

NEW PERSPECTIVES ON SPINAL MOTOR SYSTEMS

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The production and control of complex motor functions are usually attributed to central brain structures such as cortex, basal ganglia and cerebellum. In traditional schemes the spinal cord is assigned a subservient function during the production of movement, playing a predominantly passive role by relaying the commands dictated to it by supraspinal systems. This review challenges this idea by presenting evidence that the spinal motor system is an active participant in several aspects of the production of movement, contributing to functions normally ascribed to 'higher' brain regions.

INTERNAL MODEL

A representation used by the nervous system to account for the properties of the motor apparatus and the environment. Such properties could include features of the limbs, such as their lengths and their masses, and could also include features of an object to be manipulated.

SET-RELATED ACTIVITY

Neuronal activity that reflects the behavioural 'set' of the animal, which can include information about a planned movement or about the state of readiness of the animal.

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The production of every movement, whether it be a fundamental motor pattern such as walking or a complex motor skill such as playing a musical instrument, requires the control of a vast number of variables, ultimately involving the coordinated activation of muscles across the entire body. The central nervous system controls these variables by a cascade of computational processes such as the transformation of sensory information into an appropriate motor plan, the estimation of INTERNAL MODELS, and the use of feedback for adaptation and learning. Traditional views of the architecture of complex motor control have usually stressed the active contributions of the cortex, basal ganglia and cerebellum with the spinal cord contributing only passively, in the final execution of movement. This review discusses three lines of evidence that indicate that the spinal motor system is an active participant in several aspects of the production of movement. First, a recent set of technically demanding experiments show that neurons in the spinal cord are active during movement planning in a manner similar to the circuitry of supraspinal regions. Second, recent results indicate the participation of spinal motor systems in motor adaptation. Last, we review some results examining the organization of movement by spinal interneuronal systems. Taken together, these results lead to an alteration in our view of the motor system architecture and the relative contributions of spinal and supraspinal structures to complex motor control.

Preparatory activity in the spinal cord

In many everyday situations, we are aware of planning a movement before actually producing it. Waiting to accelerate at a traffic light or preparing to step over an obstacle, we often create an internal plan of the impending press on the accelerator or of the forthcoming flexion over the obstacle. In an examination of the neural substrates of such internal motor plans, Fetz and collaborators¹⁻³ have investigated the activity of spinal cord interneurons in monkeys trained to perform flexion-extension wrist movements. A distinctive feature of the training instigated by Prut and Fetz³ was the establishment of a time interval between the instruction cue and the subsequent triggered movement (instructed delay period) (FIG. 1). It is known that neural activity during the delay period reflects movement planning and occurs in the absence of muscle activity. This preparatory activity has been found to occur in many motor centres, including the primary motor cortex, the premotor cortex and the basal ganglia⁴⁻⁹. Surprisingly, some of the spinal interneurons also show SET-RELATED ACTIVITY during the instructed delay time³. This observation indicates that movement preparation develops simultaneously over a number of areas, including a region as peripheral as the spinal cord. About one third of the interneurons recorded by Prut and Fetz showed modulation of resting activity during the instructed delay time. Of these interneurons, a few increased their firing rate during the delay and then showed a further increase during the

time of movement as if they had a priming function for the motor neurons. However, most of the modulated interneurons were inhibited during the delay period and so suppressed the tendency to initiate movements.

These experiments were among the first to apply methods developed for the study of higher motor areas in behaving animals to the analysis of spinal interneuronal systems. Because of the considerable technical difficulties in recording spinal neuronal activity in

awake behaving animals, investigations on spinal motor systems have generally been undertaken in anesthetized or paralysed decerebrate preparations. The behavioural dissection of neuronal activity, commonly used to study supraspinal structures in awake behaving animals, has been extremely difficult to do in the spinal cord. By overcoming these technical difficulties, Fetz and collaborators were able to examine spinal neuronal systems with the same methods as those used in the study of supraspinal systems, clearly showing the involvement of spinal structures in functions typically reserved for supraspinal systems.

Characterization of spinal interneurons. One disadvantage inherent to the study of behaving monkeys, however, is that they generally preclude the characterization of spinal interneurons in terms of their connectivity patterns, although indirect techniques such as spike-triggered averaging can provide some information about these patterns. The strength of the reduced preparations generally used to study spinal motor systems has been the ability to systematically characterize the inputs and outputs of individual spinal interneurons by stimulating different sensory and descending pathways and recording from postsynaptic motor neurons. Such studies of interneuronal connectivity patterns have provided a wealth of information as to different classes of spinal interneurons and their potential roles in motor behaviour^{10,11}.

Ideally, we need a synthesis of the approaches used in awake behaving animals and those used in reduced preparations, to examine the activity of identified spinal interneurons in a controlled functional context. A recent example of such a synthesis is represented by the work of Bosco and Poppele^{12–14}. Their studies take a step toward revealing the functional properties of an identified class of spinal neurons — specifically, the dorsal spinocerebellar tract (DSCT) — which conveys sensory information from muscle afferents to the cerebellum. These experiments show that the activity in a subpopulation of DSCT neurons is related to the position of the foot, irrespective of the joint angles used to reach that position. On the basis of this work the authors suggest that DSCT neurons provide high-level sensory processing rather than a simple relay of information from periphery to higher centres. Although geometrical aspects of the periphery might contribute to the described properties of DSCT neurons (for example, REF 15), this work represents the examination of an identified set of spinal neurons in a clear functional context.

One interneuronal system that is clearly relevant to the interaction between spinal and supraspinal systems has been described by Alstermark, Illert, Lundberg and co-workers¹⁶. They have identified a population of neurons in the cat cervical spinal cord that mediate the supraspinal control of visually guided reaching. These neurons are located in a disynaptic pathway between cortex and forelimb motor neurons. When the output of these neurons to motor neurons is lesioned, the accuracy of reaching movements is impaired even though other aspects of the movement are unaffected. Although

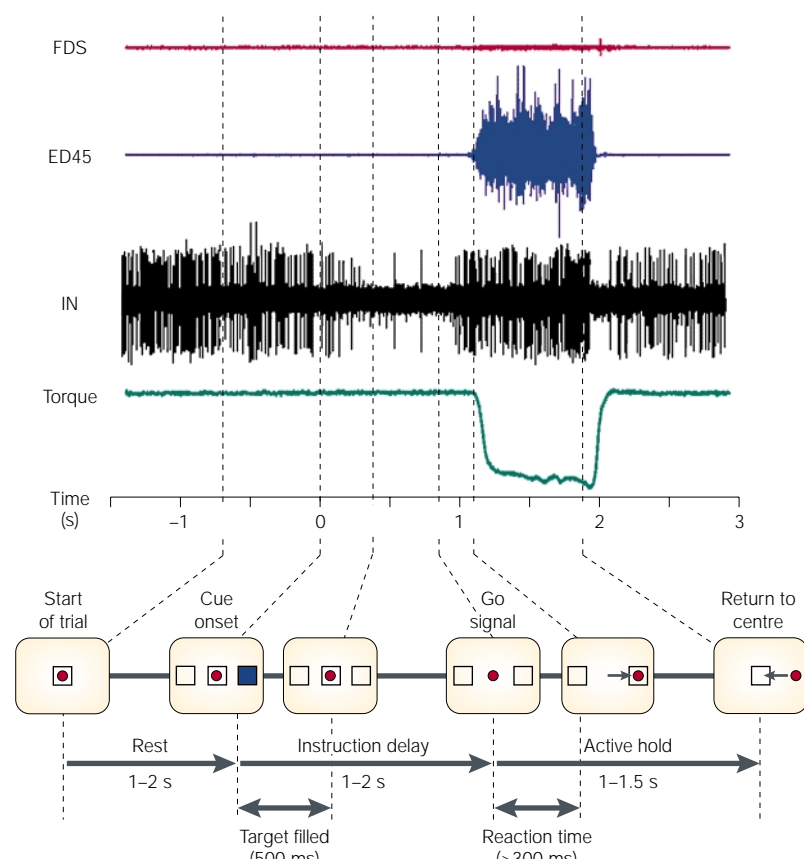


Figure 1 | The involvement of spinal interneurons in the preparation for movement. The activity of single spinal interneurons was recorded in monkeys trained to flex or extend their wrists. The movement of the wrist was prevented and the torque generated by the monkey was used to monitor the motor act. The bottom diagrams show the design of the experiments. The circle indicates the position of a cursor, controlled by the torque measured at the wrist. Proceeding from left to right through the diagram, monkeys were initially required to place the cursor within a central square target. This central cursor position reflects the production of zero torque at the wrist. After a rest period, two peripheral square targets were illuminated, one of which was filled, chosen randomly. The filled target indicated the direction of the wrist movement that the monkey was required to make. However, the monkey was trained to suppress this instructed movement. Both targets were then shown unfilled for a variable period of time. This period represents an ‘instructed delay’ during which the monkey knows the forthcoming direction of movement but is instructed to suppress this movement. At the end of this delay period the central square was removed, instructing the monkey to finally produce the wrist movement. The monkey then held the cursor in the target for a period of time by producing a constant torque, after which the monkey was instructed to release the torque and return the cursor to the central target. The top two traces illustrate the activity of two wrist muscles during a wrist extension movement (flexor digitorum sublimis (FDS, red) and extensor digitorum 4 and 5 (ED45, blue). The bottom trace (green) indicates the torque measured at the wrist. The middle trace shows the activity of a spinal interneuron (IN) during this task. This interneuron was active during the rest period but as soon as the monkey was instructed as to the direction of the forthcoming movement, the activity in this neuron was suppressed. This suppression continued until the monkey was instructed to produce the movement, at which time the activity of the neuron increased. A third of the spinal interneurons recorded showed a modulation of activity during the instructed delay period. (Adapted from REF. 3.)

there has been evidence for a homologous system in humans¹⁷, the presence of such a system in the monkey has been more controversial. Maier *et al.*¹⁸ found some evidence for this system in the macaque, but its contribution to the activation of motor neurons by the cortex was minimal. More recently, Alstermark *et al.*¹⁹ have shown that a strong contribution from this system could be revealed in the macaque after blocking GLYCINE-MEDIATED INHIBITION, indicating a stronger inhibitory control of this system in the primate than in the cat. If this system is, in fact, present in the monkey, it raises the intriguing possibility that it might mediate some of the

preparatory activity of spinal neurons observed by Prut and Fetz³. The examination of this possibility, although experimentally challenging, would clearly provide important insights into spinal cord function during the preparation and planning of movements.

Functional adaptation in the spinal cord
 One of the most remarkable aspects of the motor system is its adaptability. This adaptability is continuously challenged by changes in our environment, in our skeletomotor system, and in the motor tasks that we are asked to perform. Several lines of research have

PARALYSED DECEREBRATE PREPARATIONS

Eliminates movement of the animal. This mechanical stabilization can be accomplished by the application of paralytic agents. This paralysis is often accompanied by a precollicular decerebration in which all brain regions rostral to the superior colliculus are removed.

SUPRASPINAL SYSTEMS

The many regions of the brain that interact with the spinal cord. These systems either receive sensory information from the spinal cord or transmit information to the spinal cord.

DORSAL SPINOCEREBELLAR TRACT

A system of neurons located within the spinal cord, which receive, among other information, sensory information from muscle afferents in the limb and transmit this information to the cerebellum.

VISUALLY GUIDED REACHING

Movements of the arm that are regulated by visual feedback of the target and of the limb.

GLYCINE-MEDIATED INHIBITION

In the spinal cord, neuronal inhibition is largely mediated by the neurotransmitter glycine. This inhibition can be blocked by the neuroconvulsant strychnine.

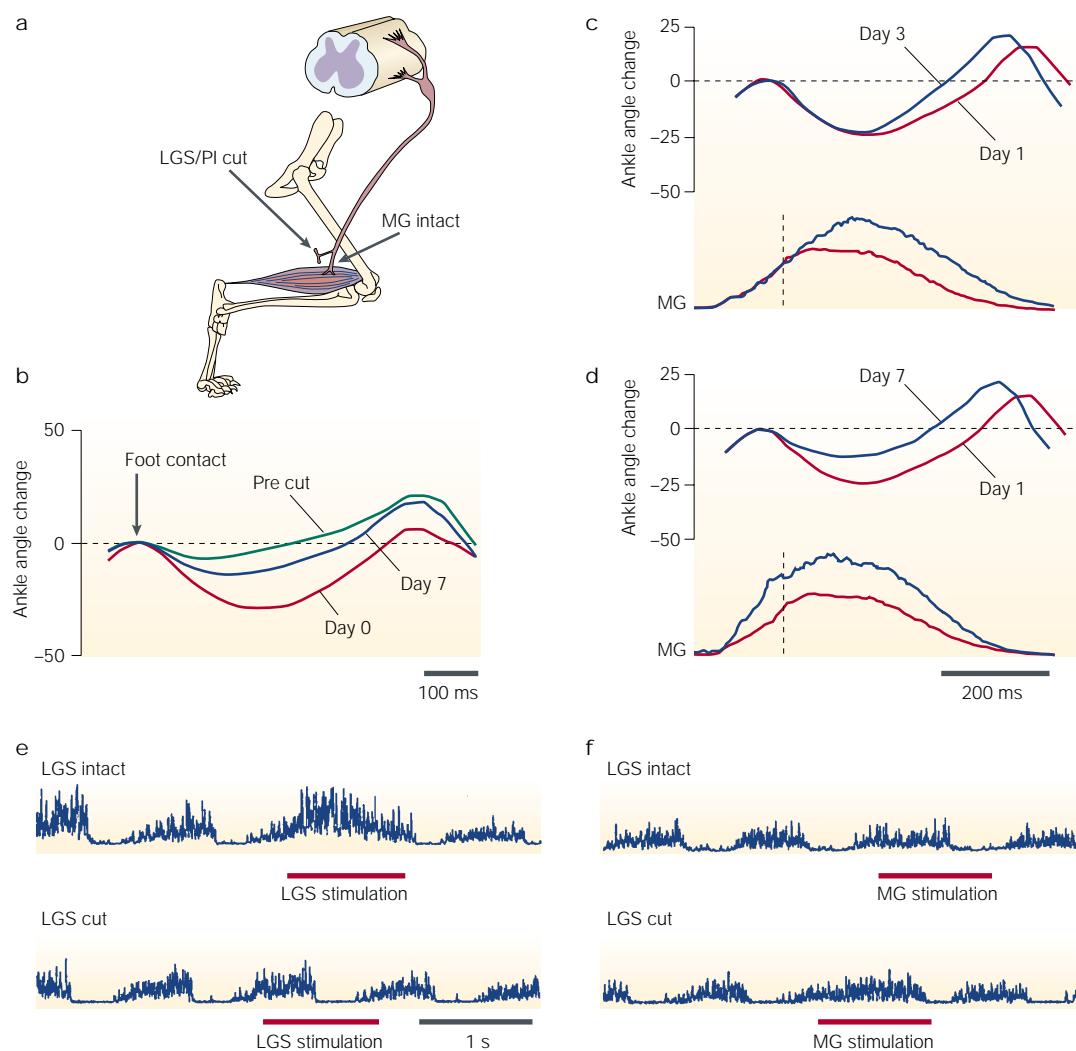


Figure 2 | The process of motor adaptation following ankle extensor nerve cut. a | The nerve projecting to ankle extensor muscles lateral gastrocnemius and soleus (LGS), and plantaris (PI) was cut, leaving intact the ankle extensor medial gastrocnemius (MG). **b** | The change in ankle angle around the time the foot contacted the ground for animals before the nerve cut ('pre'), the day of the nerve cut (day 0), and a week after the cut (day 7). The initial yielding at the ankle caused by the loss of ankle extensor function on the first day after nerve cut was largely compensated for within seven days. **c** | At three days after the nerve cut, a later component of the activation of the MG muscle (blue) was enhanced as compared to the first day after the nerve cut (red). This increase in MG reduced the later component of the ankle yield (top panel). **d** | At seven days after the nerve cut, the activation of MG before foot contact also increased, representing a predictive alteration in the locomotor pattern. **e** | In a leg with acutely sectioned LGS nerve, stimulation of LGS caused a prolongation (top trace) of the activation of vastus lateralis (VL). Bar underneath VL recording indicates period of LGS stimulation. In a leg with the LGS nerve cut chronically, the same stimulation produced no change in the VL activation (bottom trace). **f** | The small prolongation of VL activation by MG stimulation in a leg with the acutely sectioned LGS nerve (top trace) was increased in a leg with the LGS nerve cut chronically (bottom trace). After spinalization all five animals maintained the reduction of LGS efficacy, and two of the five animals maintained the increase in MG efficacy. (Adapted from REFS 27,28.)

Box 1 | Substrates of spinal plasticity

The plastic changes in motor behaviour that follow peripheral nerve cuts result from alterations in several parts of the nervous system, including the spinal cord. One particular alteration, which can be mediated by spinal cord circuitry, is the modification in the ability of peripheral nerve stimulation to prolong the locomotor cycle²⁷ (FIG. 2e,f). Existing knowledge of spinal neuronal systems suggests several candidate substrates for these spinally mediated plastic changes^{58–62}, as described in Pearson and colleagues²⁸. One obvious substrate is the monosynaptic connection between group Ia muscle afferents and motor neurons. However, intracellular motor neuron recordings have not found appropriate changes in this pathway after nerve transection²⁹. Another potential pathway is the disynaptic excitation of extensor muscles from stimulation of group Ia and Ib sensory afferents^{59–62}. This pathway is not expressed at rest but becomes evident during extensor activity. Recent work has tentatively identified a population of spinal interneurons, which might be responsible for mediating this disynaptic excitation⁶². Finally, there is a polysynaptic pathway from Ia and Ib muscle afferents to extensor motor neurons, which might be responsible for the plastic changes⁵⁹. The knowledge of these different SPINAL INTERNEURONAL SYSTEMS makes it potentially possible to identify the physiological substrate of this behavioural plasticity.

MOTOR PERTURBATION

A procedure that results in the disturbance of the normal characteristics of movement. Such perturbations could be induced by the application of a torque pulse during the movement, an alteration in the visual feedback from the limb, or the denervation of a muscle.

KINEMATIC AND DYNAMIC PROPERTIES

Kinematic properties describe the visible aspects of the limb, such as the length of the links, the angles of the joints, or the position of the hand. Dynamic properties describe the forces and torques produced that underlie visible movement.

FEEDFORWARD ANTICIPATORY ACTIVATION

A movement or muscle activation pattern that corrects for a predicted perturbation before the actual perturbation. This is in contrast to a feedback activation which is a response to the sensory signals resulting from the perturbation.

SPINALIZATION

A surgical separation of the spinal cord from the rest of the brain.

SPINAL INTERNEURONAL SYSTEMS

The set of neurons within the spinal cord that are involved in processing information transmitted to the spinal cord, either from the periphery or from supraspinal systems.

examined the principles guiding this adaptation process in human reaching movements. Recent studies have indicated that the process of adapting to MOTOR PERTURBATIONS consists of updating an existing 'internal model' of the skeletomotor system^{20–22}. Such internal models are neurophysiological representations of the KINEMATIC AND DYNAMIC PROPERTIES of the limb, such as the lengths of the limb segments and their inertias. Knowledge of these properties is necessary for the specification of the muscle activations appropriate to the production of a particular limb trajectory. When presented with a perturbation, such as a change in the visual feedback from the limb or the addition of a load, it has been suggested that the sensory feedback errors from the perturbed movements should drive the recalibration of an internal model to produce correct movements^{23,24}. Recent imaging studies in humans and single-unit recording in primates have been aimed at identifying the neural substrates responsible for such adaptation, usually focusing on higher motor areas such as cortex, basal ganglia and cerebellum.

Plasticity in spinal locomotor systems. Recent studies indicate that spinal motor systems might also function during this adaptation process. Experiments by Pearson^{25–29} and by Rossignol³⁰ and their co-workers have examined locomotion in cats after muscle denervation. This denervation causes perturbations to locomotor patterns, which animals are eventually able to correct. Pearson *et al.*²⁸ have examined in detail the changes in muscle activation patterns that follow sectioning of the nerves to ankle extensor muscles. They found that the initial compensation for the loss of ankle extensor muscles was primarily mediated by changes in a sensory feedback pathway from the limb. This component amplified the response of the remaining ankle extensor muscles to ankle flexion. Later in the adaptation process, however, they also found a change in a FEEDFORWARD ANTICIPATORY ACTIVATION of the remaining extensor muscles. Such perturbation-specific, anticipatory changes are strong evidence for the updating of an internal model of the limb during the process of motor adaptation, as sug-

gested by Pearson and colleagues²⁸. So it seems that the process of motor adaptation observed in these studies might be similar to the process observed during human motor adaptation.

In order to investigate the neural substrate of, and the role of spinal motor systems in, this adaptation process, Whelan and Pearson²⁷ transected the spinal cord of animals after they had adapted to the ankle extensor nerve cut. In the spinalized animals, they could evoke locomotor patterns by several methods to examine the state of spinal motor systems, isolated from the rest of the nervous system³¹. After such SPINALIZATION, Whelan and Pearson found that, in some of the animals, at least a portion of the motor adaptation was still present, indicating that spinal motor systems did, in fact, adapt. At present it is not clear whether the anticipatory changes in muscle activation, indicative of an acquired internal model, are also preserved following spinalization. But as hindlimb locomotion is thought to be, in large part, produced by spinally located neuronal networks^{31,32}, one might expect that such changes would be contained within the spinal cord. However, supraspinal structures, such as motor cortex and cerebellum^{33,34}, are also known to be active during locomotion, especially when corrective movements are required. Either way, these results do show that the spinal cord can contribute to the motor adaptation process (FIG. 2, BOX 1).

Distributed locomotor adaptation. A similar conclusion was reached in experiments by Carrier *et al.*³⁰. As in the Pearson experiments, Carrier *et al.* examined the adaptation of locomotion in cats after muscle nerve cuts. Animals adapted to this perturbation in a few days. After this adaptation process, Carrier *et al.* then transected the spinal cord to assess whether any of this adaptation had occurred in the spinal cord. Similarly to the results of Pearson and colleagues, Carrier *et al.* found that there was, in fact, a clear adaptation to the loss of the denervated muscles in spinal motor systems. They further showed that this spinal adaptation required an interaction between spinal and supraspinal systems: if the spinal cord was already transected when the nerve was cut, negligible adaptation occurred. However, these experiments also showed that the spinal cord was not the only site taking part in the adaptation process, because the adaptation in spinal motor systems did not compensate for the functional loss of the denervated muscles. Instead, the adapted spinal motor systems produced locomotion that was disorganized, with exaggerated knee flexion and an absence of plantar foot contact. It is not clear why such a disorganization followed spinalization in these experiments, but was not observed in the experiments by Whelan and Pearson²⁷. However, the fact that different muscle nerves were cut in the two studies might be one important difference. Nonetheless, these results indicate that the adaptation in spinal motor systems was only one part of the complete motor adaptation process: the acquisition and expression of full functional adaptation was possible only when spinal and supraspinal systems were allowed to interact with one another.

Box 2 | Combining modules for movement

To carry out the task of transforming planned movements into a set of motor commands, the central nervous system (CNS) must solve a complex inverse dynamic problem. This problem involves the transformation from a desired motion to the forces that are needed to drive the forearm and the hand. The inverse dynamic problem is a hard computational challenge because of the need to coordinate several limb segments, and the continuous changes in the mechanical properties of the limbs and the environment with which they come into contact.

A number of studies of motor learning have lent support to the idea that the central nervous system creates, updates and exploits internal representation of limb dynamics to deal with the complexity of inverse dynamics. There is evidence that such internal representations are probably built by combining modular primitives as well as other building blocks found in higher structures. For instance, experimental studies on spinalized frogs, turtles, rats and cats have led to the conclusion that the premotor circuitries within the spinal cord are organized into a set of distinct modules. Each module, when activated, induces a specific force field, and the simultaneous activation of several modules leads to the vectorial combination of the corresponding fields. We and others regard these force fields (and the set of muscles that generates individual fields) as computational primitives that are used by the central nervous system for generating a vast range of motor behaviours. Simple linear combinations of force fields, however, are only one aspect of motor programming. For the generation of movement, the CNS must activate the independent functional units, that is, the 'primitives', in a defined temporal sequence. Not much is known about the neural mechanisms of this temporal integration.

The demonstration of plasticity in spinal motor systems is not new^{25,35}. The studies described here extend previous results to examine this plasticity in a clear functional context, and show that functional motor adaptation involves both spinal and supraspinal systems. These findings complement experiments during reaching movements in humans and primates, which show that several brain regions contribute to motor adaptation. Determining the contribution of these different regions, including the spinal cord, to the adaptation of movement will be an exciting topic for future research. These findings also hold the possibility of providing a detailed neurophysiological description of the mechanisms underlying such adaptation. Existing knowledge of the spinal cord suggests several candidate interneuronal pathways for some of these spinal adaptations, all of which can potentially be tested (BOX 2).

Spinal and supraspinal interactions. Schouenbourg and co-workers^{36–41} have recently suggested that a similar interaction between spinal and supraspinal systems takes place during development. Previous research from this group showed that withdrawal reflexes in the rat are organized such that each muscle is most strongly activated by stimulation of the skin which that muscle most effectively withdraws³⁷. The neural substrate for this organizational principle is primarily located in the spinal cord³⁶. In more recent research, Schouenbourg and co-workers have shown this adult organization principle is due to an activity-dependent process during development^{39,40}. So when muscle tendons are transferred in neonatal rats, thereby changing their mechanical actions, the region of the skin from which the transferred muscles are activated changes according to this new action⁴⁰. Moreover, this activity-dependent development requires inputs from descending sys-

tems: if the spinal cord of neonatal rats is transected, the normal adult pattern of withdrawal reflexes does not develop³⁸. So even though the ultimate substrate for this behaviour is in the spinal cord, supraspinal systems are necessary for its development. Similar to the nerve cut adaptation experiments described above, the work by Schouenbourg and colleagues indicates that the acquisition and expression of normal motor behaviours require an interaction between spinal and supraspinal systems.

The composition of behaviour

It has long been known that spinal motor systems are capable of producing a wide range of motor behaviours when isolated from the rest of the nervous system. This fact, together with the descriptions of many interneuronal pathways within the spinal cord and their elaborate interactions^{10,11}, further indicate that the spinal cord cannot be viewed as a simple relay of supraspinal motor commands to the periphery. The organization of spinal motor systems will clearly place strong constraints on the production of movement by supraspinal systems.

Because of its obvious importance, the organization of movement by the spinal cord has been investigated by many researchers. One common hypothesis is that movements mediated by the spinal cord are based on the combination of a small number of behavioural units. The precise definition of such behavioural units has varied, but has often corresponded to the control of a group of functionally related muscles. According to one version of this hypothesis, proposed by Grillner³², the production of behaviour might be organized around a set of spinally generated UNIT BURST GENERATORS, with each intrinsically rhythmic 'unit' controlling a small set of synergistic muscles acting around a particular joint. In this proposal, different rhythmic behaviours could be produced through flexible combination of these unit bursters. Evidence in support of these hypotheses has come from several experiments^{31,32,42,43}. These studies, in animals such as the cat⁴⁴, the rat⁴⁵, the turtle⁴⁶ and the mudpuppy⁴⁷ have used several observational, lesion and stimulation experiments to support this idea of a flexible combination of spinally organized behavioural subunits.

The construction of movement through spinal modules.

A recent set of experiments in our laboratory^{48–56} has led to a similar hypothesis for the composition of behaviour by spinal motor systems. In this hypothesis, the flexible combination of a small set of 'spinal modules' is proposed to be used by the nervous system to produce a wide range of movement in a simple manner. A 'spinal module', according to this hypothesis, is a functional unit organized within the spinal cord that imposes a specific pattern of muscle activation. We will briefly describe a series of experiments evaluating this hypothesis to illustrate an example of the complex organization of movement by spinal motor systems and how this organization might be exploited by supraspinal systems to produce a range of behaviours in a simple manner (BOX 2).

UNIT BURST GENERATORS
Grillner's hypothesis for the spinal production of behaviour. Each spinal 'unit' is proposed to control a small set of synergist muscles acting around specific joints, which can be coupled in many ways to produce a range of rhythmic behaviours.

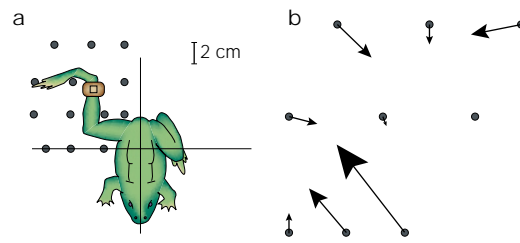


Figure 3 | The characterization of movements by the measurement of isometric force fields. **a** | The ankle of the frog was fixed in different locations of the workspace, indicated by the filled circles. With the hindlimb fixed in one of these locations, a movement was evoked by electrical stimulation of the spinal cord or by noxious stimulation of the skin. The force produced by the pattern of muscle activations underlying this movement was then measured. The hindlimb was then placed in a different location, the same stimulation was repeated, and the force at the ankle was measured. **b** | The collection of forces measured at different ankle locations. This set of position-dependent forces is termed a force field and summarizes the configuration dependent forces produced by a given pattern of muscle activation. (Adapted from REF. 48.)

Evidence for this hypothesis originally came from studies that examined the motor responses evoked by microstimulation of the interneuronal regions of the frog lumbar spinal cord. These experiments measured the isometric force at the ankle which was evoked by stimulation of a particular site in the spinal cord. By placing the ankle in different positions in the workspace, and measuring the force evoked by stimulating the same site in the spinal cord, a set of position-dependent forces (a 'force field') was collected. An example of such a force field evoked by spinal micro-stimulation is illustrated in FIG. 3. Surprisingly, systematic stimulation of different regions of the spinal cord produced only a few types of force field. Giszter *et al.*⁵¹ have shown that these force fields are not due to random motor neuron activation, direct stimulation of sensory afferents, or direct stimulation of descending systems in the spinal cord. Furthermore, Saltiel *et al.*⁵² have described a similar organization for the forces that are evoked by focal iontophoresis of NMDA (*N*-methyl-D-aspartate) into the spinal cord and have shown that these responses reflected activation of spinal interneurons. Saltiel *et al.*⁵² also showed that these different response types were preferentially evoked when NMDA was applied to particular regions of the spinal cord. Finally, similar results have also been obtained with electrical stimulation in the rat spinal cord, indicating that these results might generalize across vertebrates.⁵³

On first impression, this result of a limited number of response types that are organized by spinal motor systems is surprising. The presence of only a few units of motor output within the spinal cord is difficult to reconcile with the obvious ability of the nervous system to produce a wide range of movement during natural behaviour. However, subsequent work has indicated that the nervous system might combine these modules to produce a range of movements. Mussa-Ivaldi *et al.*⁵⁴ found that when stimulation was applied to two sites in the spinal cord simultaneously, in most cases, the result-

ing motor response was a simple linear summation of the responses evoked from each site separately (FIG. 4). The principle of summation of a small number of spinal modules potentially provides the motor system with a combinatorial mechanism that could produce a wide range of motor responses in a computationally simple manner. Furthermore, simulation studies have shown that the flexible combination of spinal modules is capable of producing a wide range of movement trajectories and reproducing the basic characteristics of normal reaching movements.

Two recent studies have provided evidence that this summation mechanism might, in fact, be used by the nervous system to produce behaviour. Tresch *et al.*⁵⁵ showed that the range of muscle activation patterns that are evoked by cutaneous stimulation of the frog hindlimb could be described as a simple linear combination of a small number of specific muscle groupings. More recently, Kargo and Giszter⁵⁶ showed that the frog WIPING REFLEX could be described as the sequential combination of different spinal modules. They further showed that a third module could be added to the ongoing behaviour to correct for imposed perturbations. These results are consistent with the hypothesis that a range of motor behaviours can be produced through the flexible combination of a small number of spinal modules.

A further question concerns whether this principle of summation might also subserve the motor responses produced by supraspinal systems. To test this hypothesis, d'Avella and Bizzi⁵⁷ examined the force fields evoked

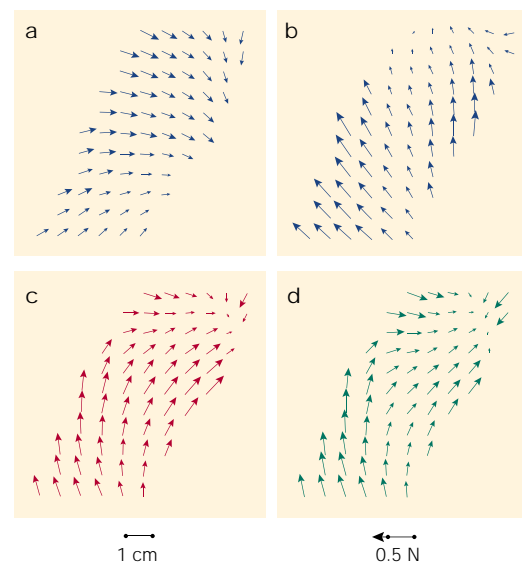


Figure 4 | Summation of force fields by co-stimulation of sites in the frog spinal cord. **a** and **b** | Two examples of force fields, evoked by stimulation of different sites in the spinal cord of a frog. **c** | Force field predicted by a simple summation of the force vectors measured at each position in the separate force fields shown in **a** and **b**. **d** | Force field actually produced by co-stimulation of the two spinal sites illustrated in **a** and **b**. The force field produced by co-stimulation of two sites in the spinal cord was very similar to the force field predicted by a simple summation of each separate force field (compare **c** and **d**). (Adapted from REF. 54.)

WIPING REFLEX

The scratch reflex in the frog in which an irritant is removed from different regions of the body by limb movements that 'wipe' the irritant off the skin.

Box 3 | Rehabilitation strategies

The ability of spinal systems to contribute to the production and adaptation of movement has led several groups to develop strategies that can enhance and exploit this ability in patients in whom the connections between spinal and supraspinal systems are completely or partially severed⁶³.

One strategy developed for animal research has been to carry out intensive locomotor training following spinal cord damage. Treadmill training, in which the initially immobile hindlimbs are placed on a moving treadmill with the hindlimb weight supported, has been shown to greatly enhance the motor capability of spinalized animals^{31,64–68}. This training is facilitated by administering neuroactive agents such as noradrenaline agonists^{65,66}, and can also be applied to cases where the spinal cord is only partially disconnected from supraspinal systems⁶⁹, a common situation in patients with spinal cord injury. On the basis of these animal experiments, several groups^{70–74} have attempted to apply such training regimes, sometimes in conjunction with pharmacological treatments, to patients with spinal cord injury. The results from these studies have shown that such approaches might provide a considerable improvement in the motor function of patients with spinal cord injury.

Another strategy that is being explored is to restore motor function by direct stimulation of the spinal cord⁶³. Although electrical stimulation of peripheral muscles has long been used to produce limb movement, the stimulation of spinal structures might have important advantages. One potential advantage is that the control of movements through spinal stimulation might be simpler than the control through intramuscular stimulation. For instance, stimulation of a combination of spinal modules might provide a way to produce coordinated movements, using only a small number of control signals. There might also be other advantages to muscle activation through direct activation of motor neurons within the spinal cord⁷⁴. Such approaches have yet to be attempted in humans, although animal experiments encourage belief in the feasibility of these approaches^{63,74}.

VESTIBULAR STIMULATION

The vestibular system senses changes in head orientation, which are produced by head movements or changes in the position of the head with respect to gravity.

PRINCIPLE COMPONENTS

A computational analysis that can be used to assess the dimensionality of a data set.

by VESTIBULAR STIMULATION in frogs. By applying a PRINCIPLE COMPONENTS analysis, they found that the dimensionality of the force fields that was evoked by vestibular stimulation was surprisingly low. This result is consistent with the idea that supraspinal systems produce movement by the summation of a small number of modules organized in the spinal cord.

The experiments discussed in this section support one particular formulation of the hypothesis that motor systems produce movement through the flexible combi-

nation of spinally organized subunits of behaviour. This work, along with the large body of spinal cord research over the past century, indicates that the spinal cord, instead of acting as a simple relay between supraspinal systems and the periphery, may be capable of making a large contribution to the neural production of movement. Understanding the organization of spinal motor systems can therefore clearly help to guide investigations of supraspinal systems. The complexity of spinal motor systems and their adaptability might also suggest rehabilitation strategies for patients with spinal cord injury, using directed training, pharmacology or functional electrical stimulation to access or augment spinal motor function (BOX 3).

Conclusions

The results described in this review clearly show that the spinal cord is an active participant in complex functions of motor control such as the planning, plasticity and organization of movement — functions typically reserved for 'higher' motor areas. This is consistent with the perspective that the production of movement is a highly distributed process involving interactions between neurons across many brain areas. This view of the distributed nature of motor control has long been acknowledged for neuronal processing across brain areas such as cerebellum, cortex and the basal ganglia. The work described indicates that neurons within the spinal cord should also be included within this distributed network. Characterizing the interactions between spinal and supraspinal systems, along with the mechanisms and principles that mediate them, will clearly be an exciting topic for future research into the neural production of movement.

Links

FURTHER INFORMATION Motor control

ENCYCLOPEDIA OF LIFE SCIENCES Motor neurons and spinal control of movement

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