CSF abnormalities in disease processes

Disease	CSF abnormality
Inflammation (e.g., encephalitis)	Increased number of white blood cells
Infection (e.g., pneumoccal meningitis)	Presence of the pathogen
Cancer (e.g., lymphoma)	Presence of cancer cells
Bleeding in the brain (e.g., burst aneurysm)	Presence of blood
Increased pressure in the brain (e.g., hydrocephalus)	Increased pressure

the nervous system, there are characteristic abnormalities of the CSF (see Table 2.2), and the physician can easily sample CSF by performing a lumbar puncture in which a needle is inserted into the subarachnoid space.

2 The Neurological Evaluation

2.1 Neurological Examination

When disease results in neurological symptoms, neurologists are frequently called to evaluate the patient, identify the diagnosis, and recommend appropriate therapy. The initial evaluation consists of obtaining a history, and performing a neurological examination. Diagnoses entertained after this evaluation are further pursued, if necessary, by laboratory testing, including blood testing, imaging, and other tests.

Neurological symptoms usually consist of difficulty with some aspect of nervous system function that we normally take for granted. The most common are problems with ambulation, coordination, strength, and the sensory functions of vision or touch. Humans are normally awake, alert, and can perform difficult cognitive tasks; neurological disease can impair level of alertness and interfere with cognition.

The first part of the neurological examination involves assessing higher cognitive functions, sometimes utilizing the "Mini-mental Status" examination [3]. Patients who have diffuse dysfunction of gray matter in the brain affecting concentration, attention, memory, recall, etc. are said to have an encephalopathy. Next, the cranial nerves (CNs) are tested: first, the optic nerve, CN II, is tested by the examiner using an ophthalmoscope, a small hand-held instrument, looking at the optic nerve head on fundoscopic examination, then by assessing vision. Eye movements are then checked, usually by having the patient follow the examiner's moving finger. Abnormalities in the conjugate movement of the eyes are common and result in the symptom of double vision, also called diplopia; sometimes diplopia is not present, but instead of smooth pursuit of a moving finger, the eye movements occur in jerky, oscillating movements called nystagmus. Eye movement testing, and testing of the pupillary response to light, tests CNs III, IV, and VI. Normal eye movements are conjugate, meaning each eye is moved equivalently. Conjugate eye movement can be impaired either by a lesion affecting one cranial nerve or by lesions of the brainstem where there are extensive connections among cranial nerves to allow for conjugate eye movements. The medial longitudinal fasciculus (MLF) is one of the connections in the brain stem and is often injured in multiple sclerosis (see Chap. 4). CN V is assessed by determining the presence of normal facial sensation and under some circumstances normal corneal reflex, the rapid shutting of the eyelid when the cornea is touched. Movement of the face tests CN VII, and hearing tests CN VIII. CN X is tested by determining that the palate moves normally and the voice is normal. CN XI is tested by measuring the strength of the sternocleidomastoid and trapezius muscles, two large muscle groups of the neck, while CN XII controls tongue movement. The motor system is tested by evaluating the strength of proximal and distal muscles in the four extremities, and by testing muscle tone and bulk. Coordination is tested by analysis of the ability to perform well-controlled movements such as rapidly moving the finger from the examiner's finger to the patient's nose. The sensory system is then examined using tests of light touch, vibration, position sense, and pin prick. Deep tendon reflexes are then tested in the arms and legs, followed by looking for any abnormal reflexes such as the

Babinski or Hoffman. The Babinski reflex is a time-honored bedside test in neurology, initially developed by Joseph Babinski, a late nineteenth century French neurologist, to differentiate psychiatric from neurological disease (Inset 2.4). Injury to descending tracts in the brain or spinal cord result in increased deep tendon reflexes and increased muscle tone. Gait is then tested, including walking one foot right before the other ("tandem gait"); inability to perform tandem gait because of problems with balance is called ataxia, a common problem in multiple sclerosis. The inability to walk well because of weakness or ataxia or abnormal muscle tone is a characteristic of many neuroimmunological diseases and is the function most important in determining the extended disability status score (EDSS), a disability scale used for measuring multiple sclerosis (see Chap. 4).

Inset 2.4 Differentiating Between "Structural" and "Psychiatric" Disease—The Babinski Reflex

Bizarre behavior is frequently caused by psychiatric disease, especially schizophrenia, which has a lifetime prevalence in the population of between 0.5 and 1%. However, behavior changes can also be called by "structural" neurological diseases, such as tumors and infections of the brain. Neurologists often struggle with making the proper diagnosis. They frequently use a test described in 1896 by Joseph Babinski, a French neurologist of Polish origin, who practiced with Charcot at the Saltpetriere in Paris. The Babinski test involves stroking the sole of the foot, and eliciting a movement of the toe upwards in individuals with damage to the corticospinal tract, but downward movement in the absence of such injury. A positive Babinski, i.e., an extensor upward movement of the toe, can be a very early sign of injury, but will be absent, i.e., a flexor downward movement, in patients with psychiatric disease.

The combination of the history and neurological examination will allow the neurologist to begin answering the two most critical questions when faced with a patient with neurological symptoms: where and what? Where is the lesion? And, what is the most likely process causing dysfunction there? For instance, the sudden onset of a left body weakness and sensory loss in a 70-year-old man with a long history of vascular disease, hypertension, smoking, and diabetes would most likely be a right cerebral stroke, while the location would be the same for a 30-year-old woman with no medical history, but the lesion causing it might be more likely to be multiple sclerosis rather than a stroke.

2.2 Imaging of the Nervous System

The neurologist frequently will confirm the likely diagnosis by some further testing. The standard tool for imaging the nervous system is computerized tomography (CT) scanning, first available for patients in 1972, which involves computer analysis of X-ray signals. Almost all hospitals in the USA have CT scanners. Another method of imaging is magnetic resonance imaging (MRI), which does not use X-rays, but instead magnetization as the primary source of signal. The principle for most types of MRI scans is that the water molecule is a dipole with the hydrogen nuclei producing a magnetic field after being aligned by an induced magnetic field or radiofrequency signals. The combination of the magnetic fields, the radiofrequency signals, and the timing of the scanning creates many potential ways to image living tissues. MRI is generally more sensitive and specific than CT scanning and does not have the potentially damaging effect of radiation dose caused by X-rays. However, it is much more expensive than CT scanning, and is not as widely available. The MRI has been especially useful in multiple sclerosis; its use in that disease will be discussed extensively in later chapters. A type of MRI called functional MRI may also become clinically useful in assessing recovery after CNS injury (see Inset 2.5). CT and MRI scan not only show areas of abnormality by their characteristic

signals but also show the absence of CNS tissue; many disease processes, especially those with a degenerative component such as Alzheimer's disease and multiple sclerosis, lead to the loss of CNS tissue which is demonstrable on imaging as atrophy.

Inset 2.5 Clinical Problem—Recovery After CNS Injury, Neural Plasticity, the Contribution of Kittens and Phantoms, and Functional MRIs

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CNS injury is unfortunately a common problem in the society, with motor vehicle accidents and strokes common causes. Neurons do not divide, and dead neurons generally cannot be replaced with new neurons. Thus, recovery of function after injury must involve processes other than growth of new cells. One of these mechanisms is neural plasticity, in which neurons involved in other functions change to pick up the lost functions from injury. The concept of plasticity and other processes are obviously of considerable interest to clinical neuroscientists who wish to optimize recovery after injury, but our knowledge of these processes remains relatively primitive.

It was thought that brain regions were "hard-wired," but this was proven wrong by pioneering experiments in the 1960s and 1970s by Hubel and Wiesel [5]. In kittens who from birth had one eyelid sewn shut, the primary visual cortex receiving inputs from the functioning eye took over the areas that normally received input from the deprived eye.

In individuals who have an amputation, rubbing of the face or lips can induce sensations perceived as if they were in the amputated, i.e., absent, limb. This is called phantom sensation, and when it is associated with pain, phantom pain. This appears to be because of downward shift of the hand area of the sensory homunculus onto the area of face representation, especially the lips, sometimes called functional cortical remapping.

The field of cortical remapping and determining whether humans can build new structural connections is an active and in 2011, a very controversial area. One of the tools of investigators in this field is functional MRI, in which activation of brain regions can be imaged by the increased blood flow caused by increased neuronal activity.

Some atrophy is due not primarily to death at the site of the atrophy visualized on imaging, but may be due to injury to a part of the nerve cell distant from the atrophy. Wallerian degeneration is axonal atrophy below an area of injury to the neuron. If the axonal injury is healed the healthy axon above the injury can grow back into the intact neurolemma, the hollow myelinated tube of the nerve, which is part of the Schwann cell or oligodendrocyte, and may not be affected by the injury. Sometimes complete recovery can occur if Wallerian degeneration goes smoothly and the neurolemma remains intact and healthy. This happens more commonly in PNS than CNS diseases.

2.3 EEG and EMG

Many patients with brain disease develop seizures or impairment of the electric signals in their brains detectable by the measurement of electric field potentials measured over the scalp, known as electroencephalography (EEG). Since measurement is over the scalp and electric fields decay rapidly with distance, the EEG mostly assesses cortical neurons close to the skull. Most of the field frequencies are about 3–20 Hz, and the amplitudes are usually 10–80 µV. The relatively low voltage is due to a great extent from damping from the skull since the signals from subdural electrodes are nearly three logs higher in amplitude than those from surface electrodes. Characteristic patterns are seen in normal awake,

drowsy, and sleeping adults, and the patterns change depending on age of the patient, and location on the skull of the electrodes tested. The most dramatic abnormalities are seen during seizures when synchronous bursts of activity can be seen as spike and wave forms which replace the normal rhythms. EEG-detected seizures may or may not have associated clinically obvious sequelae.

The electrical activity of the nervous system can also be used to detect abnormalities in the peripheral system using a test known as electromyography and nerve conduction velocity testing or EMG/NCV. In EMG, needles are inserted into muscles thought to possibly be involved in the pathological process. In a patient with ALS, Lou Gehrig's disease (see Inset 2.6) insertion of a

Morbidity/mortality. The disease is fatal, usually leading to death in 2–5 years after diagnosis.

Treatment. No treatment has been shown to be effective and there is no way to prevent the illness.

recording needle into weak muscles will demonstrate characteristic abnormalities referable to the involvement of these LMNs by the disease in the anterior horn cells of the spinal cord. NCV testing determines the velocity of nerve conduction which for most nerves is approximately 50 m/s. The most dramatic slowing of nerve conduction velocities is seen in conditions which result in the loss of myelin, such as acute or chronic inflammatory demyelinating polyneuropathy (AIDP or CIDP), conditions discussed in Chap. 9. In contrast, processes which injure axons in the PNS but generally spare myelin, e.g., the neuropathy of diabetes mellitus, will result in lower and deformed action potentials out of proportion to slowed nerve conductions.

Inset 2.6 Amyotrophic Lateral Sclerosis—UMN and LMN Findings

At-risk population. An uncommon disease affecting individuals of both sexes usually between 30 and 50 years old. The annual incidence is about 1 in 100,000.

Cause. Unknown.

Symptoms and signs. Progressive muscle weakness and atrophy. The disease is often called Lou Gehrig's disease. One of the best baseball players ever, Lou Gehrig held many records for both batting (most grand slams, most homers in a game, etc.) and for durability (most consecutive games played), until May 2, 1939, when he benched himself and sought medical attention because of his progressive weakness and was diagnosed with ALS. His retirement speech at Yankee Stadium on July 4, 1939 ("I consider myself the luckiest man on the face of the earth") was one of the most eloquent by a sports figure. He died of ALS 2 years later.

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