

Motor Control

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GLOSSARY

agonist A muscle that generates movement toward a goal.

antagonist A muscle that generates force in a direction opposite to that of an agonist.

central pattern generator Neural network in the central nervous system that produces rhythmic motor commands.

forward dynamics Computation of movements that result when muscles generate a given pattern of force.

forward kinematics Computation of limb positions for a given pattern of joint rotations.

internal model A central nervous system representation of the kinematics and dynamics of a motor task.

inverse dynamics Computation of muscle activations and forces needed to reach a goal.

inverse kinematics Computation of joint rotations or limb movements needed to reach a goal.

synergists Muscles that work together to produce a given movement.

The human motor system controls goal-directed movement by selecting the targets of action, generating a motor plan, and coordinating the forces needed to achieve

those objectives. Genes encode much of the information required for both the development and the operation of the motor system—especially for actions involving locomotion, orientation and reproduction—but every individual must acquire and store motor memories during his or her lifetime. Some of that information reaches conscious awareness, but much of it does not. This article focuses on the human motor system but draws heavily on knowledge about the motor system of other mammals, especially primates.

I. WHAT CONTROLS MOVEMENT

The motor system consists of two interacting parts: peripheral and central. The peripheral motor system includes muscles and both motor and sensory nerve fibers. The central motor system has components throughout the central nervous system (CNS), including the cerebral cortex, basal ganglia, cerebellum, brain stem, and spinal cord.

A. Peripheral Motor System

1. Muscles

Skeletal muscles consist of specialized cells, which fuse during development to form fibers (technically, a syncytium). There are two types of muscle fibers:

extrafusal and intrafusal. Extrafusal fibers, which attach to tendons and then to the skeleton, produce force and movement. Intrafusal fibers, which contain muscle spindles, attach to muscles and serve a sensory function.

Force and movement depend on muscle proteins, principally myosin and actin, both of which form strands within the muscle fibers. Molecules of myosin store kinetic energy as a result of metabolizing adenosine triphosphate (ATP), and muscle activation converts this chemical energy into mechanical force and work. Muscles generate force through a cascade of electrical and biochemical events, beginning with the release of acetylcholine by motor neuron synapses at the neuromuscular junction. This excitatory neurotransmitter binds temporarily with the muscle's cholinergic receptors, leading to depolarization of the postsynaptic membrane and mobilization of intracellular calcium ions. High intracellular calcium levels expose a site on the actin filaments to which myosin can attach. Once attached, the myosin molecules then reconfigure to force the actin and myosin filaments to slide relative to each other, which either shortens the muscle or generates force.

Whether these biomechanical events cause a force leading to movement or, alternatively, force without movement depends on the interaction of those muscles with their tendons, the skeleton, and the environment. As one consequence of the properties of actin and myosin, the length of a muscle affects the force (or tension) that it generates, a property known as the length–force (or length–tension) relation. As a muscle elongates, a given amount of activity generates a proportionately larger force. In addition, the properties of actin, myosin, and other structural elements also cause muscle fibers to behave approximately like a spring (technically termed viscoelasticity). Like metal springs, muscles have varying degrees of stiffness. For example, when pulled with a given amount of force, a spring made of thick, inflexible metal will increase its length much less than one made of thin, pliable metal. The former kind of spring is called stiff, and the latter is called compliant. Stiffness is defined as the ratio of force change to length change.

a. Rigor mortis Muscle activation increases muscle stiffness, but so does death, which leads to rigor mortis. Death causes depolarization of the muscle fibers because the eventual depletion of ATP stops the sodium–potassium pump, upon which normal cell polarization depends, as well as the hydrolysis of ATP by myosin, upon which detachment from actin

depends. In both rigor mortis and movement, attachment of myosin to actin causes stiffening of the muscle fibers.

2. Motor Neurons and Motor Units

In the ventral part of the spinal cord, motor neurons are organized into segregated motor pools, which innervate particular muscles. Alpha motor neurons send their axons from the spinal gray matter to terminate on extrafusal muscle fibers. Gamma motor neurons send their axons to intrafusal muscle fibers. Motor pools extend over two to four spinal segments, with medially situated motor pools innervating axial muscles (e.g., those of the neck and spine). Laterally situated motor pools project to limb muscles, with those contacting distal muscles located most laterally.

The term motor unit applies to a motor neuron and the muscle fibers it controls. Each motor neuron branches to innervate many muscle fibers, which receive input from only one motor neuron (except very early in development and in some disease states). The number of fibers in a motor unit varies according to function and within each muscle. Motor units that contribute to fine movements, such as those of the eye or the fingers, usually have a small number of muscle fibers. For example, motor units in the eye muscles consist of three to six muscle fibers. However, gastrocnemius, which forms the belly of the calf muscle, has thousands of muscle fibers per motor unit. Large motor neurons typically innervate more muscle fibers.

There are three basic types of motor units, each categorized by the speed with which it contracts upon electrical stimulation and its fatigability upon repeated stimulation. Fast, quickly fatiguing (FF) motor units have a short contraction time and produce a high twitch tension. However, with repeated stimulation the force they generate dissipates rapidly. Fast, fatigue-resistant (FR) motor units have an intermediate contraction time and can maintain force longer, whereas slow, nonfatiguing (S) motor units have a long contraction time and show little or no loss of force with repeated stimulation. FF motor units have large motor neurons, fast conducting, large-diameter axons, and muscle fibers of relatively large diameter. S motor units have the opposite characteristics. Muscles have various proportions of motor units: For example, S motor units make up nearly the entire diaphragm (one would not want to get tired of breathing), whereas gastrocnemius has a large proportion of FR and FF units (one certainly can get tired after a few strenuous jumps).

a. Poliomyelitis: A Disorder of Motor Neurons and Motor Units The poliovirus invades motor neurons, leaving adjacent nerve cells intact. Poliovirus receptors, located at the neuromuscular junction, allow the viruses to enter the motor neuron's axon, after which they migrate to its cell body. The infected cell either overcomes the virus or dies. If it dies, that motor unit is lost, and if the entire motor pool dies permanent paralysis results. However, some motor neurons usually survive. They develop new terminal axons that sprout to reinnervate "orphaned" muscle fibers. A single motor neuron may innervate up to 10 times the normal number of muscle fibers, restoring motor function. However, in a process called remodeling, which occurs in both healthy people and polio patients, motor units continually lose old sprouts and grow new ones. Decades after the onset of poliomyelitis, the enlarged motor units begin to break down, causing renewed weakness. According to one hypothesis, intense use of the relatively few remaining motor neurons causes this cell death.

3. Muscle Afferents

Certain sensory neurons innervate muscles and provide the CNS with information about muscle length and force. These and other sensory neurons have cell bodies in a dorsal root ganglion, with one axon projecting to sensory receptors in the periphery and another terminating in the CNS.

The diameter of muscle-afferent axons determines whether they belong to group I or group II. Group I, subdivided into groups Ia and Ib, has the larger fiber diameter and therefore faster transmission rates. Group Ia and II fibers innervate muscle spindles and are therefore called muscle spindle afferents. The term spindle refers to fine intrafusal muscle fibers that taper at the end and contain a fluid-filled capsule at the center. Muscle-afferent fibers wrap around muscular elements within the capsule. Group Ia fibers are termed primary muscle spindle afferents; group II fibers are called secondary muscle spindle afferents. Group Ib fibers innervate golgi tendon organs (GTOs), which are located in the transitional region between extrafusal muscle fibers and tendons. The role of muscle afferents in reflex responses is discussed in Section II.B.

B. Central Motor System

All levels of the CNS contribute to motor control, including the spinal cord, medulla, pons, midbrain,

diencephalon, and telencephalon. The following sections survey the major components of the central motor system, beginning with the spinal cord and progressing up the neural axis to the telencephalon. Figure 1 shows some of the major components and projections of the central motor system. Notwithstanding the impression that this component-by-component description might convey, the various components of the motor system work as an integrated neural network, not as isolated motor "centers."

1. Spinal Cord

In addition to motor neurons, spinal components of the motor system include sensory pathways, the proprioceptive system, and central pattern generators (CPGs). Sensory afferents bring information to the CNS from the skin, joints, and muscles, and both cells and fiber tracts in the spinal cord relay that information to structures involved in motor control. For example, primary afferent neurons terminate on the dorsal column nuclei in the medulla, which relay that information to the thalamus through a fiber pathway called the medial lemniscus. In addition, an extensive and intricate system of intrinsic spinal cord neurons underlies a group of miscellaneous functions collectively termed proprioceptive. Proprioceptors are sensory transducers in muscles, tendons, and other internal tissues. However, the concept of the proprioceptive system extends beyond this definition to include a wide variety of interneurons that relay somatosensory signals locally and between segments in the spinal cord as well as carry descending motor commands, largely within the spinal cord. CPGs are neural networks that generate patterned, rhythmic movements, such as those involved in walking and running.

2. Brain Stem

The brain stem contains motor neurons that send their axons through certain cranial nerves, primarily to muscles of the tongue, face, and eyes. Like the spinal motor pools, many of these cranial motor nuclei receive direct input from sensory neurons and less direct influences from proprioceptive interneurons. Brain stem CPGs generate rhythmic movements, such as those underlying breathing and chewing.

Some parts of the brain stem interact with spinal CPGs and other components of the spinal motor system. One such region has been termed the midbrain locomotion region, which is thought to trigger the

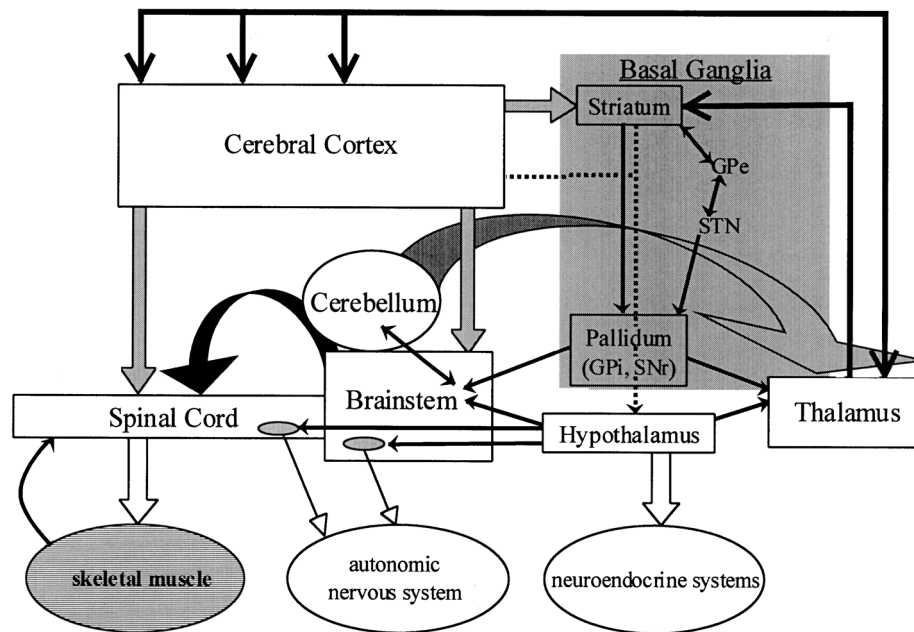


Figure 1 Major components of the motor system. Corticofugal projections are depicted as gray arrows. Projections to effectors are depicted as open arrows and arrowheads. The basal ganglia are contained within the gray box. Preganglionic autonomic motor nuclei are shown as stippled ovals. GPi, internal segment of globus pallidus; GPe, external segment of globus pallidus; STN, subthalamic nucleus; SNr, substantia nigra pars reticulata.

activity of spinal CPGs and thereby initiate locomotion. However, higher order networks, akin to CPGs but having more complex output patterns, have an important role in a number of instinctive behaviors, including aggressive posturing (a form of “body language”) and inarticulate vocalization (such as crying, laughing, and screaming). Some of these networks are located in and near a midbrain structure called the periaqueductal gray.

a. Reticulospinal System Cells in the brain stem reticular formation that project to the spinal cord make up the reticulospinal system, which extends through medullary, pontine, and midbrain levels. The reticulospinal system performs a diverse set of functions, including the regulation of muscle tone, control of posture and locomotion, and integration of lower order motor signals with those emanating from the cerebellum and cerebral cortex. Different reticulospinal pathways exert influences on flexor versus extensor muscles and on proximal versus distal parts of the limb.

Part of the reticulospinal system serves as a fast transmission route to postural motor neurons and helps prevent movements from destabilizing balance.

For example, when a person lifts a heavy object, the leg muscles need to stiffen before the elbow flexes. This postural adjustment prevents the object’s weight from pulling the person off balance. The reticulospinal system activates leg muscles to stiffen them and help preserve balance. On the whole, while people are awake the reticulospinal system has a predominantly facilitatory influence on motor pools. However, this effect changes dramatically during sleep. Then, reticulospinal neurons exert a strong inhibitory influence that, for example, prevents the performance of imagined actions during dreams.

Important influences over the reticulospinal system come from other systems, including vestibular afferents, which signal movements of the head and its orientation with respect to the earth’s gravitational field, and the motor cortex, which provides information otherwise unavailable at brain stem levels. Through vestibulospinal projections, the vestibular system can contribute directly to various reflexes that adjust eye position, posture, and limb movements. However, the vestibular afferents also provide inputs to the reticulospinal system. Consider the role of the reticulospinal system as a person runs through a field of obstacles. The signals conveyed by the reticulosp-

inal system to CPGs and spinal motor pools adjust posture and movement based primarily on vestibular and proprioceptive inputs. However, cortical and other higher order inputs supply the information needed for dynamic motor adjustments that allow people to step over and around visible obstacles.

b. Cerebellum and Red Nucleus The largest component of the brain stem motor system is the cerebellum. The medial cerebellum controls posture, whereas the lateral cerebellum participates more in voluntary movement. Accordingly, vestibular and propriospinal inputs predominate in the medial cerebellum, and inputs to the lateral cerebellum arise mainly from the cerebral cortex, relayed through mossy fibers originating in the basilar pontine nuclei. In addition, the cerebellum receives mossy fiber input from the red nucleus via the lateral reticular nucleus (which also has major spinal inputs) and from other sources. Mossy fibers terminate on the output nuclei of the cerebellum (the deep cerebellar nuclei) as well as on neurons in the cerebellar cortex. Another type of input, conveyed by climbing fibers originating in the inferior olivary complex, is thought to signal motor error or discoordination. These signals may play a central role in motor learning (see Section IV).

The output of the cerebellar cortex comes from GABAergic Purkinje cells, which inhibit neurons in the deep cerebellar nuclei and in one of the vestibular nuclei. The deep cerebellar nuclei send excitatory outputs to a variety of structures. Their largest projections terminate in the thalamus (Fig. 1), but other efferents reach the reticulospinal system, red nucleus, superior colliculus, and spinal cord. Cerebellar outputs to many of its targets are accompanied by return projections through a variety of direct and indirect pathways. One example is the cerebellar projection to the motor cortex (via the thalamus), which is returned by a cortical projection to the cerebellum (via the basilar pontine nuclei). Recurrent, excitatory circuits such as this are thought to form functional networks termed cortical–cerebellar modules.

The red nucleus plays an enigmatic role in motor control, especially in the human brain, but appears to be intimately related to cerebellar function. It receives a major projection from the deep cerebellar nuclei as well as from the motor cortex, and the largest part of the red nucleus (its parvocellular, or small-cell, component) projects predominantly to the inferior olivary complex, the source of cerebellar climbing fibers. The magnocellular (large-cell) red nucleus sends

its axons directly to the spinal cord through the rubrospinal tract, which might be particularly important in stabilizing the limb by coactivating agonist and antagonist muscles. However, the magnocellular red nucleus is said to be relatively small in the human brain, which may reflect a dominant role of cortical motor control in our species.

c. Superior Colliculus The superior colliculus, although typically discussed in terms of eye-movement control, also has an important role in the control of head movements. Generally stated, its function involves the orientation of the retina and other receptors on the head, which the superior colliculus guides through its interaction with the reticulospinal system, premotor neurons in the brain stem reticular formation, and direct projections to the spinal cord (the tectospinal system).

3. Diencephalon

The hypothalamus and thalamus are the major parts of the motor system that lie within the diencephalon. The motor functions of the hypothalamus are discussed in Section II.A. The thalamus does not serve a primarily motor function when viewed as a whole. However, a major component of the thalamus receives projections from the cerebellum and basal ganglia, which play an important role in motor control. Two general regions of the thalamus receive these inputs—the ventroanterior and ventrolateral (VA/VL) nuclei. Anterior VA/VL receives basal ganglia projections; posterior VA/VL receives cerebellar input. Each part of VA/VL sends excitatory projections to the frontal cortex and receives excitatory projections from the same cortical areas. These reciprocal connections are thought to act as recurrent cortical–thalamic modules. Although the thalamic terminals from cerebellum and basal ganglia overlap very little, the thalamocortical components of these systems converge to influence most if not all motor areas jointly.

4. Telencephalon

Two large parts of the telencephalon have important roles in motor control: the cerebral cortex and the basal ganglia. Of course, the function of both structures extends beyond motor control, but this article addresses only that role.

a. Cerebral Cortex The number of functionally distinct motor cortical fields remains unknown. One

heuristically useful view of the frontal cortex divides it into three main parts: the primary motor cortex, a group of areas collectively known as nonprimary motor cortex, and the prefrontal cortex (Fig. 2). The first two components can be referred to collectively as the motor cortex, although this term is sometimes used as a synonym for primary motor cortex.

The primary motor cortex (abbreviated M1) corresponds approximately to Brodmann's area 4. It lies in the anterior bank of the central sulcus and contains a topographic representation of the musculature. Most textbooks depict this topography in the form of a homunculus (i.e., a projection of the body onto the cortical surface). Such pictures have validity only at the most superficial level. They correctly imply that the medial part of M1 contains the leg and foot representation, that a more lateral part includes the arm and hand representations, and that an even more lateral part has the face, tongue, and mouth representation. However, at any finer level of detail, the homunculus presents an inaccurate image of M1's organization. Instead, M1 consists of a mosaic of

broadly overlapping muscle representations, with each part of the body represented repeatedly. The functions of M1 are discussed in Section III.

By current estimates, there are about a dozen nonprimary motor areas. Many of these fields occupy parts of Brodmann's area 6. However, parts of areas 8 and 24, the latter also known as anterior cingulate cortex, also contain nonprimary motor areas. A medial group of areas includes the well-known supplementary motor area (SMA), an area immediately anterior to it (the pre-SMA), and two or more cingulate motor areas. A lateral group of areas, often termed simply the premotor cortex (PM), can be divided into separate dorsal and ventral components, and these two divisions can be subdivided further into rostral and caudal parts. At least two eye-movement fields, the frontal eye field, and the supplementary eye field, have been identified. Finer subdivisions and combinations of these regions have been proposed and may have some validity. The functions of these areas are discussed in Sections III and V.B.

The primary and nonprimary motor areas project to the other components of the motor system, at virtually all levels of the neural axis (Fig. 1). The cortical output system, often called the corticofugal system, arises exclusively from layer 5 and includes a direct projection to the spinal cord (the corticospinal system). Some motor areas, especially M1, have monosynaptic excitatory connections with alpha motor neurons. Accordingly, the oxymoron "upper motor neuron" has been applied to M1's corticospinal neurons. However, M1 exerts its influence over genuine motor neurons in large measure through relatively indirect pathways, and its synapses on spinal interneurons vastly outnumber those on motor neurons. Corticospinal axons accumulate in large bundles traversing the internal capsule, cerebral peduncle, pyramidal tract, and corticospinal tract on the way from the telencephalon to the spinal cord. Because corticospinal axons run through the pyramidal tract, the term pyramidal motor system is sometimes applied to it. However, many fiber systems coexist within the pyramidal tract, such as neurons projecting to the dorsal column nuclei and other targets in the brain stem. Thus, the corticospinal and pyramidal motor systems do not correspond exactly. Additional outputs from the motor cortex include massive projections to the basal ganglia, the red nucleus, the cerebellum (via the basilar pontine nuclei), and the reticulospinal system.

b. Basal Ganglia Long considered part of the so-called extrapyramidal motor system, much of the

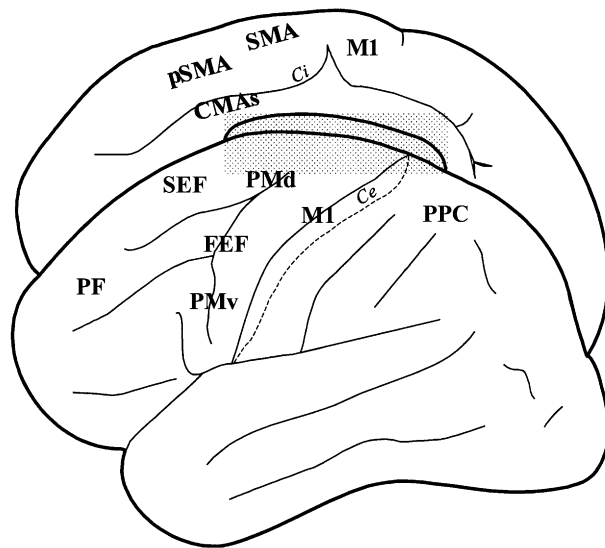


Figure 2 Motor areas of the human brain plotted onto a highly simplified sketch of the cerebral hemispheres. The lateral surface of the left hemisphere is shown below the medial surface of the right hemisphere. Rostral is to the left; dorsal is up. The dashed line indicates the fundus of the central sulcus, showing that the primary motor cortex is located mainly within the rostral (anterior) bank of that sulcus. The stippled area on the medial surface represents the corpus callosum. Ce, central sulcus; CMAs, cingulate motor areas; FEF, frontal eye field; M1, primary motor cortex; PF, prefrontal cortex; PMd, dorsal premotor cortex; PMv, ventral premotor cortex; PPC, posterior parietal cortex; SEF, supplementary eye field; pSMA, presupplementary motor area; SMA, supplementary motor area.

motor output from the basal ganglia depends, ultimately, on the pyramidal tract. Accordingly, the concept of an extrapyramidal motor system has been largely abandoned. The striatum is the basal ganglia's input structure, encompassing the putamen, caudate nucleus, nucleus accumbens, and other regions within the ventral forebrain. Likewise, the pallidum is the basal ganglia's output structure, including not only the globus pallidus but also the substantia nigra pars reticulata (Fig. 1) and additional parts of the ventral forebrain. The pallidum sends GABAergic inhibitory projections to the brain stem and thalamus. These thalamic nuclei connect to nearly the entire frontal lobe as well as additional areas, such as the inferior temporal cortex and the posterior parietal cortex.

The major excitatory inputs to the striatum come from the cerebral cortex (including the hippocampus) and the intralaminar complex of thalamic nuclei. A major input arises from the dopaminergic cells of the midbrain, located in the substantia nigra pars compacta and the adjacent ventral tegmental area. Degeneration of the striatum results in Huntington's disease, whereas degeneration of the dopaminergic neurons causes Parkinson's disease.

Much attention has recently focused on the modular organization of cortical and basal ganglia interconnections. This trend accords with the recognition of other important modules in the motor system, such as CPGs, reflex circuits, and cortical–cerebellar modules. The cortical–basal ganglionic modules, often called “loops,” consist of cortical, striatal, pallidal, and thalamic elements that form, at least in principle, a recurrent excitatory pathway. This circuit includes the so-called “direct pathway,” striatal output neurons (technically, medium spiny neurons) that project directly to the pallidal projection neurons (Fig. 1), including those in the internal segment of the globus pallidus (GPi). Another part of the basal ganglia, the “indirect pathway,” begins with projections from the striatum to the external segment of the globus pallidus (GPe). These neurons influence the subthalamic nucleus and pallidum, in turn (Fig. 1).

This sketch of the basal ganglia has heuristic value in understanding Parkinson's disease and other consequences of basal ganglia dysfunction. However, the reader should recognize that it represents a coarse oversimplification. Many other features of its anatomy are important to basal ganglia physiology. The subthalamic nucleus, for example, excites not just GPi but also GPe; the GPe sends inhibitory inputs “back” to the striatum; and the motor cortex sends a direct, excitatory projection to the subthalamic nu-

cleus. Furthermore, in addition to dopaminergic inputs, serotonergic inputs arise from the raphe nucleus, and there are a large variety of intrinsic neurons using other neurotransmitters, including acetylcholine.

c. Parkinson's Disease According to one current view, dopamine acts to support activation of the direct pathway's striatal neurons but to suppress those of the indirect pathway. Accordingly, the direct pathway's inhibitory influence over GPi might wane in the absence of dopamine. This decrease in inhibition from the striatal direct-output pathway would lead to GPi neurons having greater activity and therefore greater inhibitory output to the thalamus. The indirect pathway, may also contribute to greater inhibition of the thalamus. This increased inhibitory influence on recurrent cortical–thalamic modules may cause the slowing of movement (technically, bradykinesia) that is a symptom of Parkinson's disease.

II. WHAT THE MOTOR SYSTEM CONTROLS

The motor system controls innate behavior, which is encoded genetically; a wide variety of reflex responses, defined as output generated relatively directly by sensory inputs; and voluntary movements.

A. Instinctive Action

The hypothalamus plays a central role in the control of instinctive behaviors, such as those involved in locomotion, orientation, and reproduction, and in neuroendocrine function. Pools of neuroendocrine neurons in the periventricular parts of the hypothalamus secrete hormones into the vascular system. Their terminals in the neurohypophysis (posterior pituitary) release oxytocin and antidiuretic hormone (vasopressin). Although it might seem counterintuitive to consider such secretions as motor in function, they serve as a mechanism through which the CNS controls other parts of the body, just as alpha motor neurons do.

Different cells in the periventricular hypothalamus serve a less direct endocrine control role. These neuroendocrine cells secrete higher order control hormones, often termed releasing factors, into the portal blood supply of the pituitary. The adenohypophysis (anterior pituitary) responds to these hormones,

such as corticotropin-releasing factor, which increase or decrease the secretion of pituitary hormones such as adrenocorticotropin. These hormones play crucial roles in regulating growth and in homeostatic and reproductive functions.

The hypothalamus also affects the body through its control of the autonomic nervous system (ANS). The hypothalamus sends descending projections to the autonomic motor nuclei in the spinal cord and brain stem. There, neurons send outputs to the peripheral ganglia of the two components of the ANS, the sympathetic and parasympathetic systems. Sympathetic motor neurons are located at thoracic and lumbar levels of the spinal cord. Parasympathetic motor neurons are found in the sacral spinal cord as well as in the brain stem, from which they give rise to parts of cranial nerves V (trigeminal), VII (facial), IX (glossopharyngeal), and X (vagus). Autonomic motor neurons, like alpha motor neurons, project to the periphery and release acetylcholine. In the sympathetic nervous system, most of these cholinergic influences terminate on ganglia relatively near the CNS. These sympathetic ganglia contain neurons that release noradrenaline, which induces a generalized arousal of the “fight, flight, and fright” variety. In the parasympathetic system, cholinergic motor neurons project to ganglia relatively far from the CNS, near their visceral targets. Thus, the ANS can address the targets of the parasympathetic system more specifically than it can for the sympathetic system. Most parasympathetic postganglionic synapses use acetylcholine as a transmitter, although many neuropeptides, such as vasoactive intestinal peptide, are released along with acetylcholine. The hypothalamus, through its control of the ANS, exerts an important influence over such motor functions as vasoconstriction, respiration, and heart rate.

However, the hypothalamus does not confine its motor functions to the ANS. Parts of the hypothalamus play an important role in ingestive behaviors (such as eating and drinking), defensive and agonistic behaviors (such as flight from danger and aggression), arousal and orientation, and social behaviors, including sexual and other behaviors involved in reproduction (e.g., rearing of progeny and other means by which genes are passed to future generations). Its motor roles thus include initiating complex action patterns, which include epigenetically expressed but genetically encoded motor programs often termed species-specific or species-typical behaviors. For example, aggressive displays such as snarling at or staring down an adversary might result from fear,

intermale competition, or irritation, with each state and response mediated by different, partially overlapping networks in the hypothalamus. The hypothalamus effectuates many of these behaviors via projections to the thalamus and to various brain stem structures (e.g., the periaqueductal gray).

The several systems influenced by the hypothalamus—endocrine, autonomic, and instinctive—may seem dissimilar and unrelated. However, the hypothalamus (along with components of the amygdala) coordinates these aspects into a fully coordinated behavior. Imagine combat soldiers engaged in a stressful and dangerous situation. A variety of species-typical behaviors accompany such perilous situations, including heightened states of vigilance and arousal, which require high expenditures of energy. Parts of the medial hypothalamus detect inputs that signal such situations and, through their projections to the brain stem, release and intensify arousal and vigilance behaviors. Those hypothalamic regions also influence the periventricular hypothalamus to secrete corticotropin-releasing factor, which in turn induces the release and circulation of adrenocorticotrophic hormone. This hormone stimulates the adrenal cortex to produce and release larger amounts of glucocorticoids. A parallel ANS control signal from the hypothalamus to the motor nucleus of the vagus promotes insulin secretion by the pancreas. Thus, the neuroendocrine system (through glucocorticoids) induces the liver to release more glucose at the same time as the ANS (through insulin) promotes the uptake of glucose into cells, especially muscle fibers. Together, the hypothalamus coordinates an adaptive response to a stressful state: the mobilization and utilization of stored nutrients to support high energy expenditure as well as the actions appropriate to that state.

B. Reflex Responses

The motor system controls a large number of reflexes, of which this article highlights only withdrawal and muscle-afferent reflexes.

1. Withdrawal Reflexes

Activation of cutaneous and deep receptors by a potentially damaging stimulus gives rise to an ipsilateral flexion reflex, accompanied by contralateral extension, called the crossed-extension reflex. A polysynaptic network in the spinal cord mediates this

response, which acts to retract the limb from the noxious stimulus (the flexion reflex) and enhance postural support, especially from the legs (the crossed-extension reflex).

2. Muscle-Afferent Reflexes

Two feedback systems, both involving muscle afferents, regulate force and muscle length through reflexes. Muscle spindle afferents transduce muscle length, whereas GTO afferents transduce muscle force.

a. Force Feedback GTOs lie in series with the extrafusal fibers and receive no motor innervation. They send force information to the spinal cord, where interneurons receive input from the brain that specifies the amount of force that a muscle should produce. If that muscle's force level exceeds this set point, the GTO inputs inhibit the alpha motor neurons innervating that muscle, which lowers the force produced unless some other mechanism cancels that signal.

b. Length Feedback In contrast to GTOs, muscle spindles lie in parallel with extrafusal fibers and have contractile elements that are activated by gamma motor neurons. Without efferent innervation, the muscle spindles would become slack when extrafusal fibers shorten. The spindle afferents would then become silent and the CNS would lose information about muscle length. Gamma motor neurons activate muscle spindles during contraction to maintain that information flow. During movement and steady posture, muscle spindle afferents sense muscle length with respect to a bias length set by their gamma motor neurons. When the gamma motor neurons have high levels of activity, the bias length is relatively short. If the muscle length exceeds this bias length, muscle spindle afferents increase their discharge rate and excite alpha motor neurons innervating the same muscle. Of course, this increase in activity tends to shorten the muscle, bringing it closer to the bias length. Generally, however, gamma motor neuron activity allows the CNS to control the sensitivity of muscle spindle afferents, which may play their most important role in regulating muscle stiffness.

Information regarding limb position does not depend entirely on muscle spindles. Other sources of input include cutaneous and joint capsule receptors, both of which contribute information about limb position and joint angle. In addition, group III and IV afferents also innervate the limbs but receive informa-

tion primarily from deep receptors in the muscle and cutaneous receptors that appear to respond mainly to painful stimuli rather than force or limb position. Despite this diversity of receptors, the muscle spindles appear to be especially important for sensing muscle length, as demonstrated by the following experiment: Imagine a blindfolded person, seated with his or her elbows on a table and his or her forearm held in a vertical posture. If someone else moves one forearm, the blindfolded person can indicate the position of that arm by matching it with the other, free arm. People perform this task very accurately in normal circumstances. However, if vibration is applied to the belly of biceps, people consistently overestimate the angle of extension at the elbow. The explanation for this phenomenon involves muscle spindle afferents. Vibration provides a very powerful stimulus to muscle spindles, and the CNS wrongly interprets their increased discharge as reflecting a longer biceps muscle, which translates to increased extension at the elbow.

Muscle spindle afferents also mediate stretch reflexes, among which the monosynaptic stretch reflex is also known as the myotactic reflex or the knee-jerk response. For example, when one taps the skin surface over the knee's patellar tendon, this stretches the quadriceps muscle. Prior to the involvement of stretch reflexes, this increase in length makes the muscle generate more force through the length-tension relation. However, stretch also results in an elongation of the muscle spindles in the quadriceps, which in turn causes increased firing of the primary and secondary muscle spindle afferents. This sensory input excites alpha motor neurons and causes a knee-jerk within 15–20 msec. Particularly for the muscles of the arm, wrist, and fingers, a second pathway exists through which muscle stretch can activate motor neurons. This pathway, called the long-loop stretch reflex, also begins with muscle spindle afferents. Information from these afferents is transmitted to the thalamus and then to the somatosensory and motor cortex before returning to the spinal cord through the corticospinal projection. It takes 40–50 msec for the information to traverse this entire circuit. Although the long-loop reflex takes longer than the short-loop one, the brain can reprogram the long-loop response in a highly flexible manner. For example, if a stretch is expected, people can suppress the long-loop component of the reflex or choose to respond especially vigorously. The major role of stretch reflexes probably involves responses to an unexpected perturbation. If, during a movement, something suddenly displaces the arm, this input elicits a compensatory response from

both the short- and long-loop reflexes. These reflexes tend to change the activation levels of motor neurons in a manner that stabilizes and stiffens the limb as it moves along the desired trajectory. Reflexes may help the motor system overcome impediments that have never been experienced. If a person's goal includes producing the sound "pa," the lips must touch each other to achieve this goal. However, if an experimenter pulls on the lower lip, the motor system needs to produce more force than usual to make the lips contact each other (technically, occlusion). This response does not depend on experience with such perturbations; it occurs the first time the lip is pulled.

c. Disorders of Long-Loop Stretch Reflexes in Parkinson's Disease Normally, people can voluntarily suppress the long-loop component of the stretch reflex. In Parkinson's disease, however, patients appear to lose this ability. Regardless of the instructions given to them, stimulation of primary muscle spindle afferents produces a large response. In Huntington's disease, by contrast, there can be a complete loss of the long-loop stretch reflex. The relation between the basal ganglia and control of these reflexes remains unknown, but it probably involves its influence over the motor cortex. Recent research suggests that loss of the long-loop reflexes accounts for the jerky movements characteristic of Huntington's disease.

3. Role of Reflexes in Voluntary Movement

To what extent are reflexes used for generation of voluntary movements? Studies of patients with degeneration of large-fiber afferents (peripheral neuropathy) have led to the conclusion that reflexes play only an indirect role in volitional action. Such patients lose their stretch reflexes, limb position sense, and their ability to detect limb motion, but they can still make voluntary movements. In normal individuals, an electromyograph (EMG) pattern composed of three discrete bursts of activity characterizes the execution of a rapid, one-joint voluntary movement. First, the agonist muscle activates (AG1), followed by the antagonist muscle (ANT) and, finally, a second activation of the agonist muscle (AG2). AG1 accelerates the limb, ANT brakes the limb, and AG2 stabilizes the limb and dampens oscillations around the final position. When peripheral neuropathy patients make a rapid thumb flexion, the typical three-phase EMG pattern described previously (AG1, ANT,

and AG2) appears in the normal manner. Therefore, the EMG pattern of voluntary movements appears to originate from descending motor commands to alpha motor neurons and does not depend on reflex loops. The motor command signal, however, may pass through some of the same neurons used in reflex loops, increasing the capacity of the system to integrate peripheral and central information.

C. Voluntary Movement

This article concentrates on the voluntary control of forelimb reaching movements. However, similar processes apply to other types of voluntary movements. These processes include generating torques on an articulated chain of limb segments, promoting stability through agonist–antagonist architecture, positioning end effectors, translating goals into plans for action, computing the joint rotations and patterns of force needed to implement those plans, and compensating for other forces.

1. Generating Torques on Articulated Limb Segments

A limb consists of a chain of articulated segments, with the muscles acting as the motors technically, actuators that control torques around those segments. Each segment of a limb can rotate with respect to the more proximal segment. The axis of rotation centers on the joint that connects the two segments, and muscles provide torques on that joint. For example, a person usually has to flex his or her elbow to lift a coffee cup and sip from it. Commands from the motor system reach the biceps muscle, activating it and producing force, which results in flexion torques on the elbow joint. As the elbow flexes, the resulting movement stretches the triceps, which in other circumstances would result in increased force output from the triceps because of the length–tension relation. This increased force would cause an extension torque on the elbow joint. For the hand to reach the mouth, flexion torques need to exceed extension torques. Thus, while sending the activating commands to the biceps to initiate the movement, the motor system usually sends an inhibitory command to the triceps' motor pool as well. This reduces some of the extension torque produced by the triceps, diminishing the resistance to the voluntary flexion that brings the cup to the mouth.

2. Producing Stability Through Antagonistic Architecture

To hold a coffee cup steady requires a different approach: The motor system sends commands to activate both biceps and triceps. This coactivation results in both flexion and extension torques on the elbow joint. If the net torque, which is the sum of these two torques, equals zero, then the forearm will remain still. Why not simply shut down both muscles rather than waste the torques (and energy) to no effect? The answer has to do with limb stability. Consider what happens if an object suddenly hits a person's hand and causes the arm to flex at the elbow. During coactivation, the muscle that gets stretched because of the impact (triceps) will vigorously resist because intrinsic muscle stiffness increases with activation level. Without coactivation (i.e., with an inactive triceps), the impact would result in a much larger flexion of the elbow. Thus, coactivation promotes limb stability.

3. Positioning End Effectors

Although the final motor commands act on muscles to move limb segments, the goal of a movement often involves the positioning of an end-effector. For example, to sip from a coffee cup, most people attend to the cup and not to what the elbow is doing. Signatures provide another case in point. Everyone has a unique signature, and its distinctive character persists even if different joints and muscles perform the signing movement. This principle has been called motor equivalence. Its basis is that the pencil serves as an end effector regardless of which muscles move it. The preservation of unique elements in a signature indicates that the highest levels of the CNS represent voluntary movements not as a pattern of muscle activations but as a kinematic pattern, specifically the desired motion of an end effector.

Of course, signatures consist of complicated movement trajectories. In principle, an infinite number of possible hand trajectories can be made between two points—some straight, others curved to varying degrees. However, unless the goal includes a curved trajectory, people show a remarkable similarity in the movements that they produce in reaching from a given hand position to a target. The hand moves with a unimodal, smooth, and symmetric velocity over the time course of the action, and it takes a straight-line path. Even blind people show this feature in their arm movements. When an experimenter demonstrates the target to a blind person by moving his or her hand to

the target position (later returning it to the original location), he or she makes straight and smooth reaching movements just like sighted people. This smoothness in hand trajectory contrasts sharply with the changes that occur in joint positions during the same movement. For example, consider a movement of the right arm that starts with the hand at the far left of the midline and reaches to a target at the far right. For most people, this movement would be a straight line in terms of hand position. However, examination of joint angles shows that the elbow initially flexes and then extends. Therefore, its velocity is not unimodal. Human arm movements generally appear simple when described in terms of hand positions and velocities but are complex when described in joint coordinates. This regularity remains when people perform movements with different end effectors. For example, movements remain smooth and simple when our hands hold a long stick. In this case, the end of the stick moves smoothly and in a straight line.

4. Translating Goals into Action

a. Inverse Kinematics The smooth and simple hand trajectory described previously represents a kinematic plan. Before that plan can be formulated, the motor system must estimate both current hand position and the direction and magnitude of the movement needed to reach the target. Estimation of current hand position is based on two sources: Vision and proprioception. Muscle afferents from the arm provide the information necessary for estimating the orientation of each limb segment relative to its proximal joint. If the motor system has this information, it can compute the hand position with respect to the body. The computation of limb position from a proximal, joint-coordinate-based system to a distal, hand-centered coordinate system is called forward kinematics. If someone moves a blindfolded person's hand, he or she still has a pretty good idea of that hand's location. This ability depends primarily on the computation of forward kinematics from the length sensors in the muscles. If the motor system knows the length of the limb's muscles, it knows the angles of its joints and, through forward kinematics, can compute the location of the hand. The inverse of this computation maps hand position to the joint angles that are appropriate for it. In order to move the hand to a desired position, the motor system needs information about what joint angles the muscles need to achieve in order to move the limb segments to that position. This computation is termed inverse kinematics. In other

words, if the motor system knows the desired hand position, it can compute the joint angles needed to put the hand in that position through the computation of inverse kinematics.

b. Inverse Dynamics In addition to computing the positions of the joints and the hand for a desired limb trajectory (kinematics), the motor system must estimate how much torque to produce on each joint (dynamics). Accordingly, the motor system must translate a desired motion of the end effector into a pattern of muscle activations. This does not imply that the brain calculates or represents the joint torques in absolute terms, joint by joint, but rather that the neural network must solve this problem to generate motor commands that will achieve the goal. Consider the torques needed to lift a full cup of coffee in contrast with those needed to lift an empty cup. Although the hand trajectories in the two cases may match perfectly, torques on the elbow will differ. Therefore, the motor system must take into account the weight of objects before it sends motor commands to the muscles. The computation that estimates the motion that will occur as a result of an applied force is called forward dynamics. The mass of objects held in the hand affects this computation: Activation of the biceps at a certain level will flex the elbow by a smaller amount for a full cup than for an empty cup. Forward dynamics consists of predicting the elbow angle after the biceps receives its activation command. The ability to predict the sensory consequences of motor commands relies on this computation. The inverse of this computation, called inverse dynamics, allows the motor system to transform the desired motion of the limb into the patterns of muscle activation that produce the torques required for the task.

However, in everyday life, even movements as simple as lifting a coffee cup can encounter impediments. When something disturbs arm movements (e.g., an unexpected change in the load on the hand), movements lose their smooth and regular character. However, provided that the perturbations have high predictability, with practice the movements again become straight in terms of hand trajectory. This convergence toward a straight, simple trajectory in hand coordinates (rather than joint coordinates) further supports the idea that the motor system plans movements in terms of the position of the hand and other end effectors rather than joint angles or patterns of muscle activity. In other words, the motor system plans in terms of goals rather than the components of movement. Motor learning and memory often under-

lies the ability to make smooth, straight movement despite external perturbations and the forces of each part of a limb acting on the others.

III. MECHANISMS OF MOTOR CONTROL

Neurophysiologists have only begun to understand the mechanisms of the motor system, and this section should be considered a highly provisional account of these mechanisms. Most of the relevant information comes from studies of neuronal activity in awake, behaving monkeys.

In generating the plan for a simple reaching movement, the initial problem involves kinematics, figuring out the current location of the end effector (often the hand), the location of the target, and perhaps the path between them. Both the premotor cortex (PM) and the posterior parietal cortex (PPC) appear to have key roles in solving this problem. The general locations of these cortical regions are depicted in Fig. 2.

A. Location of Targets and Initial Hand Position

PPC, in particular, plays an important role in determining the location of objects that could serve as the target of a reaching movement. Cells in one part of the PPC, the parietooccipital area (PO; approximately corresponding to areas V6 and V6A), respond to visual stimuli and, unlike most visual areas, their receptive fields have no bias toward the foveal representation. This characteristic suggests that the visual information PO processes relates to the control of movement rather than the analysis of an object's features. Some PPC neurons signal the presence of a target in retinal coordinates (i.e., the location of a target with respect to the fovea). These cells could be particularly important in controlling eye movements to that target, but they might also function to compute reaching, head, and eye movements within a single coordinate framework. One PPC region, the lateral intraparietal cortex, appears to be particularly important for eye movements, whereas a nearby region, the medial intraparietal cortex (MIP; also known as the partial reach region, PRR), plays a larger role in reaching movements. Other cells in PPC show an influence of "extraretinal" signals such as eye and head position. Some PO neurons, for example, appear to indicate target location with respect to the head (i.e., in head-centered coordinates). These signals mark the beginning stages of transforming visual information from a

receptor-based (retinal) coordinate frame into one more useful for reaching movements. For those movements, it is more useful to represent the target location relative to the end effector that will make the movement. Other parts of PPC play a larger role in determining the initial position of the end effector. One part of parietal area 5, for example, encodes hand position with respect to the shoulder. These and other parts of PPC operate in cooperation with the motor cortex, including both PM and M1.

Like the PPC, cells in the dorsal part of PM respond to a combination of signals relevant to voluntary reaching movement, including visuospatial and proprioceptive input, as well as inputs reflecting gaze direction, the location of objects in the environment, the orientation of spatial attention, and nonspatial visual information (such as color and form). Gaze effects show that the location of the target relative to eye position has some importance in motor control, perhaps for coordinated movements of eye and hand when people reach one place while looking at another. Attentional signals might be important when not all reaching targets can be foveated, as often is the case for a sequence of movements in a cluttered visual scene. In addition to these target-related signals, cells in dorsal PM (along with many in M1) are sensitive to the initial position of the hand, possibly through both proprioceptive and visual inputs. Similarly, cells in the ventral part of PM respond to both somatosensory and visual inputs as well as spatial acoustic signals. Whereas the PPC coordinate systems seem to reflect eye-, head-, and body-centered frames, ventral PM appears to be more specialized for the particular body-centered coordinate frame that is most useful for a given movement. In ventral PM, when a body part having a tactile receptive field moves, the visual receptive field moves in the same way: Visual receptive fields on the hand move with the hand, and those on the head move with the head. Therefore, it appears that these PM cells encode the potential targets of action relative to the body and update this map whenever the pertinent body part moves. Thus, PPC and the motor cortex derive much of the information needed for formulating a kinematic trajectory, including the starting position of the hand and the target of movement in each of several relevant coordinate frameworks.

B. Dynamics

At least two brain structures mediate the generation of force profiles that move the hand smoothly to a target:

M1 and the cerebellum. The nonprimary motor cortex and basal ganglia appear to be less involved in this function.

It is likely that the network computing inverse dynamics includes the cerebellum. Damage to it results in movements that suggest an inability to compensate for the complex dynamics of multijoint reaching movements, including forces that arise due to interaction among limb segments (interaction torques). For example, the intact motor system approximates the inertia of the arm in programming activations of muscles, whereas cerebellar damage results in movements that suggest a deficit in this transformation. Normal individuals produce coordinated motion of the joints during reaching movements, whereas cerebellar patients produce movements that often consist of a sequence of single-joint motions. Neurons in the cerebellum have properties consistent with this view, including Purkinje cells that reflect movement velocity and the forces needed to achieve a certain trajectory.

M1 plays a role in limb dynamics as well, in part through its reciprocal interaction with the cerebellum. A century-long controversy has surrounded the question of whether M1 neurons encode primarily kinematics or dynamics. This problem, known informally as the muscle versus movement debate, consists of at least two parts. One part concerns how M1 addresses muscles. Some studies in the 1970s suggested that the M1 neurons address individual muscles, but refinements in research techniques have led to the understanding that individual neurons in M1 address multiple motor pools, usually of synergistic muscles. This view is consistent with the branching of corticospinal neurons to multiple motor pools and with the fact that they terminate principally on spinal interneurons rather than alpha motor neurons. These results support the “movement” side of the debate, but there is another issue. It involves the motor-control signal that M1 sends to the motor pools, and it yields a different answer—one more consistent with the “muscle” side of the debate.

A pure force signal in M1 neurons would support the view that they control muscles. Neurophysiologists have not completely settled this question, but three facts have been clearly established. First, when the hand generates a force that does not lead to movement (as happens when the hand pushes against an object so rigid that it does not move), cells in M1 have approximately the same patterns of activity as when the limb moves. Second, loads exerted on the hand can either assist a movement or oppose it. Neither kind of load changes the kinematics of movement appreciably,

but the forces involved in making the movement can differ greatly. Many cells in M1 differentiate between these two conditions, and they therefore appear to reflect limb dynamics. Third, the posture of the arm, which changes both joint angles and limb dynamics, affects the activity of M1 cells, even when the end effector path has nearly identical kinematics. The predominance of signals related to limb dynamics supports the muscle side of the debate and, therefore, a role for M1 in controlling limb dynamics. However, this view should not be taken to an extreme. There is evidence that limb kinematics is reflected by M1 cell activity, as well.

C. Kinematics

There is no evidence for a purely kinematic signal in M1. A purely kinematic signal would be invariant to loads on the limb or the initial posture of the arm. Such invariance has been observed in PPC (area 5), supporting the idea that it is mainly involved in movement planning in kinematic terms rather than movement execution in terms of limb dynamics. However, in M1 evidence points to a combination of kinematic and dynamic signals, as shown in the following experiment: Like people, monkeys can move their fingers upward by bending the wrist in different ways. If the palm is up, then the wrist can be flexed (i.e., moved in the palm's direction) to move the fingers upward. If the palm is down, then the wrist can be extended to achieve the same results. Some M1 neurons reflect only limb dynamics (i.e., flexion or extension), but others show an intermediate pattern of activity that takes into account both kinematics (end effector movement) and dynamics (muscle activity).

Large parts of nonprimary motor cortex, especially those on the lateral parts of the hemisphere, appear to function in the sensory guidance of movement at a kinematic level. For example, neurons in the dorsal and ventral PM have greater activity during visually guided movements than during memorized sequences, but they are not much affected by loads. The former observation points to a specialization for sensory guidance of movement, the latter to a specialization for kinematics. As noted previously, the activity of both PPC and PM neurons reflects the location of movement targets. However, this is not a purely sensory response in either PPC or PM. Instead, their activity reflects the motor significance of those signals at different levels. A term that has been used for motor significance in this sense is intention. For example,

when monkeys indirectly move a spot on a video monitor by pushing or pulling on a joystick, researchers can distinguish neuronal signals related to the direction of spot movement from those reflecting the direction of limb movement. Many neurons in at least one part of PPC, MIP, signal the direction of hand motion, not spot motion. Also, they signal the location of movement-guiding spots only when the spot directs a reaching movement and not when it directs an eye movement. A population of cells in dorsal PM and the vast majority of cells in M1 do so as well. As another example, when a visual cue indicates the location of the next target of a reaching movement, but movement needs to be delayed until some future time, cells in both the PPC (area 5) and dorsal PM cortex signal the direction and amplitude of the planned movement. This “delay-period” activity begins about 100 msec after the cue appears and can continue for several seconds. PPC neurons do not distinguish between objects that will be the target of the next reaching movement and similar objects that indicate (e.g., by their color) that they will not be the subject of immediate action. Thus, PPC neurons signal potential movements or movement targets but not necessarily those that are currently planned. PPC neurons also reflect, in their activity, the expected benefit to be gained by moving toward a potential target. Neurons in dorsal PM, in contrast to PPC neurons, have delay-period activity only when the object will be the target of the upcoming movement. Thus, at the level of the nonprimary motor cortex, especially PM, neural activity appears to relate mainly to the implementation of near-term kinematic plans and other relatively high-level goals.

Cells in the basal ganglia, also reflect the kinematics of reaching movements, such as direction and amplitude. However, the basal ganglia is unlikely to have a significant role in solving the inverse dynamics problem or computing the motor plan. Most basal ganglia activation or inactivation occurs too late to have a very large role in movement initiation or the planning that precedes it. Instead, the activity in basal ganglia develops at about the same time as muscle activity and continues during movement. Accordingly, it has been proposed that pallidal output plays a predominantly modulatory role. According to one hypothesis, motor-control signals depend, in part, on recurrent, mutually supporting activity in cortical–thalamic modules (or loops) that include motor cortex. Pallidal output may affect limb kinematics by facilitating or suppressing these recurrent circuits during an ongoing movement. It appears paradoxical that when the

motor parts of the basal ganglia's output projection are surgically destroyed, patients with Parkinson's disease can initiate movements more easily and move faster than before the surgery. Damage to motor-control structures usually causes rather than relieves motor dysfunction. However, the movement-modulation hypothesis resolves this paradox. Applying the brakes will slow a car, even though the brakes are not part of the movement-generation system. It is also thought that the basal ganglia function in context-dependent movement selection as well as in sequential and internally generated movements.

D. Goal Achievement

1. Limb Trajectory

M1 neurons reflect information about the direction, magnitude, and speed of the movement, in addition to postural signals. They have their greatest discharge rate for movements in one direction, with systematically less activity as the direction of movement diverges from that direction. They are therefore broadly tuned for movement direction, although this preferred direction can change with variations in starting hand position, the posture of the limb, and many other factors. On the assumption that these cells contribute to movements in their preferred direction, it is possible to compute a single vector, termed the population vector, representing the net contribution of a neuronal population. The M1 population vector anticipates the direction of limb movement for straight-line reaching movements (as well as for a variety of curved trajectories) by 30–120 msec.

Cells in the nonprimary motor cortex have properties similar to those of M1 cells but with some important differences. For example, cells in M1 are generally specific for the limb used, usually the limb contralateral to the hemisphere in which the cell is located. Cells in dorsal PM have activity broadly tuned for reaching direction like M1 neurons but have nearly the same directional preference for movements of the left hand or the right hand to the same visuospatial target. This finding shows that dorsal PM cells reflect the movement in terms of either visual targets or the trajectory of an end effector (in this case, a handle that the monkey moves). Evidence points to the former explanation. It appears that PM and M1 differ in the degree to which the visual inputs that guide a movement affect the activity of its neurons. Experiments have been done in which the monkey must follow a

visual trajectory, but this visual input is projected directly to its eyes so that the relationship between vision and movement can be altered. Sometimes the visual target trajectory and the movement trajectory, perhaps an oval, are the same, but sometimes the hand trajectories must be circular to match an oval visual input or vice versa. PM populations reflect the visual target trajectory with more fidelity than the end effector trajectory, whereas M1 populations more closely reflect the movements of the end effector (the hand). This supports the idea that the motor system computes movement trajectories in terms of end effectors, with visual target trajectory predominant in PM and limb trajectory predominant in M1.

2. Compensation for External Perturbations

A part of the long-loop reflex, M1, receives somatosensory information that helps compensate for unexpected perturbations during movement. For example, when a hand movement is stopped in progress by an external force, M1 neurons that precede and accompany the movement with a burst of activity renew or increase that activity in response. This signal probably arises from the muscle spindles, which shorten in concert with the extrafusal fibers due to their input from gamma motor neurons. When the limb is stopped, both alpha and gamma motor neurons continue to discharge according to the motor plan. The extrafusal fibers build up force, but the muscle cannot shorten. The muscle spindle fibers continue to contract, which generates a signal comparable to that evoked by a muscle stretch. This signal is relayed to M1 and it causes the motor-control signal to be augmented. The resulting increase in activity serves to compensate, at least partially, for the perturbation, although it may not be adequate to overcome the impediment. This kind of mechanism could account for the achievement of goals upon the initial presentation of a particular perturbation.

IV. MOTOR MEMORY

A. Implicit and Explicit Memory Systems

The brain regions that store motor memories differ from those that store conscious memories. The former comprise an aspect of procedural memory or knowledge and the latter declarative memory or knowledge. Psychologists often refer to procedural knowledge as implicit memory and to declarative knowledge as

explicit memory. Some psychologists use the term “habit” interchangeably for procedural knowledge, but this usage should not be confused with its biological meaning, which involves instinctive behavior.

The idea that different brain structures underlie explicit versus implicit memory comes from observing the effects of brain damage. Damage to structures in and near the medial temporal lobe (MTL) results in loss of certain recently acquired information. Amnesic patients with MTL lesions can learn and retain skills such as mirror tracing, rotary pursuit, bimanual tracking, and compensation for complex forces applied to the limb during reaching movements. Despite this motor learning, the patients may not be able to recall the training episodes.

The distinction between an explicit memory system, which depends on the MTL, and an implicit motor memory system has several implications for motor control in the human brain. Voluntary actions have been defined as those that are learned, attended, and based on a comparison among alternatives. This awareness depends on the explicit memory system. Other actions, including but by no means limited to reflex movements, proceed without conscious awareness. Some subconscious movements bear obvious markings of this unawareness, such as the stretch reflex or the vestibuloocular reflex (VOR). The latter serves as a case in point. When people move their head left while looking at something, their eyes move equally fast and equally far in the opposite direction. They are probably aware of the object at the focus of attention. However, they cannot report anything about the motor memory that allows them to keep looking directly at that object, regardless of their head movements. Adjusting the VOR involves motor learning in the broadest sense but differs dramatically from that underlying voluntary movement. People cannot make VOR-like eye movements voluntarily. Movements such as the VOR and other reflexes can only be controlled implicitly.

Other movements that can be made without conscious awareness closely resemble voluntary actions. They can be guided either implicitly or explicitly. The best studied example of this phenomenon is termed blindsight. Normally, pointing to visible targets is accompanied by explicit knowledge of the action and the goal. However, some people with damage to the visual system can point to a visual stimulus while denying that they see it. Thus, some of the visuomotor networks remain functional even when the networks underlying visual perception fail. Phenomena such as

blindsight have led to a distinction between CNS systems underlying vision for action (and therefore implicitly guided action) and those involved in vision for perception (which may or may not lead to explicitly guided action). The distinction between these two information processing systems does not depend on brain damage. Normal people can make finger movements that accurately match the size of objects they touch but nevertheless describe the size of those objects incorrectly due to visual illusions. People can also make accurate saccadic eye movements to fixate a visible target, although they report that the target moved in some different direction due to different kinds of illusions.

Which brain structures underlie motor memories, implicitly guided action, and procedural knowledge? To answer this question, it is useful to distinguish reflexes (such as for the VOR) from explicitly guided movements. Much of the information underlying the former is stored at the brain stem level, including the cerebellum. The cerebellum also has an important role in classical conditioning, through which sensory inputs are linked to stimuli that trigger reflex responses. Accordingly, it is clear that the cerebellum plays an important role in motor learning and memory at the reflex level. However, the situation is more complex for movements that are sometimes voluntary and under conscious control (explicitly guided action) but that also can become automatic and unattended as they become routine (implicitly guided action).

The oldest and most common idea holds that the MTL subserves explicit knowledge, whereas the basal ganglia underlies implicit knowledge. Patients with Parkinson’s disease show particular deficits on tasks involving implicit estimation of event probabilities, for example, along with a wide variety of tasks involving motor skills. A newer idea holds that explicit knowledge is stored in prefrontal cortex and an associated part of the basal ganglia, along with the MTL, whereas some aspects of implicit knowledge are stored in motor cortex and their associated parts of the basal ganglia, along with the cerebellum. [The distinction between prefrontal and MTL function is that between long-term information storage of many months or years (prefrontal cortex) and intermediate-term storage of many weeks or months (MTL)]. Brain imaging studies, especially those that have explored the concept of attention to action, appear to be more consistent with the newer view. In motor learning, attention to one’s actions and explicit knowledge of those actions (and outcomes) dominate the early part of training on a novel task. As a motor task becomes more automatic,

fewer attentive resources are engaged, and eventually it might be performed without awareness. Neuroimaging results have consistently shown increased blood flow, an indirect marker of synaptic activity, in the prefrontal cortex as subjects begin to perform motor tasks that involve learning a new skill. This increased activation generally declines to baseline as the task is extensively practiced and becomes automatic. Conversely, as a sequence or skill becomes more automatic, cerebellum (especially posterior parts), nonprimary motor cortex, and PPC show increases in activity. These findings support the hypothesis that prefrontal cortex–basal ganglionic modules subserve voluntary movement, whereas the motor cortex–basal ganglionic modules (along with the cerebellum and the PPC) underlie more automatic movements of the same kind.

Besides neuroimaging experiments, other evidence also implicates the cerebellum in motor learning. In a monkey trained to stabilize the wrist against an externally imposed load, for example, the cerebellum has been inactivated by cooling it. This manipulation eliminated the previously learned, predictive component of the muscle activity, which would oppose the imposed load. Furthermore, development of motor memory has been associated with an increase in the number of synapses onto the Purkinje cells in the cerebellum. Significant synaptic remodeling on Purkinje cells takes place within 1–4 hr after completion of initial training.

B. Internal Models

1. Acquisition

When a novice operator learns to control a novel mechanical system, the brain solves three types of computational problems: optimization of the task performance criteria to arrive at a kinematic plan (i.e., learning how the mechanical system should behave in order to accomplish the goals of the task), learning a model of the forward dynamics of the mechanical system (i.e., acquiring an ability to predict how the mechanical system will behave as a function of current input, and learning a model of the inverse dynamics of the controlled system (i.e., acquiring an ability to predict the inputs that should be provided to the mechanical system for a given desired change in state of that system). For example, consider the case of an operator acting on a joystick that controls the thrust produced by the motors of a remote underwater vehicle. The task involves moving the vehicle from point A to point B. The kinematic plan specifies a

smooth vehicle trajectory. The forward model specifies how the vehicle will behave as the operator moves the joystick. The inverse model estimates how the operator should move the joystick so that the vehicle moves along the planned trajectory. An internal model (IM) is a blanket term used to describe the information contained in the solution to these three types of computational problems, and motor memory refers to the representation of IMs in the brain.

People use IMs in nearly every voluntary movement. For example, consider trying to lift an empty bottle of milk that has been painted white on the inside so that it appears full. The motor system will generate muscle activation patterns in the arm that provide the forces appropriate for lifting a full bottle, resulting in a flailing motion. This fact indicates that in programming the motor output to the muscles of the arm, the motor system uses certain visual characteristics of the object to predict and compensate for its mechanical dynamics. Learning IMs has been investigated in experiments in which a subject reaches to a target while holding the handle of a lightweight robotic arm. Disengagement of the robot's motors results in smooth and straight-line movements. Motor learning starts when the investigator programs a pattern of forces for the robotic arm to produce. These forces represent novel dynamics. When a person starts the training process, the computations that the brain performs in programming muscle activations do not take into account the novel forces, resulting in jerky hand movements. To compensate, initially people stiffen the entire limb through general coactivation of the muscles. This results in improved arm stability but serves only as a temporary and relatively ineffective strategy for responding to the perturbations. With training, stiffness returns to normal levels at the same time as the brain builds an IM of the novel dynamics. The motor output changes to specifically account for the additional forces. The development and use of a new IM can be demonstrated by turning off the robot's motors at the onset of movement. The resulting movement is a mirror image of that observed early in the training process. Therefore, the motor command that reaches the muscles includes a prediction by the IM of the forces required to overcome the imposed mechanical dynamics. The motor system retains this skill for months after the training session.

2. Consolidation

As one of its fundamental properties, the neural substrate of explicit memory gradually undergoes a

change, becoming more resistant to disruption. Newly acquired memories are more sensitive to new experiences and more susceptible to interference or brain injury. Posttraining treatments, including electric shocks, removal of key anatomical sites, or inhibition of protein synthesis, retard this progression and often result in loss of the recently acquired information. These interventions, however, have little effect on recall once a window of time has passed since acquisition. Consolidation refers to this time-dependent process. Does such a process occur in the storage of motor memories?

Until recently, little evidence supported the idea that time affected properties of motor memory. For example, it was found that whereas electroconvulsive shock interfered with conscious memories, it spared retention of a newly acquired skill (e.g., reading words in mirror image). Recent work, however, has found evidence for a temporal gradient in motor memory. The results suggest that within 4–6 hr after completion of training in a reaching task, functional properties of the motor memory gradually change. Subjects learned reaching movements in force pattern 1, leading to an internal model termed IM1, and then a second force pattern, termed force pattern 2, leading to an IM2. Their ability to learn IM2 depended on the time that had passed since completion of practice in force pattern 1. If only a short time had intervened (less than 4 hr), learning of IM2 was impaired compared to that of naive subjects. By the time 6 hr had elapsed, the interference caused by their training in force pattern 1 had subsided. This evidence points to the limited capacity of the system initially engaged in learning new skills. With time, the information maintained in this system fades, allowing the learning of additional skills. If this limited-capacity system serves a kind of intermediate-term memory stage for motor skills pending consolidation into a long-term memory store, then one would predict that its disruption might lead to an inability in long-term recall of motor memories. Indeed, learning IM2 within 4 hr after performing the movements in force pattern 1 results in an inability to recall IM1 in tests of long-term recall.

a. Apraxia as a Disorder of Motor Memory Apraxia occurs in numerous forms, of which at least two may represent disorders of motor memory. Ideomotor apraxia is characterized by kinematic errors made as patients copy movements or perform according to verbal instruction. Ideational apraxia is revealed by the incorrect miming of an action appropriate for a tool. In these patients, the ability to make the

movements is relatively intact, but the motor system fails to produce the motor program that should be called up by the input, be it verbal or nonverbal instructions, as in ideomotor apraxia, or an object with a well-known use, as in ideational apraxia. The brain areas that fail in these situations have not been definitively established, but both PM and PPC appear to be involved. PM plays an important role in retrieval of a motor response as cued by visual or auditory stimuli, and PPC lesions cause some forms of apraxia. For example, a dentist with PPC damage suddenly complained that he “did not know” how to use a drill. This has been viewed as an example of a loss of a previously learned motor skill.

V. FLEXIBILITY IN MOTOR CONTROL

The ability to store motor memories enables the motor system to select a wide variety of movements in a highly flexible manner. People can select actions from a large repertoire of skills that have been previously learned, depending on context. In many contexts, achieving the goal of the motor system depends on movements made directly to targets, such as reaching to grasp an object. In others, more flexible relationships need to be established between objects and actions.

According to current thinking, different kinds of motor flexibility are afforded by different parts of the frontal cortex. Lateral nonprimary motor areas (such as dorsal PM) are thought to compute arbitrary mappings based on external (sensory) cues, whereas medial nonprimary motor areas (such as SMA) play an analogous role for internally generated actions, including memorized movement sequences. M1 is thought to enable a different sort of flexibility through the fractionation of motor synergies. Thus, it is commonly held that M1 functions mainly to permit motor “fractionation” (i.e., the independent control of muscle groups that usually work in concert). For example, the long muscles of the arm attach to several fingers to either flex or extend them. However, people can move their fingers one at a time.

A. Sensorimotor Mapping

Many reaching movements are made directly toward a target object. The term standard mapping applies to these kinds of movement. People often look at an object, orient attention toward it, and reach directly to

touch or grasp it. However, human behavior would be scarcely recognizable were it limited to standard mapping. People can also look in one direction while attending to a different place and reaching to a third, and everyone can use both spatial and nonspatial information to guide action.

1. Transformational Sensorimotor Mapping

In explaining the difference between standard and nonstandard mapping, prism adaptation serves as a case in point. When a diffracting prism distorts visual input, objects that lie directly in front of a person might appear to be 10° off to the right. When the person tries to reach to the object, he or she will reach $\sim 10^\circ$ too far to the right. However, the motor system can recognize this error and correct it through the process of motor adaptation, similar to that described previously for studying internal models (see Section IV.B). This behavior serves as a paradigmatic example of standard mapping: The motor system achieves the goal of directing the hand to the object, even though the prism distorts the object's location. In contrast, people can decide voluntarily to make a movement $\sim 10^\circ$ to the right of an object's location. This behavior serves as an example of nonstandard mapping. The motor system can produce an output that uses the spatial information in an object and transforms it according to some algorithm (such as 10° to the right) to produce a more flexible motor output than a system limited to standard mapping. This form of nonstandard mapping can be termed transformational mapping because the motor output depends on some transformed function of the spatial input.

2. Arbitrary Sensorimotor Mapping

Both of these spatially guided movements contrast with another form of nonstandard mapping termed arbitrary mapping. When nonspatial visual inputs, such as color, are used to determine the goals of action, an arbitrary mapping must be learned. Imagine a building with rooms of two colors: yellow rooms that require doorknobs to be twisted clockwise and blue rooms that require the opposite. Reaching toward the doorknob relies on standard mapping. Opening the doors requires arbitrary mapping, at least to do so reliably on the first attempt. Although this example is artificial, most signal- or symbol-guided behavior, including almost all language-guided behavior, depends on arbitrary mapping. Examples include stopping at a red light or at the sound of the word "stop."

B. Internal versus Sensorimotor Mapping

The idea that lateral nonprimary motor areas (such as PM) underlie external control of action, whereas medial areas (such as SMA) subserve internal control, has a link to related ideas concerning the motor functions of the basal ganglia and the cerebellum. It has been proposed that the cerebellum functions preferentially in externally guided action, whereas the basal ganglia controls mainly internally guided action. However, the functions of these structures are more complex than can be captured by such a simple dichotomy. The cerebellum participates in movements based on internal as well as external cues, and the basal ganglia plays a role in movements modulated by sensory as well as nonsensory information. Furthermore, contrary to earlier views, influences from both cerebellum and basal ganglia converge on both medial and lateral nonprimary motor areas.

How can these differing views be reconciled? Some progress can be made by recognizing functional subdivisions with both the basal ganglia and the cerebellum and by eschewing all-or-none dichotomies. Cells in caudal parts of one deep cerebellar nucleus, the dentate nucleus, have a preference for movements based on visual inputs (externally guided action) compared to kinematically similar movements generated from memory, whereas rostral parts have fewer cells with such preferences (i.e., they are relatively nonselective). Likewise, cells in the dorsal parts of the GPi have a strong preference for memorized sequences (internally guided action), whereas the ventral parts of GPi lack such selectivity. M1 and SMA receive their largest inputs (via the thalamus) from the less selective parts of the basal ganglia and cerebellum. Accordingly, M1 and SMA play a fairly general role in motor control and lack strong specializations for either internal or external control.

In contrast, PM receives its predominant inputs from the part of the dentate nucleus more selective for externally guided movements. Accordingly, PM has a large role in externally (often visually) guided action. For example, lesions to or inactivation of dorsal PM prevent monkeys from using color (or other nonspatial visual information) to choose an action.

The internally selective (dorsal) part of GPi preferentially influences the pre-SMA, which likewise appears to be specialized for internally guided action. Cells in pre-SMA have their greatest activity for internally guided movements, including movement sequences, and show other sequence- or order-specific patterns of activity. Temporary inactivation of the pre-

SMA disrupts the ability to produce a memorized (internally guided) sequence but not a visually triggered one. Brain imaging and brain lesion research also suggests the involvement of medial nonprimary motor areas in the learning of both limb- and eye-movement sequences and the “spontaneous” generation of action. In particular, pre-SMA, has been proposed to function in changing or updating motor plans based primarily on signals internal to the CNS.

Therefore, both medial and lateral parts of the motor cortex contain generalized as well as specialized components. Generalized parts include SMA (medially), and M1 (laterally). Specialized elements include the laterally situated PM, which maps sensory information onto motor outputs in a highly flexible manner, and the medially situated pre-SMA, which along with SMA maps a vast array of memorized and other nonsensory information onto motor output. A medial specialization for internal information accords with the role recently proposed for the rostral cingulate motor area in linking incentive magnitude to the selection of action, as occurs when one must choose an action based on some estimation of preferred outcome.

VI. EVOLUTION OF THE MOTOR SYSTEM

The motor system was born, not made, and many of the characteristics of the human motor system reflect its history. The CNS's chief function involves the acquisition of a behavioral repertoire, which can be stored both genetically and epigenetically, and the selection from that repertoire of the actions most likely to enhance an individual's fitness, in the inclusive sense of that term.

It seems likely that the ability to move in a goal-directed manner developed in an invertebrate ancestor of vertebrates. Many experts believe that the coordinated guidance of action represents the principal function of the CNS and comprises, in all likelihood, the crucial adaptive breakthrough made by the vertebrates and their ancestors. (Other animals made the same leap, but this article focuses on the human lineage.) The emphasis on motor control in evolution may seem paradoxical because, to us, complex and sophisticated cognition seems to be the principal characteristic of advanced animals, not motor control. However, in evolutionary history, long before our ancestors possessed the capacity for language, abstract reasoning, or highly general problem solving, they moved in relation to objects and places in their

environment. It seems likely that the invertebrate ancestors of vertebrates (technically, cephalochordates) evolved from filter-feeding ancestors. They could swim in a coordinated manner, and they directed those actions with a brain and sense organs concentrated on the head, including paired eyes. The ability to do these things allowed our very distant ancestors to adopt a hunting life, one probably dominated by olfaction and vision. According to the fossil record, this revolutionary advance occurred about 500–550 million years ago. The human motor system, along with that of other vertebrates, has developed its capabilities by building on the original system. The motor system that people use to run, walk, talk, and manipulate objects evolved from the same one that originally evolved to control swimming and that was adapted to control flying, burrowing, and galloping in other species.

Thus, the motor system has a high degree of functional plasticity, at least as measured over geologic time. This plasticity of function contrasts with the conservatism of this basic morphological organization throughout vertebrate evolution. In the past, authorities have speculated that the brain evolved from caudal to rostral. That is, early comparative anatomists thought that the basal ganglia, for example, being located mainly in the telencephalon, evolved relatively recently in evolution. Anatomical names such as neostriatum testify to this notion. However, recent evidence from comparative morphology shows that the basal ganglia evolved very early in vertebrate evolution, probably at about the same time as the appearance of the first true vertebrates. Most of the remainder of the motor system also reflects our inheritance from our distant vertebrate ancestors. In addition to the basal ganglia, the superior colliculus, the red nucleus, the reticulospinal system, CPGs, and the alpha motor neurons retain their basic organizational patterns and functions from the earliest history of the vertebrate brain. The evolution of the cerebellum remains less certain, but it clearly emerged relatively early in the history of vertebrates as well.

What has changed in the past 500 million years or so? Of course, many of the basic components of the motor system have been elaborated and modified in many ways. In addition, an entirely new component has been added. In contrast to the ancient components of the motor system enumerated previously, the motor areas of neocortex have evolved much more recently. In a form that people can recognize as distinctively neocortical, a clear-cut motor cortex appears only in mammals. Thus, a separate motor cortex appears to

have evolved only approximately 180 million years ago, a short time by evolutionary standards, especially compared to the ancient lineage of the motor system's other main components. The relatively recent development of the motor cortex suggests that an important aspect of motor cortex function involves the modulation and control over subcortical motor systems, including the introduction of novel levels of flexibility in the motor system, such as transformational and arbitrary mapping, and the fractionation of relatively hardwired motor synergies.

See Also the Following Articles

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