

Review

Coordination and localization in spinal motor systems

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Abstract

We review here experiments examining the hypothesis that vertebrate spinal motor systems produce movement through the flexible combination of a small number of units of motor output. Using a variety of preparations and techniques, these experiments provide evidence for such spinally generated units and for the localization of the networks responsible for producing them within different regions of the spinal cord. Such an organization might help to simplify the production of movement, reducing the degrees of freedom that need to be specified by providing a set of units involved in regulating features common to a range of behaviors.

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1. Introduction

Motor coordination is the process by which the many degrees of freedom of the nervous system are assembled together to produce a purposeful, integrated movement [9]. This problem of coordination can be formulated at many different levels of the motor system: between limbs,

between joints, muscles, motor units, or amongst the neuronal systems involved in the production of movement. At each level of the motor system, this problem is ill-posed: i.e., in general, the goal of a motor task can be accomplished by any of a number equivalent movements. How the central nervous system (CNS) copes with these excess degrees of freedom, exploiting them to produce flexible and adaptive movements, is central to the study of motor control.

In this review, we discuss experiments that address this issue of motor coordination within a particular class of movements: those produced by spinal motor systems.

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Ultimately, the large majority of movements are accomplished through neuronal systems within the spinal cord. Understanding the organization of spinal motor systems is therefore critical to our understanding of the control of movement by the rest of the nervous system. In particular, we discuss experiments which suggest that spinal motor systems are organized into a number of distinct ‘units’ of motor outputs which can be combined flexibly in order to produce a range of different behaviors. Such a modular organization of spinal motor systems represents one strategy evidently used by the vertebrate nervous system to cope with the problem of motor coordination.

2. Centers, units, modules, primitives, synergies: variations on a theme

The basic hypothesis of a modular organization of spinally produced movements is not a new one [22,23,57,76], and has been proposed in several different forms, each with slightly different emphases. The first such formulation of this hypothesis was proposed by Brown [12] based on the work of Sherrington [69] in the early part of the last century to explain the production of locomotion by the cat. This ‘half-center’ hypothesis postulated two aspects of the production of locomotion. First, it proposed that locomotion consisted of the alternation between two units of motor output, one devoted to limb flexion and the other devoted to limb extension. These two basic units, or ‘half centers’, were proposed to be the same flexion and crossed extension identified by Sherrington in his study of withdrawal reflexes. Second, this hypothesis proposed that the alternating rhythm between these two units was driven by fatiguing inhibition between the units. Thus, as opposed to Sherrington’s original suggestion that alternation was due to reflex chaining through sensory reafference, the half center hypothesis proposed that the generation of the rhythm was produced through mechanisms intrinsic to the nervous system.

Grillner subsequently elaborated this hypothesis, suggesting that instead of a strictly exclusive alternation between two units of motor output, the details of the locomotor pattern consisted in the combination of several different ‘unit bursters’ [23,24]. Each unit was proposed to control the activation of a small set of synergistic muscles acting around a single joint and to be intrinsically rhythmic. Different rhythmic motor behaviors could then be produced by flexibly coupling these different units together, allowing for the production of a range of different motor behaviors in a relatively simple manner.

Jordan expanded on these ideas to postulate the existence of devoted networks of neurons in the spinal cord responsible for producing these different units of motor output [33]. Each of these ‘modules’ was suggested to consist of the neurons responsible for activating a particular set of motor neurons, as well as the neurons

responsible for inhibiting the motor neurons of antagonistic muscles. Thus, these coupled excitatory and inhibitory populations of spinal interneurons within each module worked together to produce a consistent and unified effect on motor output.

This basic scheme and its elaborations have provided a context for many of the experiments performed on the spinal production of rhythmic behaviors such as locomotion and scratching. Many of these experiments have focused on the rhythm generating aspect of this scheme, identifying the networks, neuronal classes, or membrane properties and synaptic interactions within the spinal cord which contribute to the production of the rhythm underlying these behaviors. In the present review, we focus instead on the pattern generating aspect of this scheme: the hypothesis that the spinal cord produces complex behaviors through the flexible combination of a small number of basic ‘units of motor output’.

Such ‘units’ have been referred to using many different terms (e.g., half-center, unit burster, module, primitive, muscle synergy) with differences in their connotations and in their implications about physiological implementation or functional interpretation. Such an abundance of terms and diffusion of connotations has often confused this topic. Stein and Smith [76] clarified many of these terms and hypotheses nicely, characterizing their distinguishing features. For the purposes of the present review, however, we wish to emphasize their commonality: that they each propose that the spinally generated motor behaviors are produced by combining units of motor output. In this context, we will generally refer to such a ‘unit of motor output’ as consisting of the coupled activation of a group of muscles.

The possible involvement of such units in the production of normal behaviors produced by the intact nervous system has been evaluated in several previous reviews [26,38,43]. The present review describes studies which examine the organization of spinal neuronal systems isolated from the rest of the nervous system in the context of this hypothesis of a modular organization of spinal motor systems. We include here two different lines of experiments used to evaluate this hypothesis. One experimental approach examines the coordination patterns of muscle activations, assessing whether different behaviors can be described as a combination of a small number of units of motor output. The other approach examines the neurophysiological substrates of such units, assessing the localization of the responsible neuronal networks within the spinal cord. Although the term localization has been used to refer to the ‘structural plan of anatomical interrelationships’ [9] within motor networks, the experiments described here mainly address localization as referring to a topographical organization of spinal motor systems. In particular, these experiments examine whether the networks responsible for different units of motor output are preferentially located in particular regions of the spinal cord. We then discuss the

potential interpretations and implications of such an organization in the context of the more general problem of the production of normal movements by the intact nervous system.

3. Evidence for a modular organization of vertebrate spinal motor systems

Evidence in support of such a modular organization of spinally generated motor behaviors has come from observational and physiological experiments performed in a range of different preparations. Here we summarize results obtained from examinations of the turtle, mudpuppy, frog, rat, and cat spinal motor systems.

3.1. Modular organization of turtle motor behaviors

Perhaps the most systematic examination of the modularity of spinal motor systems has been performed in studies of the turtle spinal cord by Stein and collaborators [73,75,76]. In the spinalized turtle, sustained cutaneous stimulation of different regions of the body surface evokes a rhythmic motor behavior which acts to remove the stimulus [46,55]. Depending of the site of stimulation, one of three different forms of scratch reflexes can be evoked. These three different forms of the scratch reflex are characterized by a temporal reconfiguration of three fundamental units of motor behavior: although all three have a basic alternation between hip flexion and extension, the timing of knee extension differs between the three different forms of scratches. In rostral scratches, the knee extension occurs late in the hip flexion; in pocket scratches, the knee extension occurs during hip extension; in caudal scratches, the knee extension is activated at the end of the hip extension.

Moreover, these units can be reconfigured flexibly, showing a great deal of independence from one another. For instance, the units controlling hip extension during rostral scratches can be deleted in individual cycles [56,77]. Such ‘hip extension deletions’ can occur spontaneously or can be promoted by hemisection of the contralateral thoracic spinal cord. Interestingly, following such deletions produced by contralateral hemisection, the hip extension phase can be reinserted into the rhythm and the full rostral scratch motor pattern restored if a site on the body surface is stimulated in addition to the one used to evoke the rostral scratch [74]. These results demonstrates a strong bilateral aspect to the spinal networks involved in the production normal motor behaviors.

Another example of a flexible reconfiguration of these spinal units is illustrated in the case of ‘hybrid blends’. Such hybrids occur when two behaviors are evoked simultaneously and the biomechanical demands of each behavior are not mutually exclusive [72]. For instance, when two sites are stimulated simultaneously, one which

evokes a rostral scratch and another which evokes a caudal scratch, the resulting behavior is in some cases a blending of the two motor patterns, in which both sites are scratched during the same motor rhythm. In such a ‘hybrid blend’ the behavior consists of the basic alternation between hip flexion and hip extension common to each scratch but has a double burst of knee extension: this double burst is seen in both immobilized (Fig. 1) and moving preparations. The timing of each of these knee extensor bursts within the hip cycle corresponds to the timing of the knee extensor bursts exhibited in the scratch evoked from stimulating each site separately. Thus, the two behaviors are ‘blended’ together by reconfiguring a small number of basic units of motor output. A more recent study has demonstrated a blend between the motor patterns involved in swimming and rostral scratch [15]. Swimming can be evoked in the spinalized turtle by electrical stimulation of the descending dorsolateral funiculus [34]. When swimming is evoked in this way and a rostral scratch is evoked simultaneously, the resulting motor pattern is a ‘hybrid’ of the two responses evoked individually. Thus, the rostral scratch is ‘merged’ into the ongoing hip flexion phase of swimming and the resulting pattern of muscle activation contains features of the hip flexion phase both of the rostral scratch and of swimming.

The experiments described above were performed mainly by observing the patterns of motor output evoked during different behaviors, and examining how the range of different behaviors could be characterized as the reconfiguration of a small number of spinally organized units of motor output. Further evidence for such an organization has come from physiological experiments examining the neuronal substrates of these behaviors.

Mortin and Stein [47] examined the consequences of removing different spinal segments on the production of the three different forms of the scratch reflex. One of their main results was that the basic ability to produce a rhythmic motor output was distributed throughout many different spinal segments, although rostral segments had higher rhythmogenic capability than caudal spinal segments. They also found evidence for localization of the neuronal networks responsible for the different units of motor output involved in the production of scratches. Thus, regardless of which scratch form was studied, when rostral segments were removed there was a tendency for the hip flexion phase to be deleted while when caudal segments were deleted there was a tendency for the hip extension phase to be deleted. These results suggested that distinct neuronal networks, preferentially located in particular regions of the spinal cord, were responsible for the production of a particular component of the motor behavior.

A similar conclusion was obtained in a more recent set of experiments by Berkowitz and Stein [5,6] and Berkowitz and Stein [7,8] examining the activity patterns of unidentified spinal interneurons during the production of different forms of the scratch reflex. By examining the

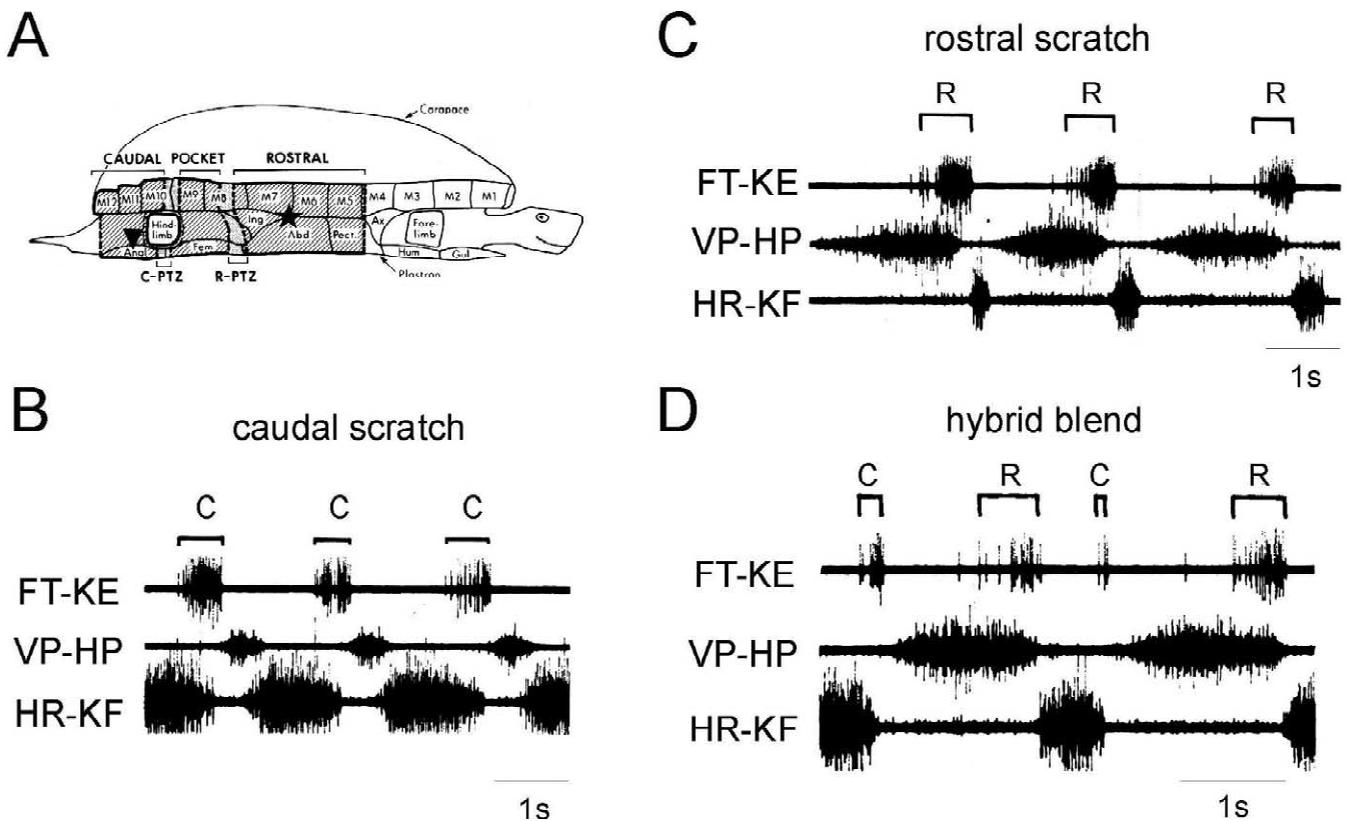


Fig. 1. Hybrid blend of motor patterns by the turtle spinal cord. (A) Schematic of the turtle shell and body surface. The three zones of the shell and skin surface from which the different forms of the scratch reflex can be evoked (caudal, pocket, rostral) are indicated. The filled triangle indicates a site from which a caudal scratch was evoked. The filled star indicates a site from which a rostral scratch was evoked. (B) Electroneurogram (ENG) recordings of the knee extensor nerve (FT-KE), hip flexor nerve (VP-HP), and the hip extensor nerve (HP-KF) during three caudal scratches in the immobilized turtle. Periods of FT-KE activity distinguishing the different forms of the scratch are indicated by bars above the ENGs, labelled with 'C' for caudal scratch. (C) ENGs recorded during three rostral scratches. The 'R' above each bar indicates periods of FT-KE activity characteristic of a rostral scratch. (D) ENGs during a hybrid blend, in which stimulation was applied to both caudal and rostral scratch eliciting regions of the skin. Note the double bursts in the FT-KE nerve. Adapted from Ref. [72], with permission.

activity of neurons in each of the different forms of the scratch, they found that neurons were broadly tuned to the region of the body surface used to evoke the forms of the scratch reflex. Thus, each neuron could be activated in several different forms and there was no clear localization of the neurons that were most active in one form or another [5]. These results were consistent with the lesion experiments performed by Mortin and Stein [47] showing no clear localization of the systems producing each distinct form of scratching: the networks responsible for each scratch were for the most part shared. In addition to examining the tuning of neurons to different forms of the turtle scratch reflex, Berkowitz [6] examined the relationship of individual neurons to different phases of the scratch reflex. He found a weak localization of different neurons within the spinal cord according to when they were active during the scratch cycle. Although within any spinal segment neurons could be active in any phase of the scratch cycle, there was a tendency for neurons which were related to hip flexion to be located in rostral segments of

the spinal cord while neurons related to hip extension tended to be located in caudal segments of the spinal cord. Although this tendency for localization was not strong, it was consistent with the lesion studies of Mortin and Stein [47] suggesting a relative localization of hip flexor and extensor related activities to rostral and caudal regions of the spinal cord, respectively. Since the experiments of Berkowitz sampled the activity of heterogeneous populations of unidentified neurons, a stronger localization of neuronal activity might be found for subsets of neurons more directly involved in the production of the scratch reflex.

Taken as a whole, this evidence obtained from both observational and physiological investigations of the turtle spinal cord, suggests that spinal motor systems are organized into a small number of fundamental units of motor output. Further, these different units of motor output appear to be preferentially localized within different regions of the spinal cord, although there is also a large degree of overlap.

3.2. Spinal neuronal networks responsible for walking in the mudpuppy

Experiments performed in the mudpuppy (*Necturus maculatus*) reached a similar conclusion about the organization of spinal neuronal systems involved in the production of forelimb locomotion [13]. When the spinal cord of this preparation is isolated in vitro and NMDA is applied to the bath, a rhythmic walking motor pattern in forelimb muscles is evoked [13,81]. In this preparation, even a single cervical segment is capable of producing a stable motor rhythm, either in response to bath applied NMDA or to electrical stimulation of the spinal cord [13]. Such a distribution of rhythmogenic capability throughout the spinal cord is similar to what has been described in other preparations. Interestingly, Cheng et al. [13] found that different spinal segments were specialized for the production of particular components of the motor rhythm. In particular, they found that a single rostral spinal segment produced rhythmic activation of flexor muscles while a single caudal spinal segment produced rhythmic extension (Fig. 2). If regions of both segments were left in continuity, the normal alternation between flexion and extension could be produced. These results suggested that the locomotor activity produced by the mudpuppy spinal

cord consisted in the combination of motor outputs produced by distinct neuronal networks localized in different regions of the spinal cord. This localization appeared to parallel the topographical organization of motor pools, so that the interneuronal circuits responsible for controlling a particular group of motor neurons are located in proximity to those motor neurons. These results in the mudpuppy support the notion that the complex behavior of locomotion is produced through the combination of a small number of basic units, controlled by functionally and anatomically distinct neuronal networks.

3.3. Modularity in frog spinal motor systems

A recent set of experiments performed by the present authors and collaborators has also led to the development of a similar hypothesis of a modular organization of spinal motor systems in the frog spinal cord [10,11,21]. This hypothesis was originally motivated by experiments examining the organization of motor outputs evoked by electrical microstimulation of spinal interneuronal regions [10,20]. These experiments found that only a few distinct types of motor outputs could be evoked by such stimulation. However, when stimulation was applied simultaneously to two different sites in the spinal cord, each of which when stimulated individually produced a different type of motor output, the resulting motor output was a simple combination of the separate motor outputs [39,48]. Based on these observations, it was proposed that complex movements might be produced by the flexible combination of a small number of spinally generated motor patterns. Subsequent work demonstrated that a similar organization could be found in the motor outputs evoked from activation of spinal interneuronal systems by focal iontophoresis of NMDA [60,61].

Two experiments have provided evidence in support of such a hypothesized spinal modular organization underlying natural behaviors produced by the frog spinal cord. Tresch et al. [80] applied a computational analysis to the muscle activation patterns evoked by cutaneous stimulation of different regions of the skin surface of the hindlimb. This analysis attempted to identify patterns of covariation amongst subsets of muscles, each corresponding to a muscle synergy, within the observed motor outputs. The analysis then combined these synergies with different weightings in order to describe the observed muscle activation patterns. The results of this study showed that the muscle activation patterns involved in hindlimb withdrawal reflexes could be explained in terms of the combination of a small number of muscle synergies, consistent with the hypothesized modular organization of spinal motor systems.

Strong evidence in support of the hypothesis that behaviors can be produced through the combination of a small set of motor elements has come from recent experiments by Kargo and Giszter [35]. Those experiments

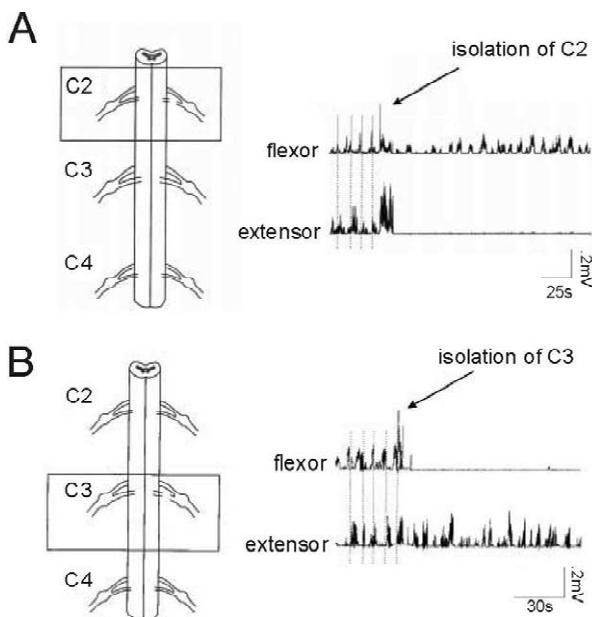


Fig. 2. Isolation of flexor and extensor generating networks in the mudpuppy. (A) Left schematic shows the mudpuppy spinal cord. The overlaid box indicates the region of the spinal cord which is surgically isolated from the rest of the spinal cord. The right traces show flexor and extensor muscle activity evoked by bath applied NMDA (60 μ M). At the time indicated by the arrow, the C2 segment indicated to the left was isolated and only rhythmic flexor activation persisted. (B) Same conventions as A, showing persistence of rhythmic extensor activity following isolation of C3. NMDA concentration was 80 μ M in B. Adapted from Ref. [13], with permission.

examined the organization of wipe reflexes and their responses to perturbations in the spinalized frog. In response to strong noxious stimulation of the hindlimb, spinalized frogs will produce a form of a scratch reflex, in which both hindlimbs are moved together and the unstimulated hindlimb is used to remove the noxious stimulus: i.e., the stimulus is removed by ‘wiping’ it off the hindlimb. The first observation of Kargo and Giszter was that the electromyographic (EMG) patterns during a wipe could be split into at least three partially overlapping components, one corresponding to an early flexion phase, followed by a second phase characterized by strong hip extension, and ending with a final knee extension phase. Both the hip extension and the knee extension phases could be added or removed from the motor response without strongly affecting the other muscles, similar to the ‘deletions’ described above for the turtle [20]. Thus, the patterns of normal motor output during a wipe reflex could be characterized in terms of a staggered and overlapping combination of units of motor output.

Kargo and Giszter [35] then showed that the spinalized frog is able to produce corrective movements in response to unexpected perturbations (Fig. 3). They placed an

obstacle in the path of the unstimulated hindlimb, i.e., the hindlimb which would be used to remove the stimulus. When the leg hit the obstacle, the frog produced a hip flexion bringing the hindlimb around the obstacle so that the wiping behavior could be executed correctly. Remarkably, this corrective response was integrated seamlessly into the ongoing behavior and the resulting behavior was able to complete the intended wipe reflex. Thus, the original muscle activation patterns observed during unperturbed trials were essentially preserved when the obstacle was encountered: the set of muscles involved in the corrective hip flexor response were simply inserted into the wiping reflex. Further, this hip flexor response was clearly composed of the coupling between the activation levels in a group of muscles: both their temporal profiles and their amplitudes covaried. These observations provide strong evidence suggesting that the wiping reflex and its modifications in response to perturbations can be explained in terms of the flexible combination of a small number of muscle synergies.

It also appears that there is a topography to these different types of responses within the spinal cord, as revealed by focal NMDA iontophoresis. Saltiel et al. [60]

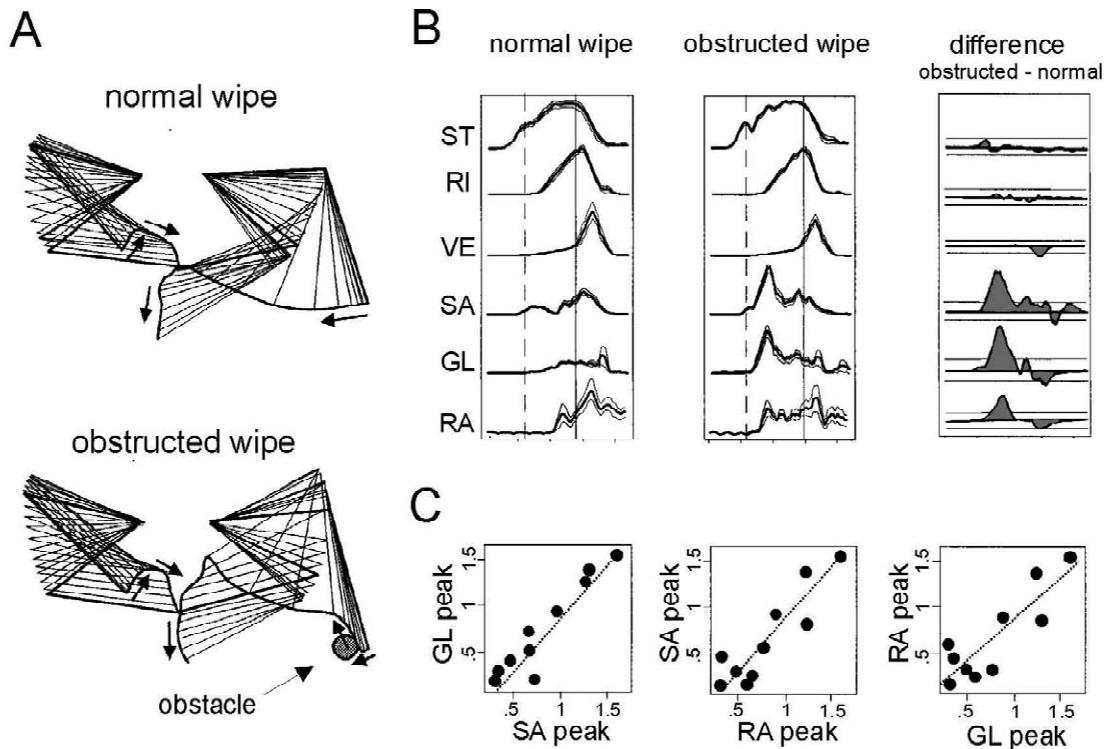


Fig. 3. Motor patterns during wipes in the spinalized frog. (A) Stick figures of the configurations of left and right hindlimbs during wipe reflexes. Ankle position is indicated by solid continuous line and small arrows indicate the direction of motion for each ankle. In the top response with no obstruction, the two hindlimbs whisk against each other near the midline of the frog in order to remove the noxious stimulus on the left hindlimb. In the bottom response with an obstacle in the path of the right hindlimb, the obstructed limb initially flexes to move around the obstacle. After this flexion, the wipe continues and the two hindlimbs are able to whisk against each other. (B) Electromyographic (EMG) patterns during normal (left) and obstructed (middle) wipes and their difference (right). Traces show average EMG activity across 10 wiping trials. The difference plot shows three muscles activated in response to the obstruction. Muscle abbreviations are ST (semitendinosus), RI (rectus internus), VE (vastus externus), SA (sartorius), GL (gluteus), and RA (rectus anterior). (C) Peak muscle activations for those three muscles plotted against one another, showing strong covariation. Adapted from Ref. [35], with permission.

described that NMDA iontophoresis evoked responses that were either a simple sustained, tonic pattern of muscle activation or a more complex rhythmical pattern consisting of a combination of several different phases. These rhythmic responses appeared to be sequential combinations of the more simple, tonic responses. It was also observed that certain classes of rhythmic movements were evoked more frequently than others. Examination of the anatomical location of the sites evoking tonic responses suggested that the different types of responses were localized to distinct rostrocaudal regions of the spinal cord. Examination of the sites from which different types of rhythms were observed, however, did not reveal such a discrete localization. Instead, a particular type of rhythm could be evoked from several different regions of the spinal cord. These regions, however, appeared to correspond to the regions from which those tonic responses composing the rhythm were evoked. Thus, if a rhythm was composed of an alternation between knee flexion and hip extension of the limb, this rhythm could be evoked either from the region of the spinal cord which evoked tonic knee flexion or from the region of the cord which evoked tonic hip extension. These results suggested that the production of a motor rhythm might be due to the coordination between simple units of motor output organized within particular regions of the spinal cord.

It seems to us that this organization is very similar to that proposed for the production of the rhythmic scratches in the turtle [5–8,47]. As described above, in the turtle it appears that the networks in the spinal cord involved in producing the different forms of the scratch are shared to a large degree between the forms. Thus, for each different form, the full pattern of rhythmic motor output requires an overlapping set of several spinal segments and neurons recruited in each form are distributed throughout the spinal cord. However, both lesion experiments and neuronal recordings suggested that there was a tendency towards localization, although not exclusive, of the units of motor output from which the behaviors were composed. The production of rhythmic scratches, therefore, could be seen as the differential coordination between the units organized within different regions of the spinal cord. Although there are differences in the details of this organization and in the methods used to examine it, it seems that this organization is similar in principle to that suggested in the frog.

3.4. Modularity of mammalian spinal locomotor systems

Although the half-center and unit-burster hypotheses described above were first developed to explain mammalian locomotion, there is still no clear consensus as to whether either organization is actually instantiated in the mammalian spinal cord. Part of the difficulty with evaluating this hypothesis is that locomotion is in general difficult to evoke in acutely spinalized animals (e.g., Refs. [3,51]). The main reliable way of evoking stable locomotor

rhythms in acutely spinalized animals is by application of noradrenergic agonists, such as clonidine or the noradrenergic precursor L-DOPA [57], along with perineal stimulation or tail pinching. Both of these agents are capable of evoking a slow rhythmic motor pattern which exhibits many of the characteristic features of locomotion: there is a basic alternating activity between flexors and extensors within one hindlimb, and between homologous muscles in opposite hindlimbs. In many aspects, however, the motor pattern produced in the acutely spinalized animal is simpler than the pattern produced during normal locomotion (Fig. 4) [22,50,51]. Thus, there is a generally similar temporal activation profile of all flexor muscles and of all extensor muscles during L-DOPA or clonidine locomotion, while in intact locomotion there are more individuated activation profiles. This simplified pattern of locomotion does not appear to simply reflect spinal shock in the acutely spinalized preparation because it is preserved in animals examined several days after the spinalization [51]. However, there are aspects of this pattern that do not fit into a simple alternation between the activation of flexors and extensors. For instance, the activation of some intrinsic foot muscles occurs in only a portion of the flexor phase [62]. Also, application of the potassium channel blocker 4-AP in acutely spinalized animals can cause more individuated responses in muscles (Fig. 4) [14,51], although these effects can be difficult to interpret [22]. These details are similar to those observed during normal locomotion and are maintained in deafferented or paralyzed preparations.

Further suggestions that the pattern produced by the isolated spinal cord, although simpler than that observed in normal locomotion, was not simply an alternation between flexion and extension came from observations of ‘exceptional cases’, in which the activity levels of subgroups of muscles can be shown to vary independently of other groups of muscles. Such observations are similar to the observations of additions and ‘deletions’ described in the turtle and frog. For instance, Grillner and Zangger [25] reported cases of rhythmic activity in a set of flexor muscles acting at one joint with simultaneous tonic activity in flexor muscles acting at another joint. Similarly, they reported a strong coupling between flexor muscles acting at one joint with a looser coupling between flexor muscles acting at different joints. These observations along with other similar ones were the original evidence which led Grillner to suggest the idea that the basic spinally generated motor rhythm might be produced through the combination of a set of ‘unit bursters’ [23,24]. These experiments therefore suggest that the acutely transected spinal cord contains networks capable of producing a motor pattern similar to normal locomotion, though substantially simplified, and which can be explained as the combination of a small number of units of motor output.

Subsequent work has also shown that the same spinalized animals can recover a motor pattern very similar to

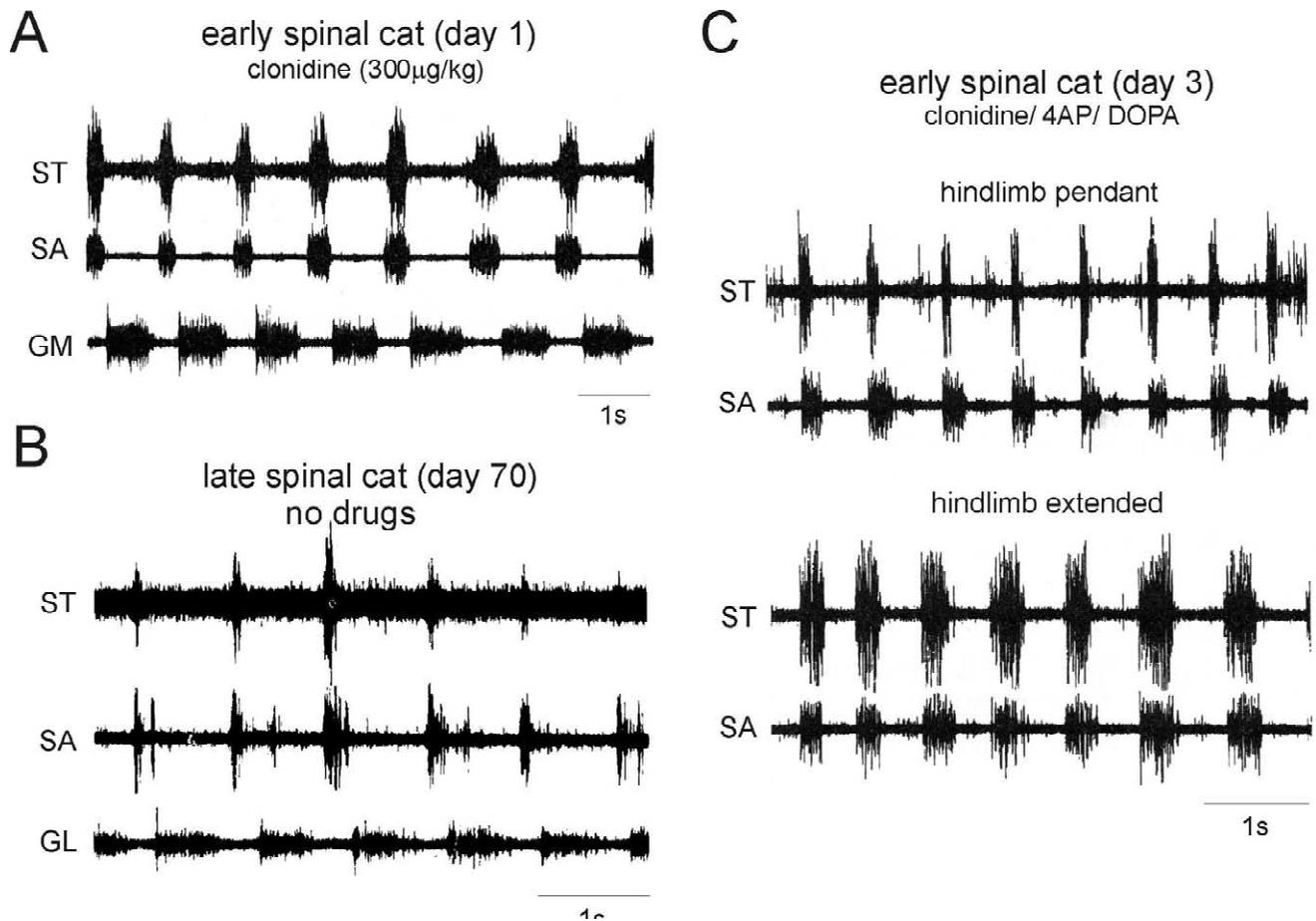


Fig. 4. Muscle activation patterns during locomotion in immobilized spinal cats. (A) The ENG activity in hindlimb muscles in an acutely spinalized cat (day 1) following clonidine and pinching the skin of the perineum. Muscle abbreviations are ST (semitendinosus), SA (sartorius), and GM (medial gastrocnemius). (B) The ENG in a cat spinalized 70 days previously and given locomotor training. Note the more individuated activation patterns of the hindlimb flexor muscles SA and ST as compared to those in the acutely spinalized cat. Similar variability was observed in locomotion evoked by clonidine. Muscle abbreviations are same as A plus GL (lateral gastrocnemius). (C) ENGs of SA and ST in an acutely spinalized cat given clonidine, 4-AP, and DOPA. With different static limb configurations (pendant or extended) the duration of ST was abbreviated as compared to that of SA. Such limb configuration dependent effects were not observed in acutely spinalized animals with only clonidine. Adapted from Ref. [51], with permission.

that observed in normal locomotion when given locomotor training postspinalization (Fig. 4) (see Refs. [16,58]). When animals are given repeated rehabilitation training, such as with a locomotor treadmill or strong cutaneous stimulation, over the course of weeks following spinalization the locomotor pattern becomes both stronger and more similar to normal locomotion. This similarity is true of locomotion evoked with or without the aid of pharmacological agents. There are still differences, both in the muscle activation patterns [51] and in the kinematics [4] of the movements, but many of the details of muscle activations are observed even in paralyzed animals [4,51]. Thus, following this type of intense rehabilitative training, the neural networks in the spinal cord are capable of adaptation necessary to reproduce a version of locomotion similar to that observed in intact animals. Whether these changes following training are due to a general increase in the excitability of spinal locomotor systems or reflect func-

tional plasticity by the spinal cord is not entirely clear at present [16,50,51].

There is some evidence, although scant and scattered at present, suggesting a tendency towards anatomical localization of interneuronal systems involved in producing different units of motor output in the mammalian spinal cord. In one study it was shown that last order interneurons projecting to elbow extensor muscles could be segregated based on their rostrocaudal location and their activity pattern: neurons with extensor related activity, presumably excitatory, were located caudally while neurons with flexor related activity, presumably inhibitory, were located rostrally [29]. Similarly, in the neonatal rat it has been shown that the majority of ventromedially located neurons in rostral segments of the spinal cord are flexor related while the majority of neurons in caudal segments are extensor related [79]. These results in the neonatal rat are consistent with the principle described in the mudpuppy of a colocali-

zation between motor neurons and the interneuronal network controlling them [13]. Also consistent with this principle, it has been shown that Ia inhibitory neurons are active during the same phase of locomotion as the motor neuron pool of the muscle from which they primarily receive Ia afferent input and these neurons are also located in proximity to the same motor pool [52]. A similar organization has been described for Renshaw cells [52]. There is also a population of interneurons located in midlumbar regions of the cat spinal cord characterized, among other criteria, by monosynaptic group II input [17,18,31]. This population (in L4) appears to show primarily flexor related activity [68], consistent with the idea that flexor related activity is located rostrally in the spinal cord. There are also interneuronal populations characterized by group II input but located in lower lumbar and sacral segments of the spinal cord [32,54]. Although the exact relationship between the different populations is not clear at present [54], it would be interesting to examine the activity of these other populations during locomotion: in particular, it would be interesting to examine whether these more caudally located populations are activated during the extensor phase of locomotion. Finally, a preliminary report in the cat [44] has identified a population of last order interneurons located in caudal spinal segments (L7 see Fig. 2 in Ref. [44]) which has been implicated in providing excitation to extensor muscles during locomotion, both mediated by the pattern generating networks and mediated by state dependent reflexes. These observations, although taken from a number of different studies on different interneuronal populations none of which is definitively responsible for the production of locomotion, suggest a localization of interneuronal systems related to the different phases of the motor pattern underlying locomotion. In particular, these observations suggest that flexor related activity is localized to rostral spinal segments while

extensor related activity is localized to caudal spinal segments.

3.5. Modular organization of mammalian withdrawal reflexes

A set of recent experiments has suggested a modular organization of the spinal systems involved in producing withdrawal reflexes in the rat and cat. Schouenborg and co-workers [27,42,63–66] have examined the activation of individual hindlimb muscles in response to noxious stimulation of different regions of the skin surface in anesthetized rats [64] and cats [41]. They found that the region of the skin surface from which each muscle was maximally activated was also the region of the skin surface which that muscle removed most effectively from the stimulus (Fig. 5, [66]). In this scheme, the withdrawal behavior is organized in terms of a number of modules controlling the activity of individual or small numbers of synergistic muscles, with each module activated by the region of the skin surface appropriate for the mechanical action of that muscle or muscles [65]. In this way, the particular set of muscles activated in the withdrawal reflex results from the patterns of overlap between the receptive fields for each module, the activation of each module occurring in parallel.

The organization described above is clearly seen in intact animals, especially for distal muscles. In the spinalized animal, however, this organization is greatly degraded [63]. The skin region from which a muscle is activated expands dramatically for most muscles and the apparent precision which was characteristic of the intact animal is coarsened. Similarly, in animals which were spinalized as neonates, the precise relationship between sensory input and motor output was also degraded [42]. These results suggest that, similar to the observations made for

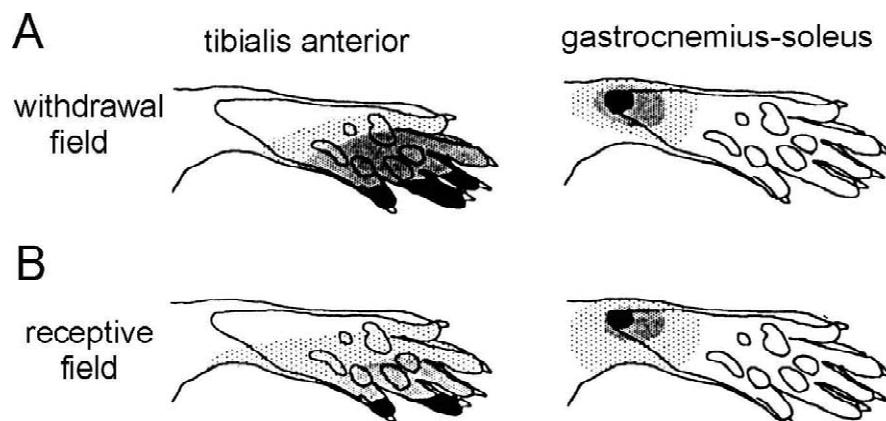


Fig. 5. Matching between muscle action and activation during withdrawal reflexes. (A) The regions of the skin surface which are maximally moved by activation of tibialis anterior and gastrocnemius-soleus. Darker regions indicate regions of the skin which are moved the most rapidly. (B) The regions of the skin surface from which the same muscles are activated during withdrawal reflexes. Darker regions indicate the skin regions which maximally activated each muscle. Note the close similarity between the regions of skin surface which are moved by a muscle and the regions of skin surface which activate the same muscle. Adapted from Ref. [66], with permission.

locomotor behavior described above, the withdrawal behaviors produced by spinal motor systems when isolated from the rest of the nervous system do not show the details and precision which are characteristic of the normal, intact behavior. Interestingly, it was reported that the regions of skin from which semitendinosus and biceps femoris were evoked, although different in the intact animal, were similar following spinalization [63]. If a similar convergence of activating regions were to be found for other muscles, it might suggest that following spinalization the activation of a set of muscles was coordinated into a unit. However, although such an alteration in motor function following spinalization might reflect a simpler spinal motor strategy being revealed after removal of contributions from descending systems, it might also reflect physiological consequences of the spinalization procedure itself on the function of spinal systems.

4. Interpretation and implications of a modular organization of spinal motor systems

The experiments described in the present review, focusing on the organization of spinal motor systems, are in general consistent with the hypothesis of a modular organization of spinal motor systems. In a recent review of adaptation in spinal motor systems [50], the evidence in favor of such a modular organization of motor behaviors was characterized as ‘not very compelling’. Although the experiments described here provide support for this hypothesis, we agree that they are not definitive for several reasons. Observations of the motor output of spinal systems often is obtained from only a small number of muscles, making a clear evaluation of the complexity of spinal motor output difficult. The examination of movements in a simplified behavioral context, though helpful to examine the systematic regulation of particular behaviors, might itself impose constraints on the organization of motor outputs. Systematic evaluations of such an organization also will likely require analytical and computational techniques which have not been generally employed to evaluate these questions. Such techniques can also be applied to intact behaviors in order to fully evaluate the complexity of these motor patterns. More generally, most of these experiments implicitly assume that the organization of spinal motor systems observed in the isolated spinal cord is also the organization present when the nervous system is intact. The alterations in spinal function which take place following transection will clearly contribute to organization of movements observed in spinalized animals.

Similarly, neurophysiological experiments suggesting that neurons and neuronal networks related to different phases of the behavior are localized to distinct regions of the spinal cord do not definitively establish that the

networks are involved in controlling the activation of a set of muscles rather than of individual muscles. The effects of lesions described thus far are equally consistent with a control of individual muscles as they are with a control of a group of muscles. Similarly, recordings of the activity of single spinal interneurons have not clearly evaluated whether such activity is related to the activation of single or multiple muscles. Also, although the present review has emphasized the tendency toward localization of different neuronal activity, there is a high degree of overlap and intermingling between neurons related to different components of behavior. Further experiments, both observational and neurophysiological, examining the pattern generating capabilities of spinal motor systems are clearly required to fully evaluate the hypothesis of a modular organization of spinal motor systems.

What might be the implications of such a modular organization of spinal motor systems, if it were in fact clearly demonstrated, to the production of movement by the rest of the nervous system? This question has often been evaluated in terms of ‘Bernstein’s’ problem: i.e., how does the nervous system cope with the large number of degrees of freedom of the motor system to produce purposeful, integrated behavior [9]. It has often been proposed that one solution to this problem is to reduce the degrees of freedom in the nervous system by coupling excess degrees of freedom together. The finding of modularity in spinal motor systems would clearly represent such a solution: by coupling together the activation levels of a number of muscles, the degrees of freedom of the motor system could be significantly reduced. This reduction would therefore potentially simplify the production of movements by the rest of the nervous system. At the extreme, this interpretation of modularity implies that spinal motor systems present a motoric bottleneck through which all movements must pass. In this context, the spinally encoded units of motor output could be seen as abstract computational entities, allowing a simple and efficient mechanism underlying the production of movement.

Alternatively, the existence of individual spinal units of motor output might be involved in the control of particular features of movement rather than acting primarily to simplify the production of movement by reducing degrees of freedom. In fact, Bernstein suggested that the large number of degrees of freedom in the motor system should be considered less as a problem for the nervous system to overcome and more as a capability for the nervous system to exploit [9]. In his view, the structured motor output observed in stereotyped behaviors, such as locomotion or basic repetitive reflexes, should be considered as reflecting the action of a control law developed to solve the goals of the behavior. Such a solution involves the selection of the degrees of freedom relevant to the behavior and their regulation in the face of unexpected perturbations. Degrees

of freedom can become coupled when they are involved in the control of a particular feature or phase of the behavior. Such features might include kinematic, as emphasized by Bernstein, or potentially biomechanical aspects of the task.

In this context, the spinal central pattern generators for relatively stereotyped and fundamental behaviors such as locomotion, scratching, or withdrawal might be interpreted as instantiations of solutions, potentially derived through evolution, to the demands of each behavior. The decomposition of these behaviors into a small number of units of motor output might then reflect the coupling together of degrees of freedom which, by working together, control particular features, either biomechanical or kinematic, of the movement. Thus, the reduction in degrees of freedom afforded by such units would reflect not primarily simplification of control, but rather the identification and regulation of behaviorally relevant features of the movement. As the requirements of motor behaviors become more demanding and the neural systems controlling them become more elaborated and specialized, the control exhibited by the entire nervous system acting in concert might become more fractionated and detailed. The motor patterns encoded within spinal motor systems might therefore be difficult to recognize in the natural behaviors of the complex motor systems of intact animals, which reflect the concerted action of many additional systems.

Rather than a bottleneck of motor output, then, such spinally generated units of behavior might represent strategies, organized within the spinal cord, relevant to the control of particular features of the motor output. Since movements are ultimately produced by acting through the spinal cord, the rest of the nervous system would therefore have to take this organization of spinal motor systems into account in some manner. The most direct way for descending systems to take this organization into account would be to take advantage of it, utilizing the spinal units of motor output in the production of normal movements. If the behavior to be produced by the intact nervous system shared control features in common with the motor patterns produced by spinal systems, descending systems might simply use these patterns in the production of movement. For instance, although the full motor patterns underlying quadrupedal locomotion might not be directly utilizable in human bipedal locomotion, individual components controlling particular features of the movement might be shared and therefore used by descending systems. This interpretation is similar to other recent proposals [30,53,78] for the production of movement by the nervous system. Such a possibility also resembles the accumulation and combination of simple systems utilized in the development of robotics control strategies [71]. In this context, the units of motor output organized in the spinal cord might simplify the production of movement by providing solutions to motor control problems that are common across a wide class of movements.

However, it is clear from existing anatomical and physiological evidence that descending systems have options other than using spinal units of behavior when producing movement. One clear option is for descending systems to bypass spinal interneuronal systems altogether by activating motor neurons directly. The monosynaptic connections between cortex and motor neurons observed in primates [40] is a clear demonstration of such a bypassing of spinal systems. Such bypassing systems might serve to modulate the activity of muscles independently or might serve to create their own patterns of coordination (e.g., Ref. [45]). Another powerful option that descending systems have access to is to modify the functionality of spinal motor systems. Mechanisms such as neuromodulation of synaptic efficacy or of intrinsic neuronal properties [70], presynaptic inhibition of primary afferents [59] or of interneurons [1,19], or inhibitory regulation of pathways (e.g., Refs. [2,28]) all provide means by which descending systems can fundamentally alter the state of spinal networks and consequently the organization of their motor output. Such mechanisms might explain how simple coordinative structures organized by spinal motor systems could be transformed into the complex and precise patterns of adaptive motor behaviors exhibited by intact animals. Whether the organization of spinal motor systems is exploited, is sculpted, or is some combination of the two, it is clear that this organization will strongly influence how descending systems utilize the spinal cord to produce movement.

5. Conclusions

In this review we have discussed experiments which provide evidence in support of the hypothesis that spinal motor systems in vertebrates produce movement through the combination of a small number of units of motor output. There are, of course, many important aspects of this issue which have not been addressed in the present review. In particular, we have not addressed the contribution of sensory feedback to structures organized within the spinal cord. Such feedback clearly plays an important role in the production of normal motor patterns [23,49,57]. Indeed, the interpretation of spinal modularity as reflecting the control of distinct features of movement as discussed above clearly implies a critical role of sensory feedback and it seems likely that the full characterization of an unit of motor output will require knowledge of its regulation by afferent feedback (cf. Ref. [36]). Another relevant topic concerns the developmental specification of this spinal cord organization through embryonic and postnatal life and whether independent units of motor output such as considered here can also be observed in immature animals (e.g., Refs. [37,67]). These topics and others will be interesting

to examine with regard to this hypothesis of the organization of spinal systems.

In conclusion, the hypothesis examined here of a modular organization of spinal motor systems, although first proposed at the turn of the century and influential ever since to the study of the neural control of movement, remains in flux. Although the experiments described here generally support this hypothesis, it is clear that more experiments are required to evaluate this hypothesis fully and to examine the possible utilization of such units in the production of normal motor behaviors. Future experiments utilizing novel preparations and analytical techniques will hopefully be able to shed further light on this hypothesized “framework in which the limitless combinatorial properties of the nervous elements can be brought into action to produce ‘movements ranging from ballet dance to a tight rope walk’ [23]” [57].

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