36

Locomotion

THE ABILITY TO MOVE IS ESSENTIAL for the survival of animals. Although many forms of locomotion have evolved—swimming, flying, crawling, and walking—all use rhythmic and alternating movements of the body or appendages. This rhythmicity makes locomotion appear to be repetitive and stereotyped. Indeed, locomotion is controlled automatically at relatively low levels of the central nervous system without intervention by higher centers. Nevertheless, locomotion often takes place in environments that are either unfamiliar or present unpredictable conditions. Locomotor movements must therefore be continually modified, usually in a subtle fashion, to adapt otherwise stereotyped movement patterns to the immediate surroundings.

The study of the neural control of locomotion must address two fundamental questions. First, how do assemblies of nerve cells generate the rhythmic motor patterns associated with locomotor movements? Second, how does sensory information adjust locomotion to both anticipated and unexpected events in the environment? In this chapter we address both of these questions by examining the neural mechanisms controlling walking.

Although most information on neural control of walking has come from studying the cat's stepping movements, important insights have also come from studies of other animals as well as rhythmic behaviors other than locomotion. Therefore, we shall also consider the more general question of how rhythmic motor activity can be generated and sustained by networks of neurons.

Several critical insights into the neural mechanisms controlling quadrupedal stepping were obtained

nearly a century ago when it was found that removing the cerebral hemispheres in dogs did not abolish walking—decerebrate animals are still able to walk spontaneously. One animal was observed to rear itself up in order to rest its forepaws on a gate at feeding time. It was soon discovered that stepping of the hind legs could be induced in cats and dogs after complete transection of the spinal cord. The stepping movements in these *spinal preparations* (Box 36–1) are similar to normal stepping. Nonrhythmic electrical stimulation of the cut cord elicits stepping at a rate related to the intensity of the stimulating current. Another important early observation was that passive movement of a limb by the experimenter could initiate stepping movements in spinal cats and dogs, suggesting that proprioceptive reflexes are crucial in regulating the movements.

Finally, in 1911 Thomas Graham Brown discovered that rhythmic, alternating contractions could be evoked in deafferented hind leg muscles immediately after transection of the spinal cord. He therefore proposed the concept of the half-center, whereby flexors and extensors inhibit each other reciprocally, giving rise to alternating stepping movements. Four conclusions can be drawn from these early studies.

1. Supraspinal commands are not necessary for producing the basic motor pattern for stepping.
2. The basic rhythmicity of stepping is produced by neuronal circuits contained entirely within the spinal cord.
3. The spinal circuits can be modulated by tonic descending signals from the brain.
4. The spinal pattern-generating networks do not require sensory input but nevertheless are strongly regulated by input from limb proprioceptors.

For almost half a century following these early studies few investigations were aimed at establishing the neural mechanisms for walking. Instead, research on motor systems focused on the organization of spinal reflex pathways and the mechanisms of synaptic integration within the spinal cord (see Chapter 35). Modern research on the neural control of locomotion dates from the 1960s and two major experimental successes. First, rhythmic patterns of motor activity were elicited in spinal animals by the application of adrenergic drugs. Second, walking on a treadmill was evoked in decerebrate cats by electrical stimulation of a small region in the brain stem.

At about the same time electromyographic recordings from numerous hind leg muscles in intact cats during unrestrained walking revealed the complexity of the locomotor pattern and brought to prominence the question of how spinal reflexes are integrated with intrinsic spinal circuits to produce the locomotor pattern. Soon thereafter, investigations of stepping in spinal cats demonstrated the similarity of locomotor patterns in spinal preparations and intact animals, thus firmly establishing the idea that the motor output for locomotion is produced primarily by a neuronal system in the spinal cord.

A Complex Sequence of Muscle Contractions Is Required for Stepping

For the purpose of examining the patterns of muscle contraction during locomotion, the step cycle in cats and humans can be divided into four distinct phases: flexion (F), first extension (E_1), second extension (E_2), and third extension (E_3) (Figure 36–2A). The F and E_1 phases occur during the time the foot is off the ground (*swing*), whereas E_2 and E_3 occur when the foot is in contact with the ground (*stance*).

Swing commences with flexion at the hip, knee, and ankle (the F phase). Approximately midway through swing the knee and ankle begin to extend while the hip continues to flex (the E_1 phase). Extension at the knee and ankle during E_1 moves the foot ahead of the body and prepares the leg to accept weight in anticipation of foot contact at the onset of stance. During early stance (the E_2 phase) the knee and ankle joints flex, even though extensor muscles are contracting strongly. A lengthening contraction of ankle and knee extensor muscles occurs because weight is being transferred to the leg. The spring-like yielding of these muscles as weight is accepted allows the body to move smoothly over the foot, and is essential for establishing an efficient gait. During late stance (the E_3 phase) the hip, knee, and ankle all extend to provide a propulsive force to move the body forward.

The rhythmic movements of the legs during stepping are produced by contractions of many muscles. In general, contractions of flexor muscles occur during the F phase, whereas contractions of extensor muscles occur during one or more of the E phases. However, the timing and amounts of activity are different in different muscles (Figure 36–2B). For example, a hip flexor muscle (iliopsoas) contracts continuously during the F and E_1 phases, whereas a knee flexor muscle (semitendinosus) contracts briefly at the beginning of the F and E_2 phases. Another complexity is that some

Box 36–1 **Preparations Used to Study the Neural Control of Stepping**

The literature on the neural control of quadrupedal stepping can be confusing because different experimental preparations are used in different studies. In addition to intact animals, spinal and decerebrate cats are commonly used in studies of the neural mechanisms of locomotor rhythmicity. Moreover, each of these preparations may be used in two experimental strategies, deafferentation and immobilization, depending on what is being investigated. Finally, neonatal rat and mouse preparations have proven useful for analyzing the cellular properties of neurons generating the locomotor rhythm.

Spinal Preparations

In spinal preparations the spinal cord is transected at the lower thoracic level (Figure 36–1A), thus isolating the spinal segments that control the hind limb musculature from the rest of the central nervous system. This allows investigations of the role of spinal circuits in generating rhythmic locomotor patterns.

In *acute* spinal preparations adrenergic drugs such as L-DOPA (L-dihydroxyphenylalanine) and nialamide are administered immediately after the transection. These drugs elevate the level of norepinephrine in the spinal cord and lead to the spontaneous generation of locomotor activity approximately 30 minutes after administration. Clonidine, another adrenergic drug, enables locomotor activity to be generated in acute spinal preparations but only if the skin of the perineal region is also stimulated.

In *chronic* spinal preparations animals are studied for weeks or months after transection. Without drug treatment locomotor activity can return within a few weeks of cord transection. Locomotor function returns spontaneously in kittens, but in adult cats daily training is usually required.

Decerebrate Preparations

In decerebrate preparations the brain stem is completely transected at the level of the midbrain, disconnecting rostral brain centers, especially the cerebral cortex, from the spinal centers where the locomotor pattern is generated. Because brain stem centers remain connected to the spinal cord, these preparations allow investigation of the role of the cerebellum and brain stem structures in controlling locomotion.

Two decerebrate preparations are commonly used. In one the locomotor rhythm is generated spontaneously, whereas in the other it is evoked by electrical stimulation of the mesencephalic locomotor region. This difference depends on the level of decerebration. Spontaneous walking occurs in *premammillary preparations*, in which the brain stem is transected from the rostral margin of the superior colliculi to a point immediately rostral to the mammillary bodies. When the transection is made caudal to the mammillary bodies *postmammillary* or *mesencephalic preparation*, spontaneous stepping does not occur; rather, electrical stimulation of the mesencephalic locomotor region is required to evoke walking (Figure 36–1B).

When supported on a motorized treadmill, both preparations walk with a coordinated stepping pattern in all four limbs and the rate of stepping is matched to the treadmill speed. The motor activity can be recorded during stepping, and sensory nerves can be stimulated with implanted electrodes to examine the reflex mechanisms that regulate stepping.

Deafferented Preparations

An early view of the neural control of locomotion was that it involved a "chaining" of reflexes: Successive stretch reflexes in flexor and extensor muscles were thought to produce the basic rhythm of walking. This view was disproved by Graham Brown, who showed that rhythmic locomotor patterns were generated even after complete removal of all sensory input (deafferentation) from the moving limbs.

Deafferentation is accomplished by transection of all the dorsal roots that innervate the limbs. Because the dorsal roots carry only sensory axons, motor innervation of the muscles remains intact. Deafferented preparations were once useful for demonstrating the capabilities of the isolated spinal cord but are rarely used today, principally because the loss of all tonic sensory input drastically reduces the excitability of interneurons and motor neurons in the spinal cord. Thus, changes in the locomotor pattern after deafferentation might result from the artificial reduction in excitability of neurons rather than from the loss of specific sensory inputs.

Immobilized Preparations

The role of proprioceptive input from the limbs can be more systematically investigated by preventing activity in motor neurons from actually causing any movement. This is typically accomplished by paralyzing the muscles with *d*-tubocurarine, a competitive inhibitor of acetylcholine that blocks synaptic transmission at the neuromuscular junction.

When locomotion is initiated in such an immobilized preparation, often referred to as fictive locomotion, the motor nerves to flexor and extensor muscles fire alternately but no actual movement takes place and the proprioceptive afferents are not phasically excited. Thus the effect of proprioceptive reflexes is removed whereas tonic sensory input is preserved.

Because immobilized preparations allow intracellular and extracellular recording from neurons in the spinal cord, they are used to examine the synaptic events associated with locomotor activity and the organization of central and reflex pathways controlling locomotion.

Neonatal Rodent Preparation

The spinal cord is removed from a neonatal rat or mouse (0–5 days after birth) and placed in a saline bath, where it will generate coordinated bursts of activity in leg motor neurons when exposed to NMDA and serotonin (Figure 36–1C). This preparation allows more detailed analysis of the locations and roles of the specific neurons involved in rhythm generation, as well as pharmacological studies on the rhythm-generating network.

The ability to genetically modify neurons in the spinal cord of mice allows studies on the function of identified classes of neurons in these animals.
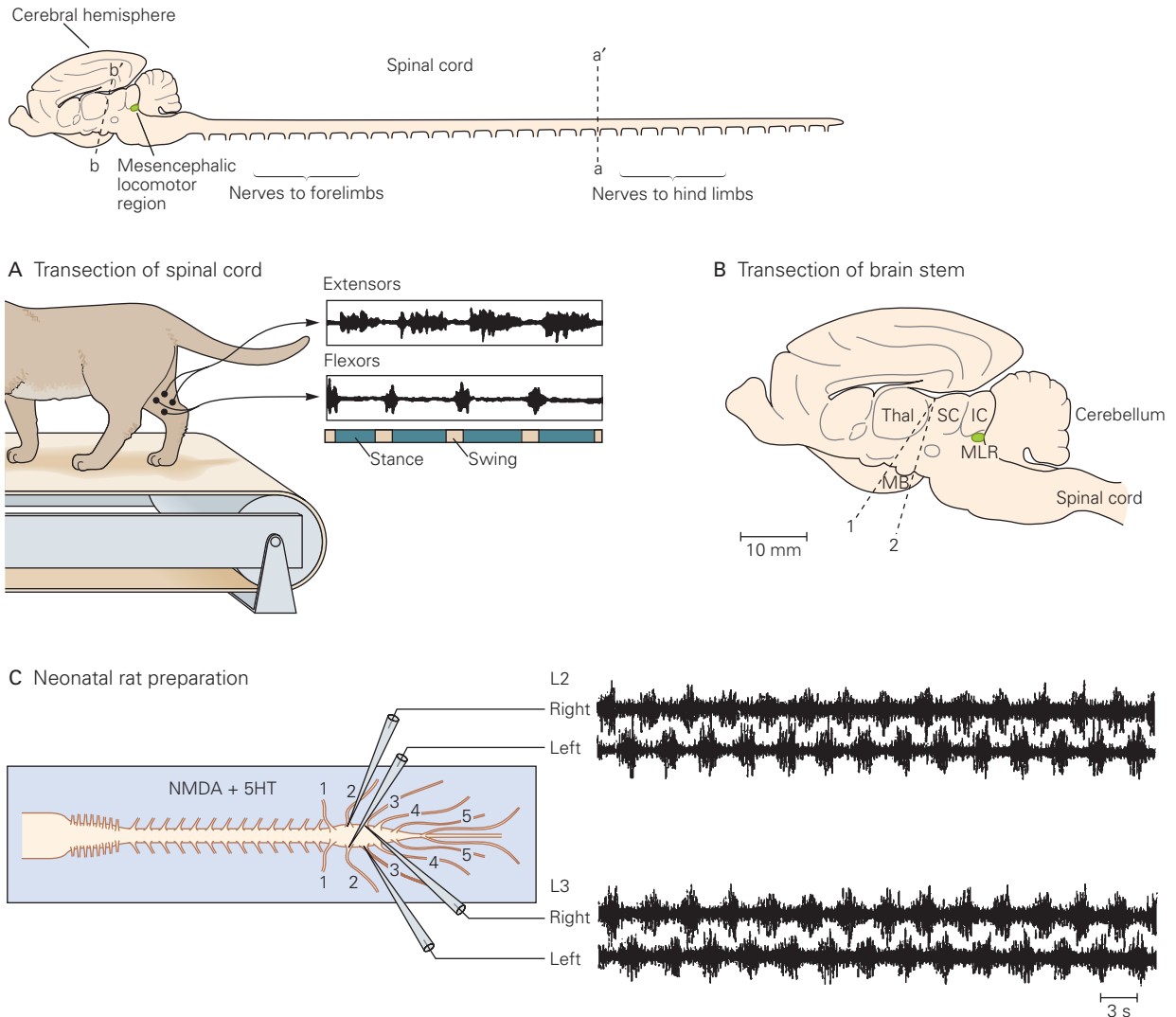

Figure 36–1 **A.** Transection of the spinal cord of a cat at the level a-a' isolates the segments of the cord with nerves that project to the hind limbs. The hind limbs are still able to step on a treadmill either immediately after recovery from surgery if adrenergic drugs are administered or a few weeks after surgery if the animal is exercised regularly on the treadmill. Transection of the brain stem at the level b-b' isolates the spinal cord and lower brain stem from the cerebral hemispheres.

B. Depending on the exact level of the transection of the brain stem, locomotion occurs spontaneously (1) or can be initiated by electrical stimulation of the mesencephalic locomotor region (**MLR**) (2). The mesencephalic locomo-

tor region is a small region of the brain stem close to the cuneiform nucleus approximately 6 mm below the surface of the inferior colliculus (**IC**). (**Thal**, thalamus; **SC**, superior colliculus; **MB**, mammillary body.)

C. The spinal cord is removed from a neonatal rat and placed in a saline bath. Addition of *N*-methyl-D-aspartate (NMDA) and serotonin (5-hydroxytryptamine, or 5-HT) to the bath elicits rhythmic bursting in the motor neurons supplying leg muscles, as shown in recordings from nerve roots of the second (L2) and third (L3) lumbar segments. Intracellular or tight-seal recordings can also be made from lumbar neurons during periods of rhythmic activity. (Adapted, with permission, from Cazalets, Borde, and Clarac 1995.)
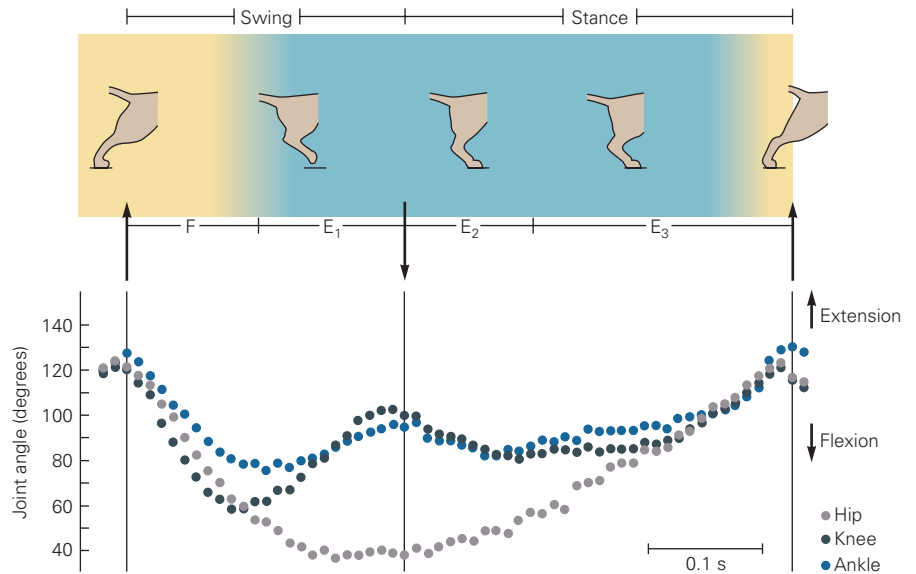
A Four phases of the step cycle

Figure 36–2 Stepping is produced by complex patterns of contractions in leg muscles.

A. The step cycle is divided into four phases: the flexion (F) and first extension (E$_1$) phases occur during swing, when the foot is off the ground, whereas second extension (E$_2$) and third extension (E$_3$) occur during stance, when the foot contacts the ground. Second extension is characterized by flexion at the knee and ankle as the leg begins to bear the animal's weight. The contracting knee and ankle extensor muscles lengthen during this phase. (Adapted, with permission, from Engberg and Lundberg 1969.)

B. Profiles of electrical activity in some of the hind leg flexor and extensor muscles in the cat during stepping. Although flexor and extensor muscles are generally active during swing and stance, respectively, the overall pattern of activity is complex in both timing and amplitude. (**IP**, iliopsoas; **LG** and **MG**, lateral and medial gastrocnemius; **PB**, posterior biceps; **RF**, rectus femoris; **Sart**$_m$ and **Sart**$_a$, medial and anterior sartorius; **SOL**, soleus; **ST**, semitendinosus; **TA**, tibialis anterior; **VL**, **VM**, and **VI**, vastus lateralis, medialis, and intermedialis.)

B Activity in hind leg muscles during the step cycle
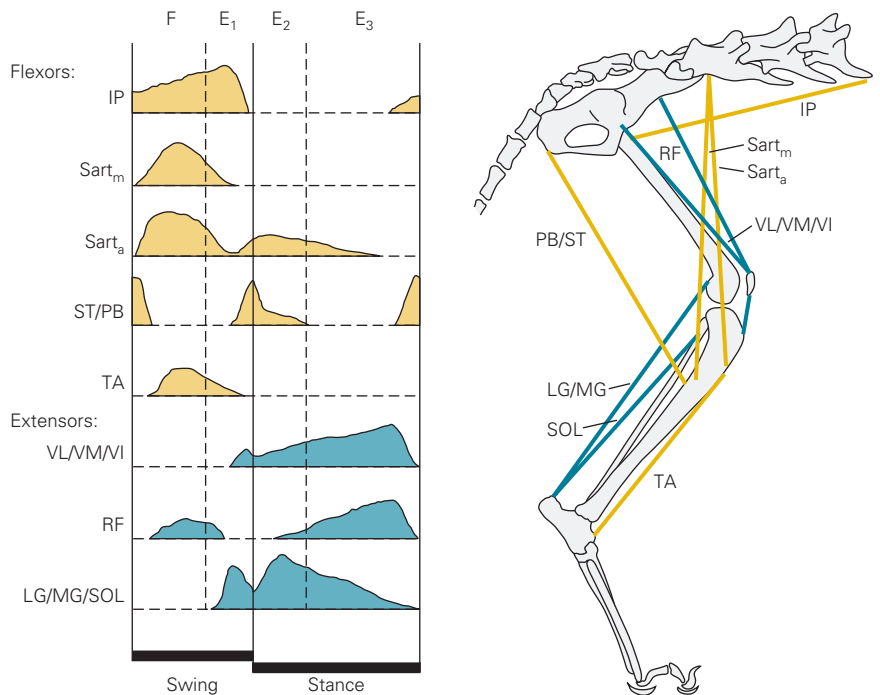
muscles contract during both swing and stance. Thus the motor pattern for stepping is not merely alternating flexion and extension at each joint, but a complex sequence of muscle contractions, each precisely timed and scaled to achieve a specific task in the act of locomotion.

The Motor Pattern for Stepping Is Organized at the Spinal Level

Transection of the spinal cord of quadrupeds initially causes complete paralysis of the hind legs. It does not, however, permanently abolish the capacity of hind

legs to make stepping movements: Hind leg stepping often recovers spontaneously over a period of a few weeks, particularly if the transection is made in young animals. Recovery of stepping in adult cats can be facilitated by daily training on a treadmill evoked by nonspecific cutaneous stimulation of the perineal region.

Electromyographic records of the hind leg muscles of chronic spinal cats during stepping are quite similar to those of normally walking animals. Many of the reflex responses that occur in normal animals can also be evoked in spinal animals. Spinal animals are not, however, able to maintain balance on the treadmill. Adequate control of balance requires descending signals from brain stem centers, such as the vestibular nuclei.

Contraction in Flexor and Extensor Muscles of the Hind Legs Is Controlled by Mutually Inhibiting Networks

From the studies by Graham Brown early in the 20th century we know that the isolated spinal cord can generate rhythmic bursts of reciprocal activity in flexor and extensor motor neurons of the hind legs even in the absence of sensory input (Figure 36–3). Graham Brown proposed that contractions in the flexor and extensor muscles are controlled by two systems of neurons, or *half-centers,* that mutually inhibit each other (Figure 36–4B).

According to Graham Brown, activity alternates between half-centers because of fatigue of the inhibitory connections. For example, if two half-centers receive tonic excitatory input, and the flexor half-center receives the stronger input, the flexor muscles will contract while the extensor half-center is inhibited. Then, as the inhibitory output fatigues, the extensor half-center's output will increase, causing inhibition of the flexor half-center and contraction of the extensor muscles until its inhibitory output fatigues. Thus the flexor and extensor muscles controlled by the two half-centers will alternately contract and relax as long as the half-centers receive sufficient tonic excitatory input.

The half-center hypothesis was supported by studies in the 1960s on the effects in spinal cats of the drug L-dihydroxyphenylalanine (L-DOPA), a precursor of the monoamine transmitters dopamine and norepinephrine. After the cats were treated with L-DOPA, brief

Figure 36–3 Rhythmic activity for stepping is generated by networks of neurons in the spinal cord. The existence of such spinal networks was first demonstrated by Thomas Graham Brown in 1911. Graham Brown developed an experimental preparation system in which dorsal roots were cut so that sensory information from the limbs could not reach the spinal cord. An original record from Graham Brown's study shows that rhythmic alternating contractions of ankle flexor (tibialis anterior) and extensor (gastrocnemius) muscles begin immediately after transection of the spinal cord.
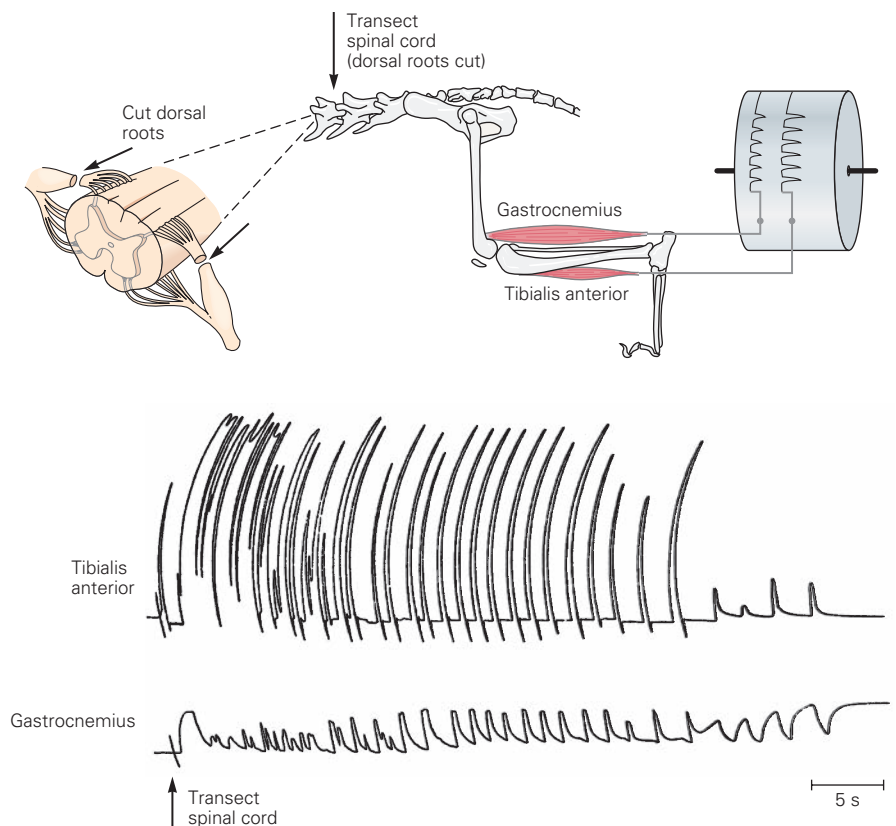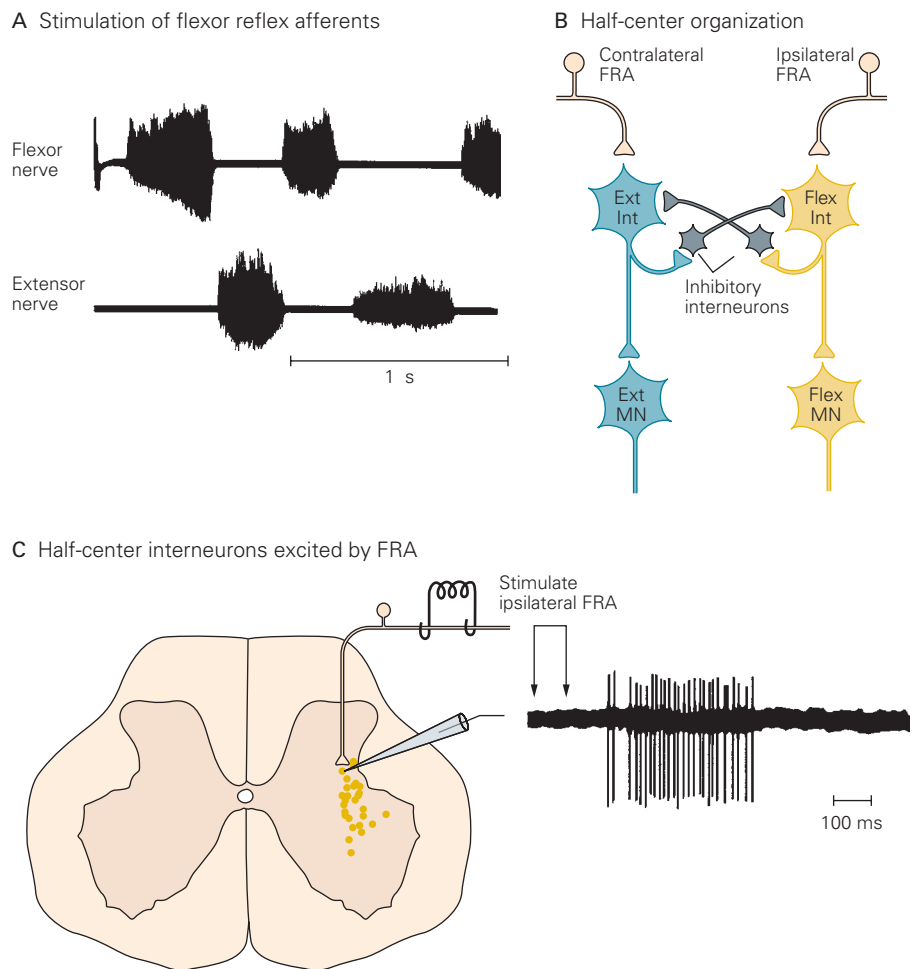
A Stimulation of flexor reflex afferents

B Half-center organization

Flexor
nerve

Extensor
nerve

1 s

Figure 36–4 Reciprocal activity in flexor and extensor motor neurons.

A. High-threshold cutaneous and muscle afferents called flexor reflex afferents (FRA) were electrically stimulated in spinal cats treated with L-DOPA (L-dihydroxyphenylalanine) and nialamide. Brief stimulation of ipsilateral FRAs evoked a short sequence of rhythmic activity in flexor and extensor motor neurons. (Adapted, with permission, from Jankowska et al. 1967a.)

B. Interneurons in the pathways mediating long-latency reflexes from the ipsilateral and contralateral FRAs mutually inhibit one another. This "half-center" organization of the flexor and extensor interneurons likely mediates rhythmic stepping.

C. Stimulation of the ipsilateral FRA evokes a delayed, long-lasting burst of activity in the half-center interneurons located in the intermediate region of the gray matter. (Adapted, with permission, from Jankowska et al. 1967b.)

Contralateral
FRA

Ipsilateral
FRA

Ext
Int

Flex
Int

Inhibitory
interneurons

Ext
MN

Flex
MN

C Half-center interneurons excited by FRA

Stimulate
ipsilateral FRA

100 ms

trains of electrical stimuli were applied to small-diameter sensory fibers from skin and muscle. These trains of stimuli evoked long-lasting bursts of activity in either flexor or extensor motor neurons, depending on whether ipsilateral or contralateral nerves were stimulated. The afferents producing these effects are collectively termed *flexor reflex afferents.* Additional administration of niala- mide, a drug that prolongs the action of norepinephrine released in the spinal cord, often resulted in short sequences of rhythmic reciprocal activity in flexor and extensor motor neurons (Figure 36–4A).

The system of interneurons generating flexor bursts was found to inhibit the system of interneurons generating the extensor bursts, and vice versa (Figure 36–4B). This organizational feature is consistent with Graham Brown's theory that mutually inhibiting "half- centers" produce the alternating burst activity in flexor and extensor motor neurons. The interneurons mediat- ing the burst patterns arising from stimulation of the

flexor reflex afferents have not been fully identified but they may include interneurons in the intermediate region of the gray matter in the sixth lumbar segment. Interneurons in this region produce prolonged bursts of activity in response to brief stimulation of either ipsilateral or contralateral flexor reflex afferents in spi- nal cats treated with L-DOPA (Figure 36–4C).

Central Pattern Generators Are Not Driven by Sensory Input

Neuronal spinal networks capable of generating rhyth- mic motor activity in the absence of rhythmic input from peripheral receptors are termed *central pattern generators* (Box 36–2). Largely because the mammalian nervous system is so complex, we lack detailed information on the neuronal circuitry and mechanisms for rhythm gen- eration by central pattern generators in the mammalian spinal cord. However, we have considerable knowledge

Box 36–2 Central Pattern Generators

A central pattern generator (CPG) is a neuronal network within the central nervous system that is capable of generating a rhythmic pattern of motor activity without phasic sensory input from peripheral receptors. CPGs have been identified and analyzed in more than 50 rhythmic motor systems, including those controlling such diverse behaviors as walking, swimming, feeding, respiration, and flying.

The motor pattern generated by a CPG under experimental conditions is sometimes very similar to the motor pattern produced during natural behavior, as in lamprey swimming (see Box 36–3), but there are often significant differences. In nature the basic pattern produced by a CPG is usually modified by sensory information and signals from other regions of the central nervous system.

The rhythmic motor activity generated by CPGs depends on three factors: (1) the cellular properties of individual nerve cells within the network, (2) the properties of the synaptic junctions between neurons, and (3) the pattern of interconnections between neurons (Table 36–1). Modulatory substances, usually amines or peptides, can alter cellular and synaptic properties, thereby enabling a CPG to generate a variety of motor patterns.

The simplest CPGs contain neurons that burst spontaneously. Such endogenous bursters can drive motor neurons, and some motor neurons are themselves endogenous bursters. Bursters are common in CPGs that produce continuous rhythms, such as those for respiration. They are also found in locomotor systems. Locomotion, however, is an episodic behavior, so bursters in locomotor systems must be regulated.

Bursting is often induced by modulatory input from neurons projecting to the rhythm generating system. Neuromodulatory inputs can also alter the cellular properties of neurons so that brief depolarizations lead to maintained depolarizations (plateau potentials) that long outlast the initial depolarization. Neurons with the capacity to generate plateau potentials have been found in a large number of CPGs, and in some systems they are essential for rhythm generation.

Rhythmicity does not always depend on bursting or plateau potentials. A simple network can generate rhythmic activity if the firing of some neurons can be enhanced or reduced according to some temporal pattern. One process is postinhibitory rebound, a brief increase in excitability of a neuron after the termination of inhibitory input. Two neurons that mutually inhibit each other can oscillate in an alternating fashion if each neuron has the property of postinhibitory rebound.

Other time-dependent processes include synaptic depression, delayed onset of activity after a depolarization (delayed excitation), and differences in the time course of synaptic actions through parallel pathways connecting two neurons.

Most CPGs produce a complex temporal pattern of activation of different groups of motor neurons. Sometimes the pattern can be divided into a number of distinct phases; even within a phase the activity of different motor neurons can be timed separately. The sequencing of activity in motor neurons is regulated by a number of mechanisms. Perhaps the simplest mechanism is mutual inhibition; interneurons that fire out of phase with each other are usually reciprocally coupled by inhibitory connections

Another mechanism is the rate of recovery from inhibition, which can influence the relative time of onset of activity in two neurons simultaneously released from inhibition. Finally, mutual excitation is an important mechanism for establishing synchronous firing in a group of neurons. Electrical synapses are often employed for mutual excitation, particularly when a rapid high-intensity burst within a group of neurons is needed.

Table 36–1 Building Blocks of Rhythm-Generating Networks

Cellular properties	Synaptic properties	Patterns of connection
Threshold	Sign	Reciprocal inhibition
Frequency-current relationship	Strength	Recurrent inhibition
Spike frequency adaptation	Time course	Parallel excitation and inhibition
Post-burst hyperpolarization	Transmission (electrical, chemical)	Mutual excitation
Delayed excitation	Release mechanisms (spike, graded signal)	
Post-inhibitory rebound		
Plateau potentials	Multicomponent postsynaptic potentials	
Bursting (endogenous, conditional)	Facilitation/depression (short-term, long-term)	

about the cellular, synaptic, and network properties of central pattern generators in invertebrates and lower vertebrates, which have less complex nervous systems than mammals. For example, the analysis by Sten Grillner of the central pattern generator controlling swimming in the lamprey has provided considerable insight into the mechanisms of rhythm generation in vertebrate motor systems (Box 36–3).

Recent studies using the spinal cord of the neonatal rat have identified several classes of rhythmically active interneurons and demonstrated that some of these interneurons can generate sustained membrane


Box 36–3 Lamprey Swimming

One of the best-analyzed central pattern generators is that for lamprey swimming. Lampreys swim by alternating muscle contrations on the two sides of each body segment (Figure 36–5). Each segment contains a neural network capable of generating rhythmic, alternating activity in motor neurons on the two sides (Figure 36–6).

On each side of the network excitatory interneurons drive the motor neurons and two classes of inhibitory interneurons, commissural and local. The axons of the commissural interneurons cross the midline and inhibit all neurons in the contralateral half of the network, ensuring that when muscles on one side of the network are active, muscles on the other side are silent. The local inhibitory interneurons inhibit the commissural interneurons on the same side.

A number of cellular and synaptic mechanisms are involved in the initiation and termination of activity on one side of the network. One important mechanism in the initiation of activity is the opening of NMDA-type glutamate receptor-channels. Once the inhibition from contralateral commissural interneurons is terminated, the NMDA-type receptor-channels in all ipsilateral neurons are opened by a brief depolarization (post-inhibitory rebound) and the voltage-dependency of the channels leads to plateau potentials.
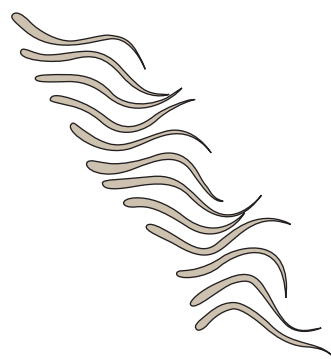
Rhythm in intact animal
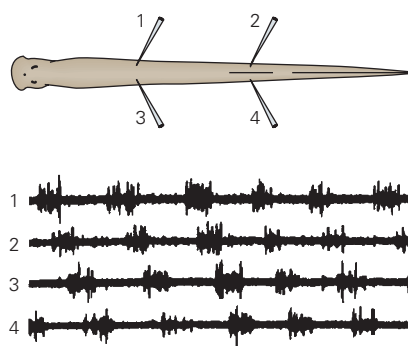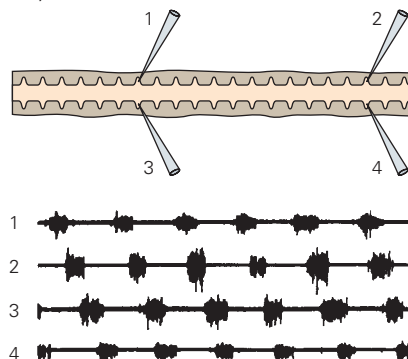
Rhythm in isolated cord

Figure 36–5 The lamprey swims by means of a wave of muscle contractions traveling down one side of the body 180 degrees out of phase with a similar traveling wave on the opposite side. This pattern is evident in electromyogram recordings from four locations along the animal during normal swimming. A similar pattern is recorded from four spinal roots in an isolated cord. (Adapted, with permission, from Grillner et al. 1987.)

depolarizations (*plateau potentials*) in response to weak synaptic input. Because this active membrane property is known to be important for rhythm generation in simpler systems, it is likely that it also contributes to rhythm generation in the mammalian spinal cord.

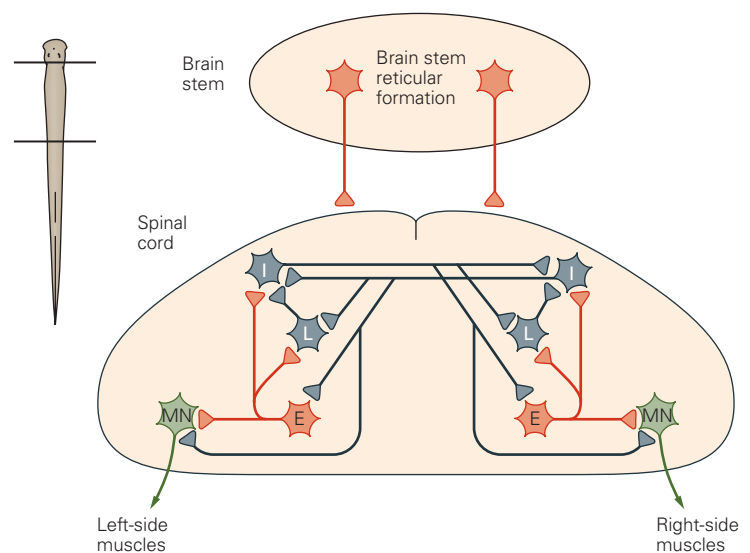## Spinal Networks Can Generate Complex Locomotor Patterns

The locomotor patterns generated in deafferented or immobilized spinal animals are generally much simpler than normal stepping patterns. Usually they

Activation of low-voltage Ca^{2+} channels further strengthens the depolarization. The influx of Ca^{2+} through these channels and the NMDA-type receptor-channels activates calcium-dependent K^+ channels. The resultant increase in K^+ conductance terminates the plateau potentials and so contributes to the termination of activity.

Two additional mechanisms contribute to the termination of activity in each half of the network. One is

a progressive decline in the discharge rate of the neurons resulting from the summation of slow afterhyperpolarizations. The other is delayed excitation of the local inhibitory interneurons. When excited, these interneurons inhibit the commissural interneurons (Figure 36–6), thereby removing inhibition from the contralateral half of the network and enabling it to become active.

Figure 36–6 Each body segment of the lamprey contains a neuronal network responsible for the motor pattern in that segment. Activity in each segmental network is initiated by activity in glutamatergic axons descending from the brain stem reticular formation. The reticulospinal neurons increase the excitability of all neurons in a segmental network by activation of both NMDA-type and non–NMDA-type glutamate receptors. On each side of the network excitatory interneurons (**E**) drive the motor neurons (**MN**) and two classes of inhibitory interneurons, commissural (**I**) and local (**L**). (Adapted, with permission, from Grillner et al. 1995.)

A Spinal cat immobilized

B Decerebrate cat walking

C Decerebrate cat immobilized
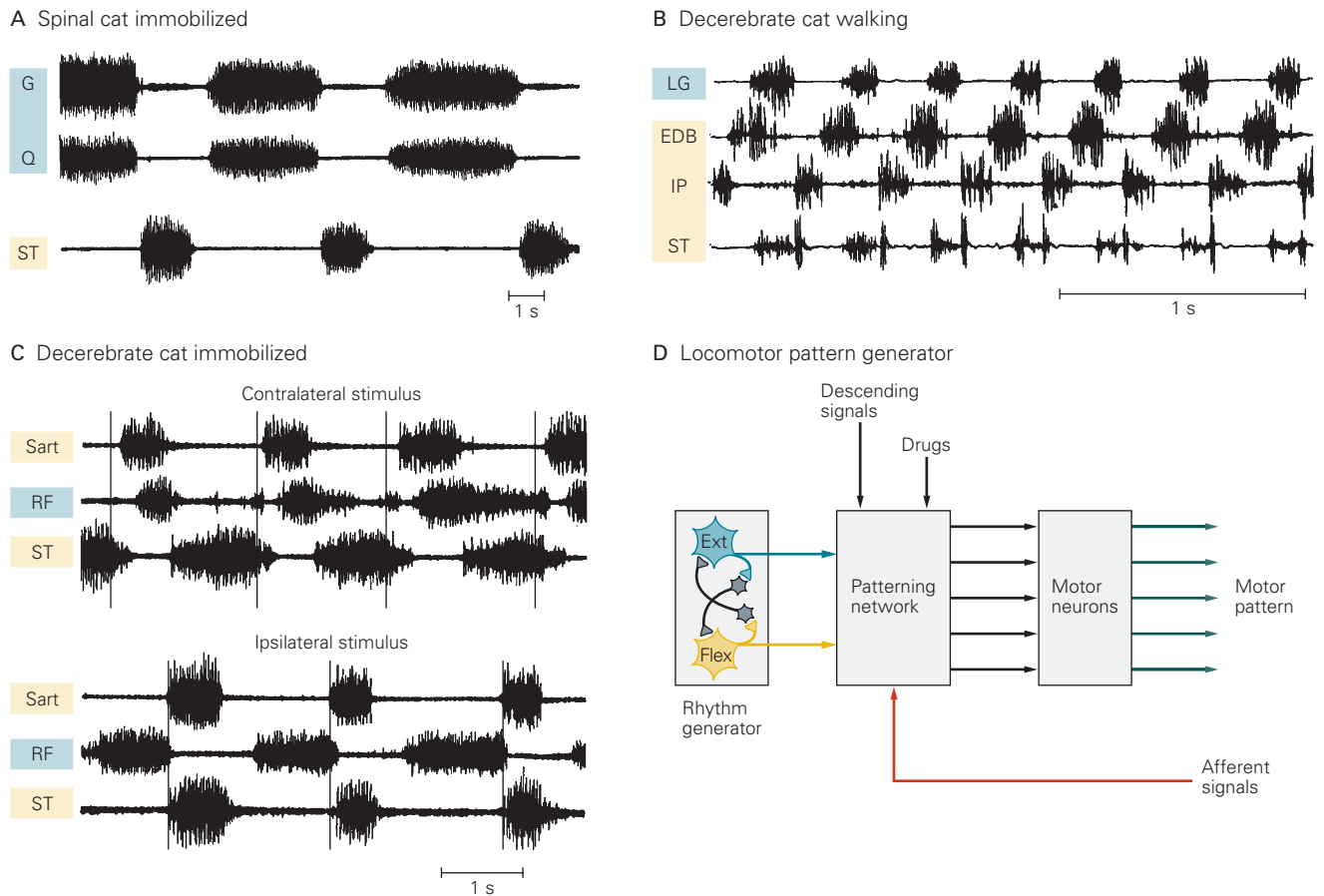

D Locomotor pattern generator

Figure 36–7 A variety of motor patterns can be generated without phasic sensory input.

A. A reciprocal pattern of activity in nerves innervating flexor and extensor muscles is seen in an immobilized spinal cat treated with L-DOPA and nialamide. (**G**, gastrocnemius; **Q**, quadriceps; **ST**, semitendinosus.) (Adapted, with permission, from Edgerton et al. 1976.)

B. A complex motor pattern is recorded from a walking decerebrate cat with deafferented hind-leg muscles. (**LG**, lateral gastrocnemius; **EDB**, extensor digitorum brevis; **IP**, iliopsoas; **ST**, semitendinosus.) (Adapted, with permission, from Grillner and Zangger 1984.)

C. Fictive motor patterns are recorded in an immobilized decorticate cat when either the ipsilateral or contralateral paw is squeezed. The patterns are radically different. (**Sart**, sartorius; **RF**, rectus femoris; **ST**, semitendinosus.) (Adapted, with permission, from Perret and Cabelguen 1980.)

D. This schematic description of a locomotor pattern generator is based on recent studies on fictive locomotion in decerebrate cats. The basic rhythmic pattern is produced by mutually inhibiting flexor and extensor half-centers. The interneurons of these half-centers drive the motor neurons through an intermediate system of interneurons (patterning network) that control the timing of activation of different classes of motor neurons. Descending signals, drugs, or afferent signals can modify the temporal motor activity pattern by altering the functioning of interneurons in the patterning network. (Adapted, with permission, from Rybak et al. 2006.)

consist of alternating bursts of activity in flexor and extensor motor neurons (Figure 36–7A). More complex locomotor patterns can be generated in immobilized spinal animals after a period of training or through the application of additional drugs such as 4-aminopyridine. Moreover, in decerebrate animals elaborate locomotor patterns can be produced in hind limb motor neurons after deafferentation (Figure 36–7B). These patterns resemble those recorded in the same animals before deafferentation. Finally, a variety of patterns can be generated in immobilized decerebrate animals, and these patterns can be altered significantly by changing the level of tonic sensory input (Figure 36–7C).

From these observations it is clear that the spinal pattern-generating network for each leg can produce a variety of motor patterns. Which pattern is generated depends on many factors, such as the supraspinal and tonic sensory inputs to the spinal pattern generators as well as the drugs used to experimentally initiate rhythmicity. This functional flexibility may be explained by a scheme in which mutually inhibiting half-centers produce the basic rhythmicity and establish a general pattern of reciprocal activity in flexor and extensor motor neurons, whereas the details of the temporal pattern are established by a network of interneurons (the patterning network) connecting the half-centers and motor neurons (Figure 36–7D).

Sensory Input from Moving Limbs Regulates Stepping

Although normal walking is automatic, it is not necessarily stereotyped. Mammals constantly use sensory input to adjust their stepping patterns to variations in terrain and to anticipated and unexpected conditions. This input is provided predominantly by three sensory systems: the visual, vestibular, and somatosensory systems. Proprioceptors in muscles and joints provide information about body movements and are involved in the automatic regulation of stepping. Cutaneous receptors in the skin, sometimes referred to as exteroceptors, adjust stepping to external stimuli and can also provide important feedback about body movements.

Proprioception Regulates the Timing and Amplitude of Stepping

One of the clearest indications that somatosensory signals from the limbs regulate the step cycle is that the rate of stepping in spinal and decerebrate cats matches the speed of the motorized treadmill belt on which they tread. Specifically, afferent input regulates the duration of the stance phase. As the stepping rate increases, the stance phase becomes shorter while the swing phase remains relatively constant. This observation suggests that some form of sensory input signals the end of stance and thus leads to the initiation of swing.

Sherrington was the first to propose that proprioceptors in muscles acting at the hip are primarily responsible for regulating the stance phase. He noticed that rapid extension at the hip joint, but not at the knee and ankle joints, led to contractions in the hip flexor muscles of chronic spinal cats and dogs. More recent studies have found that preventing hip extension in a limb

suppresses stepping in that limb, whereas rhythmically moving the hip can entrain the locomotor rhythm, that is, cause the timing of the neural output to match the rhythm of the externally imposed movements.

During entrainment a burst of activity in hip flexor motor neurons is initiated in synchrony with hip extension (Figure 36–8A). The afferent fibers that signal hip angle for swing initiation arise from muscle spindles in the hip flexor muscles. In decerebrate animals stretching these muscles to mimic the lengthening that occurs at the end of the stance phase inhibits the extensor half-center and thus facilitates the initiation of burst activity in flexor motor neurons during walking (Figure 36–8B).

Other important proprioceptive signals for regulating the step cycle arise from proprioceptors in extensor muscles. Electrical stimulation of sensory fibers from Golgi tendon organs and muscle spindles prolongs the stance phase, often delaying the onset of swing until the stimulus has ended (Figure 36–9A). Sensory fibers from both types of receptors are active during stance.

The intensity of the signal from the Golgi tendon organs is related to the load carried by the leg. Golgi tendon organs have an excitatory action on ankle extensor motor neurons during walking but an inhibitory action when the body is at rest (see Chapter 35). The functional consequence of this reflex reversal is that the swing phase is not initiated until the extensor muscles are unloaded and the forces exerted by these muscles are low, as signaled by a decrease in activity from the Golgi tendon organs. Unloading of extensor muscles normally occurs near the end of stance, when the animal's weight is borne by the other legs and the extensor muscles are shortened and thus unable to produce high forces.

In addition to regulating the transition from stance to swing, proprioceptive information from muscle spindles and Golgi tendon organs contributes significantly to the generation of burst activity in extensor motor neurons. Reducing this sensory input in cats diminishes the level of extensor activity by more than half; in humans it has been estimated that up to 30% of the activity of ankle extensor motor neurons is caused by feedback from the extensor muscles.

At least three excitatory pathways transmit sensory information from extensor muscles to extensor motor neurons: a monosynaptic pathway from primary muscle spindles (group Ia afferents), a disynaptic pathway from primary muscle spindles and Golgi tendon organs (group Ia and Ib afferents), and a polysynaptic pathway from primary muscle spindles and Golgi tendon organs that includes interneurons in the central pattern generator (Figure 36–9B). The continuous regulation of the
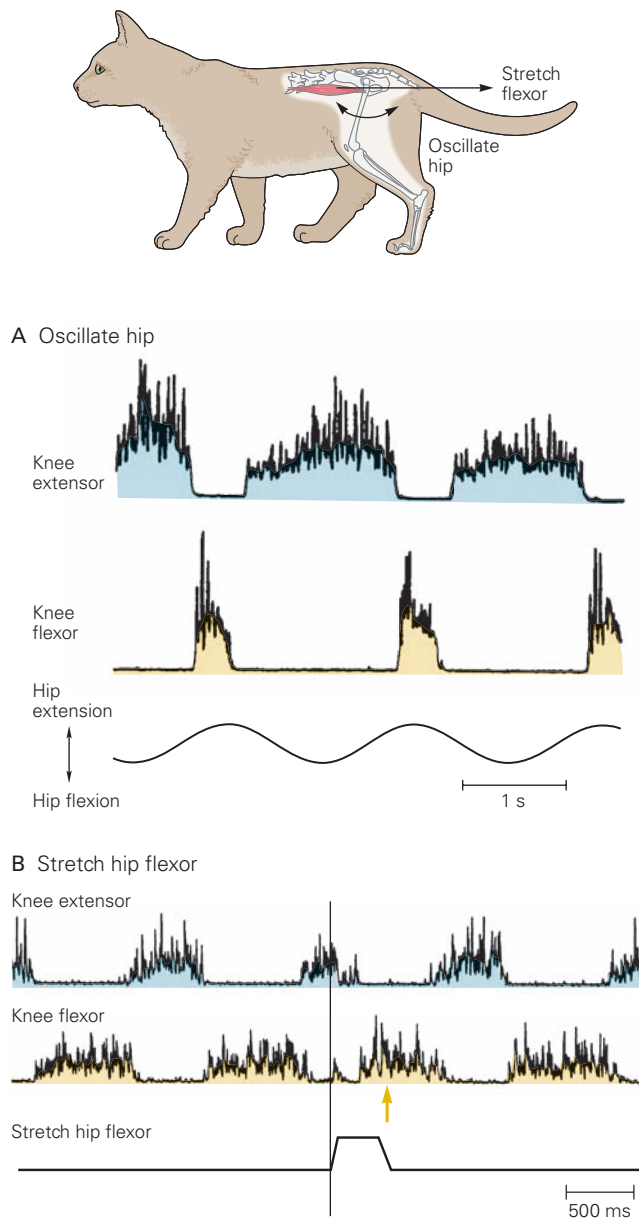
A Oscillate hip

Knee
extensor

Knee
flexor

Hip
extension

Hip flexion

1 s

B Stretch hip flexor

Knee extensor

Knee flexor

Stretch hip flexor

500 ms

Figure 36–8 Information on hip extension controls the transition from stance to swing.

A. In an immobilized decerebrate cat oscillating movement around the hip joint entrains the fictive locomotor pattern in knee extensor and flexor motor neurons. The flexor bursts, corresponding to the swing phase, are generated when the hip is extended. (Adapted, with permission, from Kriellaars et al. 1994.)

B. In a walking decerebrate cat stretching of the hip flexor muscle (iliopsoas) inhibits knee extensor activity allowing knee flexor activity to begin earlier. The **arrow** in the knee-flexor record indicates the expected onset of knee flexor activity had the hip flexor muscle not been stretched. Activation of sensory fibers from muscle spindles in the hip flexor muscle is responsible for this effect. (Adapted, with permission, from Hiebert et al. 1996.)

level of extensor activity by proprioceptive feedback presumably allows automatic adjustment of force and length in extensor muscles in response to unexpected unloading and loading of the leg.

Sensory Input from the Skin Allows Stepping to Adjust to Unexpected Obstacles

Sensory receptors in the skin have a powerful influence on the central pattern generator for walking. One important function of these receptors is to detect obstacles and adjust stepping movements to avoid them. A well-studied example is the stumbling-corrective reaction in cats. A mild mechanical stimulus applied to the dorsal part of the paw during the swing phase produces excitation of flexor motor neurons and inhibition of extensor motor neurons, leading to rapid flexion of the paw away from the stimulus and elevation of the leg in an attempt to step over the object. Because this corrective response is readily observed in spinal cats, it must be produced to a large extent by circuits entirely contained within the spinal cord.

One of the interesting features of the stumbling-corrective reaction is that corrective flexion movements are produced only if the paw is stimulated during the swing phase. An identical stimulus applied during the stance phase produces the opposite response, excitation of extensor muscles that reinforces the ongoing extensor activity. This extensor action is appropriate; if a flexion reflex were produced during the stance phase the animal might collapse because it is being supported by the limb. This is an example of a *phase-dependent reflex reversal:* The same stimulus excites one group of motor neurons during one phase of locomotion but activates the antagonist motor neurons during another phase.

Descending Pathways Are Necessary for Initiation and Adaptive Control of Stepping

Although the basic motor pattern for stepping is generated in the spinal cord, fine control of stepping movements involves many regions of the brain, including the motor cortex, cerebellum, and various sites within the brain stem. Many neurons in each of these regions are rhythmically active during locomotor activity and hence participate in the production of the normal motor pattern. Each region, however, plays a different role in the regulation of locomotor function.

Supraspinal regulation of stepping can be divided into three functional systems. One activates the spinal locomotor system, initiates walking, and controls the
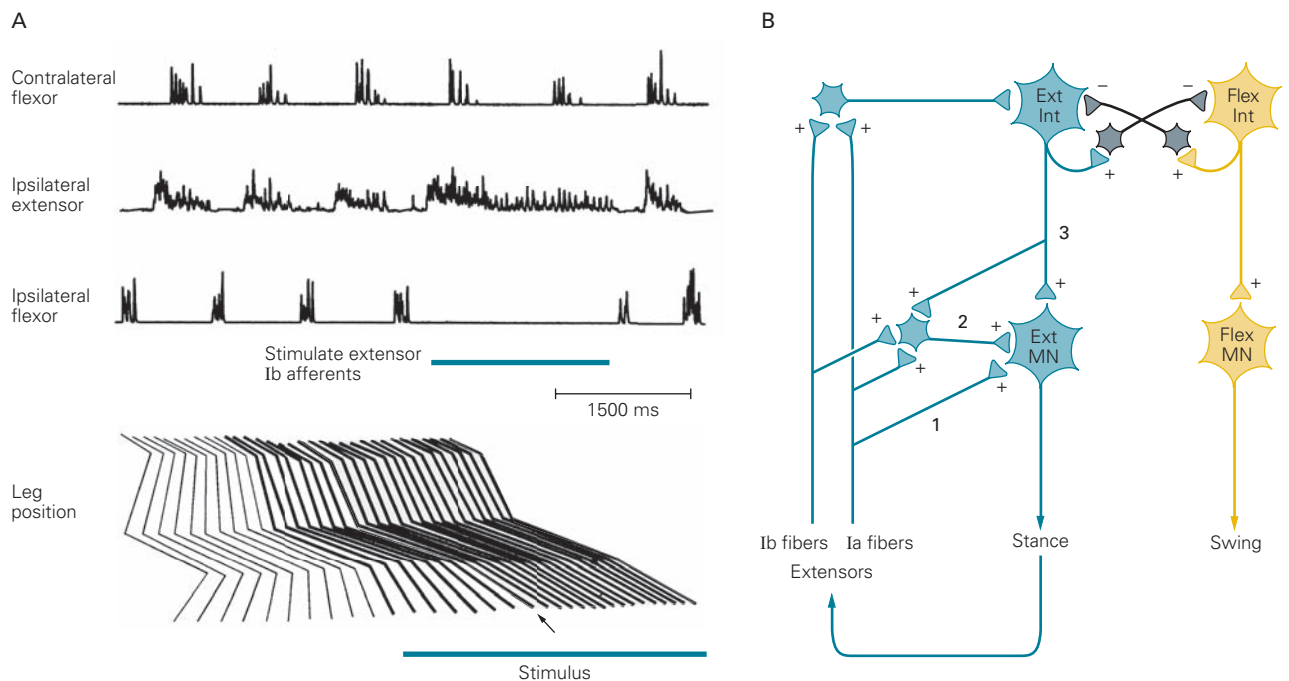
Figure 36–9 The swing phase of walking is initiated by sensory feedback from extensor muscles.

A. In a decerebrate cat electrical stimulation of group I sensory fibers from ankle extensor muscles inhibits bursting in ipsilateral flexors and prolongs the burst in the ipsilateral extensors during walking. The timing of contralateral flexor activity is not altered. Stimulating group I fibers from the extensors prevents initiation of the swing phase, as can be seen in the position of the leg during the time the fibers were stimulated. The **arrow** shows the point at which the swing phase would normally have occurred had the extensor afferents not been stimulated. (Adapted, with permission, from Whelan, Hiebert, and Pearson 1995.)

B. Afferent pathway from extensor muscles regulating stance. Two mutually inhibiting groups of extensor and flexor interneurons constitute a central pattern generator. Feedback from extensor muscles increases the level of activity in extensor motor neurons during stance and maintains extensor activity when the extensor muscles are loaded. The feedback is relayed through three excitatory (+) pathways: monosynaptic connections from Ia fibers to extensor motor neurons (1); disynaptic connections from Ia and Ib fibers (2); and a polysynaptic excitatory pathway through the extensor interneurons (3).

overall speed of locomotion; another refines the motor pattern in response to feedback from the limbs; and the third visually guides limb movement (Figure 36–10).

Pathways from the Brain Stem Initiate Walking and Control Its Speed

In their seminal studies of decerebrate cats, Mark Shik, Fidor Severin, and Grigori Orlovsky found that tonic electrical stimulation of the mesencephalic locomotor region initiates stepping when decerebrate animals are placed on a treadmill. The mesencephalic locomotor region is situated approximately 6 mm ventral to the inferior colliculus (Figure 36–11A), close to the cuneiform nucleus. The rhythm of the locomotor pattern is related only to the intensity of electrical stimulation, not

to its pattern. Weak stimulation produces a slow walking gait, which accelerates as the intensity increases; progressively stronger stimulation produces trotting and finally galloping (Figure 36–11B).

The transition from trotting to galloping is especially interesting for it involves a shift from an out-of-phase relationship between left and right legs in trotting to an in-phase relationship in galloping. This shift in interlimb coordination is also observed in spinal cats walking on a motorized treadmill as the speed is increased. Therefore it is most likely implemented by local circuits in the spinal cord.

In addition to the mesencephalic locomotor region, several other motor regions of the brain can produce locomotion when stimulated electrically. These include a subthalamic locomotor region and a nucleus
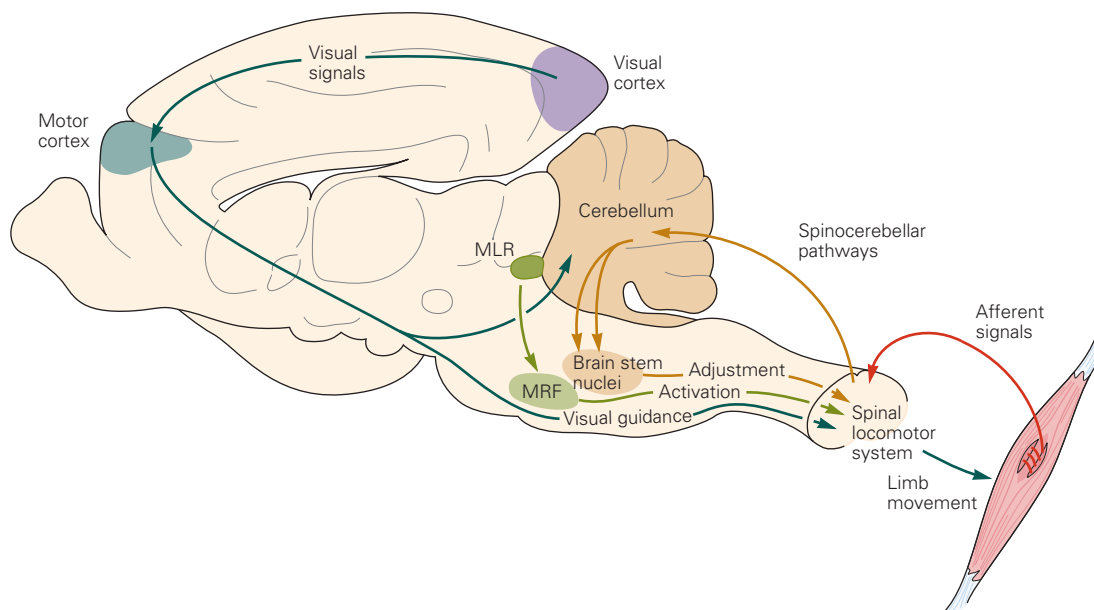
Figure 36–10 The brain stem and motor cortex control loco- motion. The spinal locomotor system is activated by signals from the mesencephalic locomotor region (**MLR**) relayed by neurons in the medial reticular formation (**MRF**). The cerebel- lum receives signals from both peripheral receptors and spinal central pattern generators and adjusts the locomotor pattern through connections in brain stem nuclei. Visual information conveyed to the motor cortex can also modify stepping movements.

in the pontine reticular formation (pontine peduncu- lar nucleus). How these different brain stem regions interact in the normal control of locomotion is not yet known.

How are signals from locomotor regions of the brain stem transmitted to patterning networks in the spinal cord? Because application of adrenergic drugs is often sufficient to initiate stepping in acute spinal animals, an early hypothesis was that the initiation and maintenance of locomotor activity depends on activity in the descending noradrenergic pathway from the locus ceruleus or the descending serotonergic pathway from the raphe nucleus. However, because locomotor activity can be evoked after depletion of norepinephrine and serotonin, neither of these amin- ergic pathways is essential for locomotion. The cur- rent view is that these transmitters are modulators that regulate the magnitude and timing of motor neuron activity in the locomotor networks in the spinal cord. Although adrenergic drugs can initiate stepping move- ments in the spinal animal, aminergic neurons may not serve this function in nature.

Clues about the identity of the descending system that initiates locomotor activity came first from stud- ies on the neonatal rat and lamprey. Administration of glutamate receptor agonists to the isolated spinal cord was found to initiate locomotor activity. In decerebrate cats administration of agonists to the NMDA-type gluta- mate receptors in the spinal cord initiates locomotor activity similar to that evoked by electrical stimulation of the mesencephalic locomotor region. The applica- tion of glutamate receptor antagonists prevents this response. These observations suggest that glutamatergic pathways are involved in initiating locomotor activity.

Considerable research has been devoted to iden- tifying the origin and course of the descending path- ways that initiate locomotor activity. The central pattern generators in the spinal cord cannot be directly activated by neurons in the nuclei near the mesen- cephalic locomotor region, for the axons of these neu- rons do not descend directly to the cord. Instead, the mesencephalic motor neurons form connections with neurons in the medullary reticular formation, whose axons descend in the ventrolateral region of the spi- nal cord (Figure 36–11A). These neurons are excited by stimulation of the mesencephalic locomotor region, and transection of their axons in the ventrolateral funiculus of the spinal cord prevents stimulation of the mesencephalic locomotor region from initiating loco- motor activity. Thus current evidence indicates that the

signals that activate locomotion and control its speed are transmitted to the spinal cord by glutamatergic neurons with axons that travel in ventral reticulospinal pathways.

The Cerebellum Fine-Tunes Locomotor Patterns by Regulating the Timing and Intensity of Descending Signals

Damage to the cerebellum results in marked abnormalities in locomotor movements, including a widened base of support, impaired coordination of joints, and abnormal coupling between limbs during stepping. These symptoms are called *ataxia* (see Chapter 42). Ataxic walking resembles a drunken gait. Because ataxic gait is apparent in patients with cerebellar lesions even when they are walking on level surfaces, we can conclude that the cerebellum is involved in regulating all stepping movements.

The cerebellum receives sensory information about the actual stepping movements as well as information on the state of the central pattern generators through
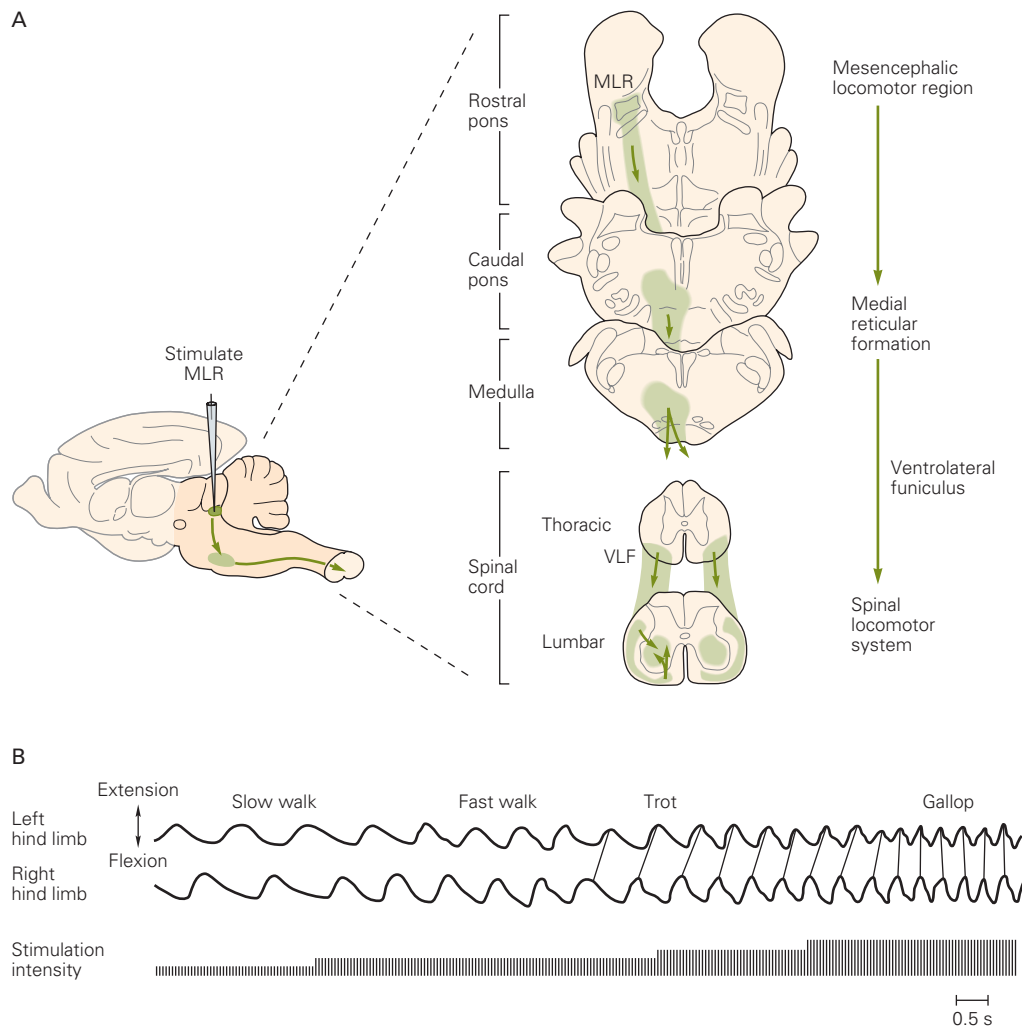

Figure 36–11 The mesencephalic locomotor region modifies stepping patterns.

A. Stimulation of the mesencephalic locomotor region (**MLR**) excites interneurons in the medial reticular formation whose axons descend in the ventrolateral funiculus (**VLF**) to the spinal locomotor system. (Adapted, with permission, from Mori et al. 1992.)

B. When the strength of stimulation of the mesencephalic locomotor region in a decerebrate cat walking on a treadmill is gradually increased, the gait and rate of stepping change from slow walking to trotting and finally to galloping. As the cat progresses from trotting to galloping, the hind limbs shift from alternating to simultaneous flexion and extension.

two ascending pathways. For the hind legs of the cat these are the dorsal and ventral spinocerebellar tracts. Neurons in the dorsal tract are strongly activated by numerous leg proprioceptors and thus provide the cerebellum with detailed information about the mechanical state of the hind legs. In contrast, neurons in the ventral tract are activated primarily by interneurons in the central pattern generator, thus providing the cerebellum with information about the state of the spinal locomotor network. The cerebellum also receives input from the motor cortex and other forebrain regions related to locomotor function.

It is thought that the cerebellum compares actual movements of the legs—proprioceptive signals in the dorsal spinocerebellar tract—with intended movements—the central commands conveyed in the ventral spinocerebellar tract and collaterals of corticospinal tract neurons. When these two types of information differ, representing an error, the cerebellum computes corrective signals and sends these to various brain stem nuclei.

During walking the cerebellum influences several brain stem nuclei, including the vestibular nuclei, red nucleus, and nuclei in the medullary reticular formation. The signals from the cerebellum to the vestibular nuclei during walking are likely used to regulate balance by integrating information about the position and movement of the head derived from the vestibular system with proprioceptive information about movements of the legs.

The Motor Cortex Uses Visual Information to Control Precise Stepping Movements

Normal walking is often guided by vision, and the motor cortex is essential for visually guided movement. Experimental lesions of the motor cortex do not prevent animals from walking on a smooth floor or even on smooth inclines, but they severely impair tasks requiring a high degree of visuomotor coordination, such as walking on the rungs of a horizontal ladder, stepping over a series of barriers, and stepping over single objects placed on a treadmill belt. Such "skilled walking" is associated with considerable modulation in the activity of a large number of neurons in the motor cortex (Figure 36–12).

Many of these neurons project directly to the spinal cord and thus may regulate the activity of interneurons in the central pattern generator for locomotion, thereby adapting the timing and magnitude of motor activity to a specific task. Electrical stimulation of either the motor cortex or the corticospinal tract in normal walking cats influences the timing of locomotor activity;

these effects are generally stronger than those elicited by stimulation of brain stem regions.

Planning and Coordination of Visually Guided Movements Involves the Posterior Parietal Cortex

When humans and animals approach an obstacle in their pathway they must adjust their stepping to either move around the obstacle or step over it. These adjustments begin two or three steps before the obstacle is reached. Recent studies by Trevor Drew and his colleagues have shown that the posterior parietal cortex has an essential role in planning these adjustments.

Small lesions in this region cause walking cats to misplace the positioning of their paws as they approach an obstacle, and to increase the probability that one or more legs contact the obstacle as they step over it. Recordings in the parietal cortex have identified sets of neurons that could be involved in the planning and coordination of stepping movements. Some neurons increase their activity as an animal approaches an obstacle, whereas others maintain their activity when an obstacle passes under the animal (Figure 36–13).

Visual information about the size and location of an obstacle is registered as the obstacle is approached, and this information is stored in working memory, a form of short-term memory, to guide the legs. In humans obstructing vision one stride before an obstacle is encountered does not influence foot clearance over the obstacle. In quadrupeds, however, such working memory is necessary because an obstacle is no longer within the visual field by the time the hind legs are stepping over it.

Many of the features of the working memory for guiding the legs have recently been established in cats. The main features are that the forelegs must step over the obstacle in order for the memory to be established, the trajectories of the hind legs are scaled appropriately for the height of the obstacle and for the relative positions of the hind paws and the obstacle, and the memory persists for many minutes without declining.

The neurobiological mechanisms underlying this form of memory remain to be established, but the persistence of the memory appears to depend upon neuronal systems in the posterior parietal cortex. With bilateral lesions of the medial posterior parietal cortex the memory is completely abolished after a few seconds (Figure 36–14). Complementing this observation is the recent identification by Trevor Drew and colleagues of neurons in the posterior parietal cortex whose activity is elevated while the cat straddles an obstacle with the forelegs on one side and the hind legs on the other side.
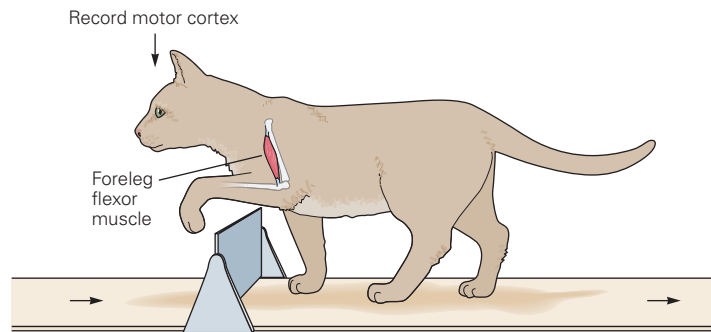
Figure 36–12 Stepping movements are adapted by visual input in the motor cortex. When a normal cat steps over a visible object fixed to the belt of a treadmill, neurons in the motor cortex increase in activity. This increase in cortical activity is associated with enhanced activity in foreleg muscles, as seen in the electromyograms (**EMG**). (Adapted, with permission, from Drew 1988.)
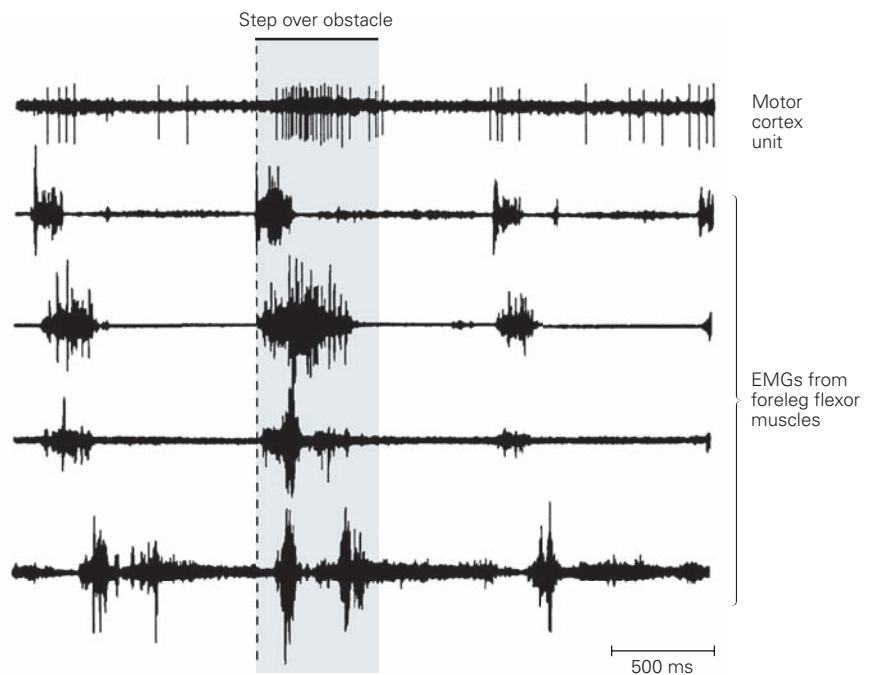
Human Walking May Involve Spinal Pattern Generators

Unlike spinal cats and other quadrupeds, humans with spinal cord transection generally are not able to walk spontaneously. Nevertheless, some observations of patients with spinal cord injury parallel the findings from studies of spinal cats. In one striking case a patient with nearly complete transection of the spinal cord showed uncontrollable, spontaneous, rhythmic movements of the legs when the hips were extended. This behavior closely parallels the rhythmic stepping movements in chronic spinal cats. In another study on a few patients with severe spinal cord injury, stepping on a treadmill was improved by clonidine, a drug influencing biogenic amines.

Compelling evidence for the existence of spinal rhythm-generating networks in humans comes from studies of development. Human infants make rhythmic stepping movements immediately after birth if held upright and moved over a horizontal surface. This strongly suggests that some of the basic neuronal circuits for locomotion are innate. Because stepping can occur in infants who lack cerebral hemispheres (anencephaly), these circuits must be located at or below the brain stem, perhaps entirely within the spinal cord.

During the first year of life, as automatic stepping is transformed into functional walking, these basic circuits are thought to be brought under supraspinal control in two ways. First, the infant develops voluntary control of locomotion. From what we know about the neuronal mechanisms in the cat, this ability could depend on the
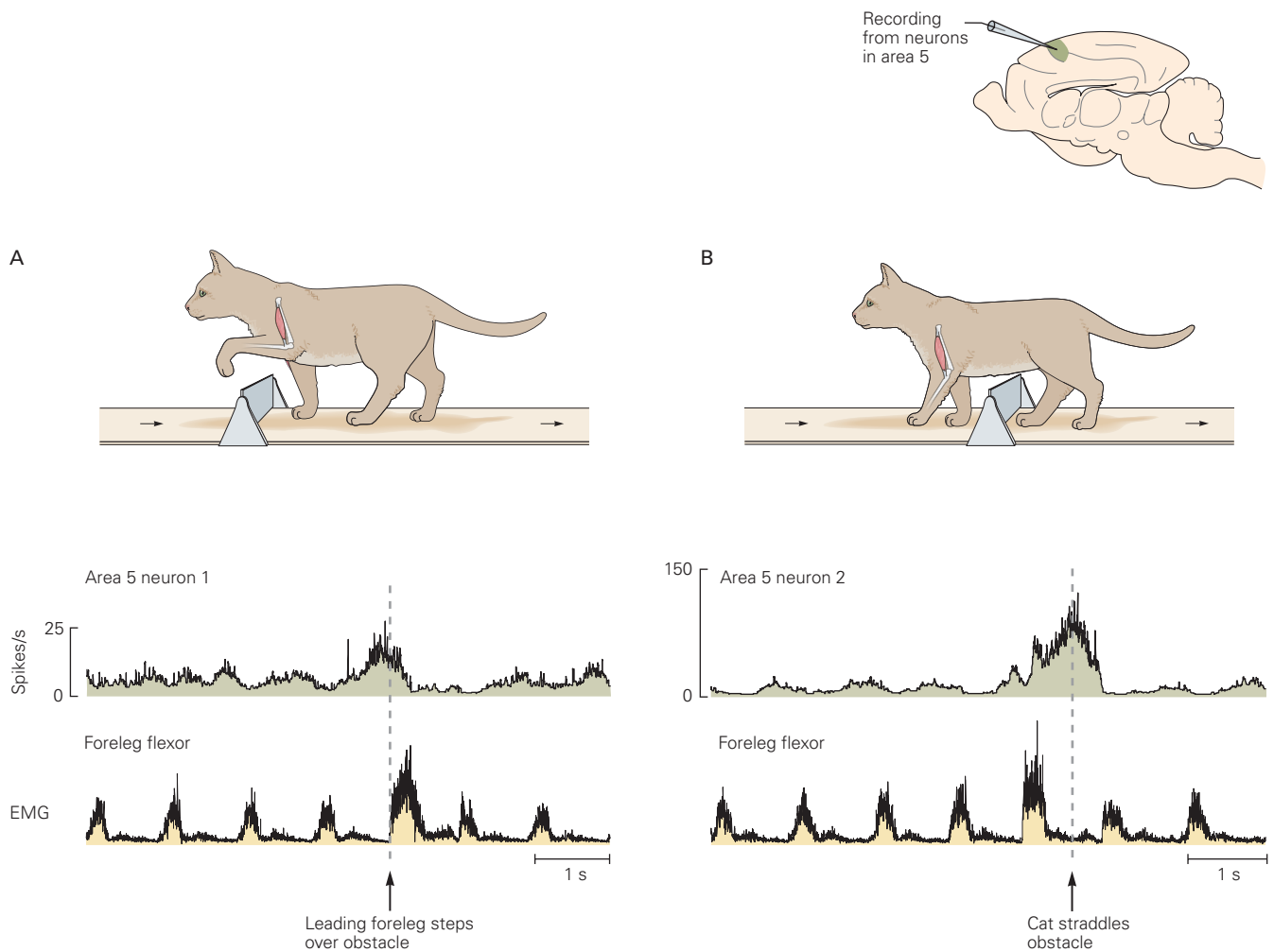
Figure 36–13 Neurons in area 5 of the posterior parietal cortex of the cat are involved in visuomotor transformations of walking. (Adapted, with permission, from Drew et al. 2008.)

A. The activity of a neuron increases as the animal approaches an obstacle and then declines the instant the leading foreleg begins to step over the obstacle.

B. Activity in a different neuron increases after the leading foreleg begins to step over an obstacle and is maximally active when the cat straddles the obstacle.

maturation of reticulospinal pathways and regions of the brain stem that project to reticulospinal neurons, such as the mesencephalic locomotor region. Second, the stepping pattern gradually develops from a primitive flexion-extension pattern that generates little effective forward movement to the mature pattern of complex movements. Again based on studies of cats, it is plausible that this adaptation reflects maturation of descending systems that originate in the motor cortex and brain stem nuclei and which are modulated by the cerebellum.

Parallels between human and quadrupedal walking have also been found in patients trained after spinal cord injury. Daily training restores stepping in spinal cats and improves stepping in patients with chronic spinal injuries. In patients with complete spinal cord injury motor patterns evoked in response to rhythmic leg movements can also be modified by daily therapy (Box 36–4). Thus the spinal networks for locomotion in humans and cats can adapt.

In light of these findings there is reason to believe that human walking relies on the same general principles of neuronal organization as quadrupedal walking: Intrinsic oscillatory networks are activated and modulated by other brain structures and by afferent input. Nevertheless, human bipedal locomotion differs from most

animal locomotion in that it places significantly greater demands on descending systems that control balance during walking. Indeed, maturation of the systems that control balance and stepping patterns is necessary for the infant to begin walking independently at the end of the first year. In contrast, horses can stand and walk within hours after birth. It is therefore likely that the locomotor spinal networks in humans are more dependent on supraspinal centers than those in quadrupeds. This dependence may explain in part the relatively few observations of spontaneous stepping movements in humans with complete spinal cord injury.
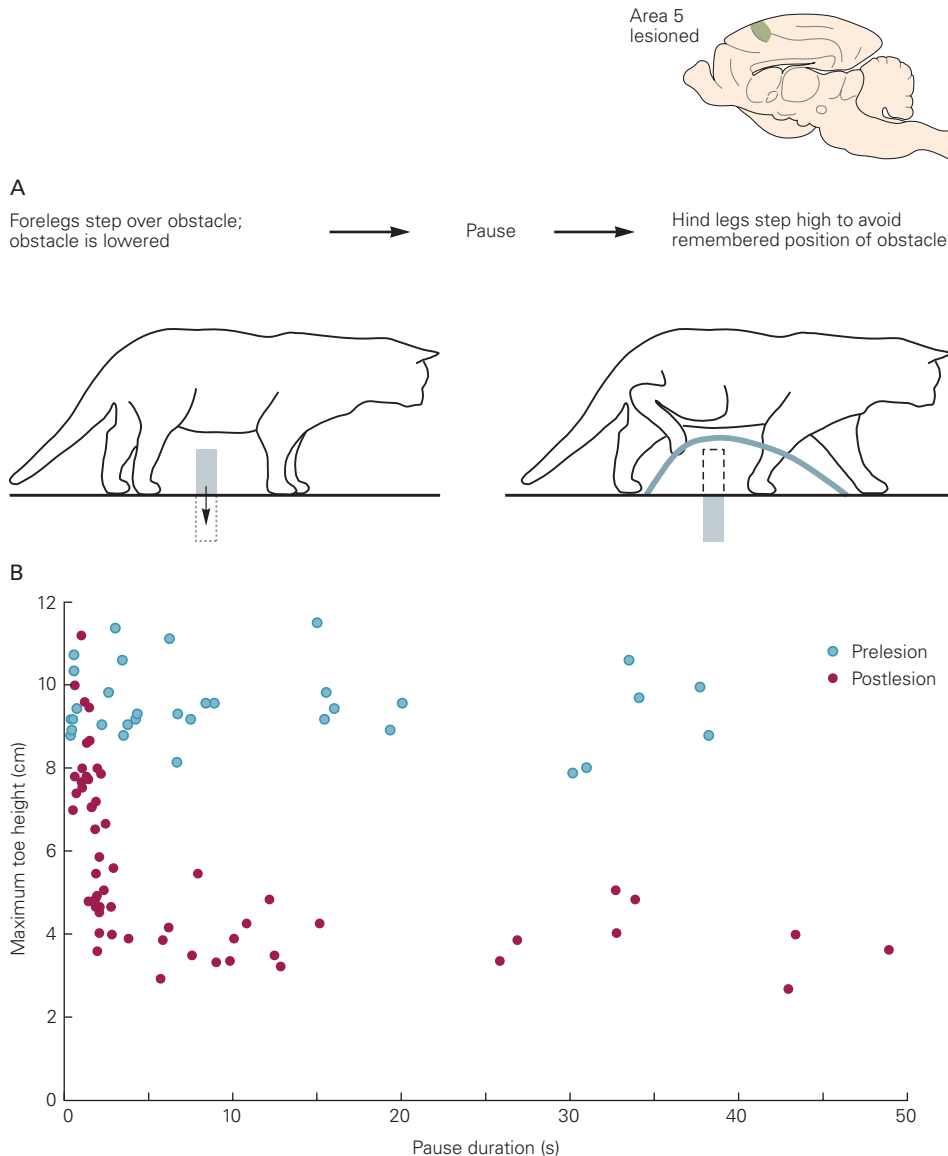

Figure 36–14 A walking cat's working memory of an obstacle is impaired following bilateral lesions of area 5 in the posterior parietal cortex.

A. A normal animal walks forward, steps over an obstacle, and pauses. While the animal pauses, the obstacle is removed. When walking resumes, the hind legs step high to avoid the remembered obstacle. The **blue line** traces the elevated trajectory of one toe.

B. The maximum toe heights of the hind legs are plotted against pause duration before and a few days after bilateral lesions of area 5 of posterior parietal cortex. The impairment of memory is indicated by the decline in maximum toe height for pause durations greater than a few seconds. (Adapted, with permission, from McVea et al. 2009.)

Box 36–4 Improving Walking After Spinal Cord Injury

Every year approximately 11,000 people in the United States injure their spinal cords, and for many this results in permanent loss of sensation, movement, and autonomic function. The devastating loss of functional abilities, together with the enormous cost of treatment and care, creates an urgent need for effective methods to repair the injured spinal cord and to facilitate functional recovery.

Over the past decade considerable progress has been made in animal research aimed at repairing the axons of damaged neurons in the spinal cord and promoting the regeneration of severed axons through and beyond the site of injury. In many instances the regeneration of axons has been associated with modest recovery of locomotor function. However, none of these strategies has reached the point where it can be confidently used in humans with spinal cord injury.

Therefore, rehabilitative training is the preferred treatment for patients with spinal cord injury. One

especially successful technique for enhancing walking in patients with partial damage to the spinal cord is repetitive, weight-supported stepping on a treadmill (Figure 36–15). This technique is firmly based on the observation that spinal cats can be trained to step with their hind leg on a moving treadmill (see Box 36–1).

For humans partial support of the body weight through a harness system is critical to the success of training; presumably it facilitates the training of spinal cord circuits by reducing the requirements for supraspinal control of posture and balance.

Although the neural basis for the improvement in locomotor function with treadmill training has not been established, it is thought to depend on synaptic plasticity in local spinal circuits as well as successful transmission of at least some command signals from the brain through preserved descending pathways.
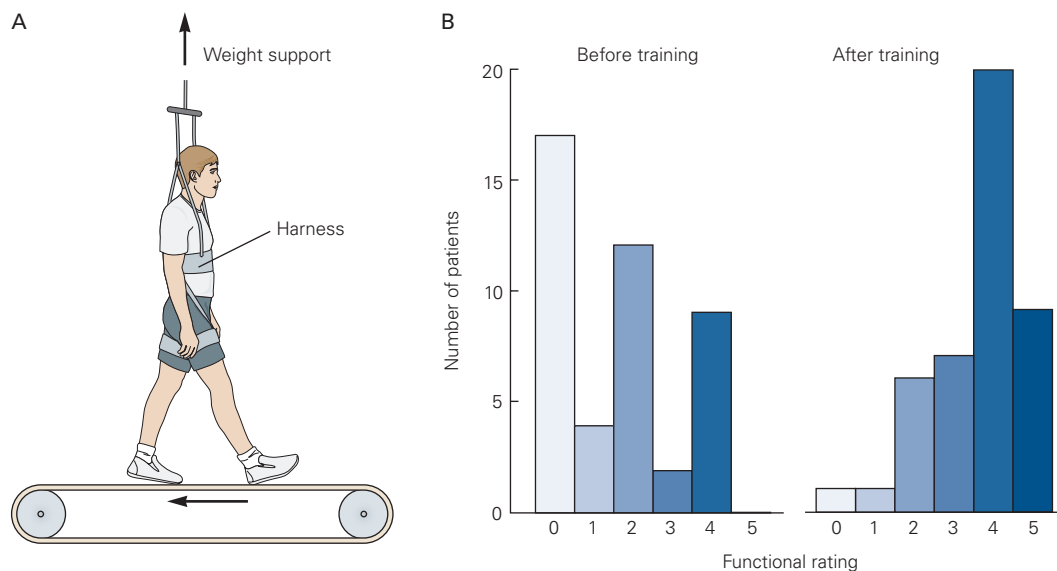

Figure 36–15 Treadmill training improves locomotor function in patients with partial spinal cord injury. (Adapted, with permission, from Wernig et al. 1995.)

A. A patient is partially supported on a moving treadmill by a harness, and stepping movements are assisted by therapists.

B. Locomotor function improved in 44 patients with chronic spinal cord injury after they received daily training lasting from 3 to 20 weeks. The functional rating ranges from 0 (unable to stand or walk) to 5 (walking without devices for more than five steps).

An Overall View

Locomotion in mammals typically involves rhythmic movements of the body and one or more limbs. These movements depend on precise regulation of the timing and strength of contractions in numerous muscles. Local spinal circuits, known as central pattern generators, can produce the basic motor pattern for locomotion even without sensory information from peripheral receptors. Numerous examples of central pattern generators have been analyzed at the cellular level, and it is clear that a wide variety of cellular, synaptic, and network properties are involved in these local networks.

Central pattern generators are extremely flexible; their cellular and synaptic properties can be modified by modulatory signals at chemical synapses. Their functioning depends on how they are activated and the pattern of afferent input they receive.

Modern research on mammalian locomotion dates from the 1960s, when two important experimental animal preparations were introduced. In the decerebrate animal stepping can be initiated by electrical stimulation of a site in the brain stem, the mesencephalic locomotor region. In the spinal preparation centrally generated locomotor activity can be evoked after the administration of adrenergic drugs.

Using these preparations, investigators have confirmed and extended fundamental observations made at the beginning of the 20th century, namely that the basic rhythm for locomotion is generated centrally in spinal networks, that the transition from stance to swing is regulated by afferent signals from leg flexor and extensor muscles, and that descending signals from the brain regulate the intensity of locomotion and modify stepping movements according to the terrain on which the animal is walking.

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