Sensory Control and Organization of Neural Networks Mediating Coordination of Multisegmental Organs for Locomotion

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INTRODUCTION

Locomotor patterns are often rhythmic or cyclic, consisting of two main phases: a power stroke of the locomotor apparatus that yields propulsion of the organism relative to its environment, may it be water, air, or the ground, and a return stroke that re-establishes the starting position for the locomotor apparatus to generate the next power stroke. In walking, the power stroke is the stance phase of a leg, and the return stroke is the swing phase. In almost all rhythmically active locomotor systems, it is clear that a complex rhythmic motor pattern is generated by neural networks within the CNS, called central pattern generators (CPGs) (Grillner 1985, 2003; Marder and Calabrese 1996). Numerous examples show that a functional motor program not only depends on centrally generated basic rhythmic motor output but is also dependent on sensory signals reporting the actual movements from the periphery (Clarac et al. 2000; Fouad et al. 2002; Grillner and Wallén 2002; Pearson 2000, 2004). Sensory feedback can influence the magnitude and the timing of motor activity (Fig. 1). This general scheme based on one internal rhythm generating mechanism suffices for the description of motor outputs that keep a given relation in timing between their output elements, e.g., the muscles driving a locomotor organ.

However, the situation is more complex when several or multi-segmented locomotor organs have to be controlled. For instance, walking is based on coordinated movement sequences of the legs, which themselves are multi-segmented. An insect leg, for example (Fig. 2A), consists of more than five segments, i.e., the coxa, the trochanter, the femur, the tibia, and the tarsal segments, which are driven by >12 muscles. To generate steps, a specific task-dependent spatiotemporal sequence of muscle activation has to be generated so that the movements of the leg segments are coordinated (Bässler and Büschges 1998; Pearson 2000). Until 10 years ago, research did not often focus on the special issues arising from controlling a multi-segmented limb. Individual influences of sensory feedback from the limb in the generation of the locomotor output were identified, but an overall picture of sensory-central interaction, which could account for the generation of a coordinated walking motor output of a multi-segmented limb, was lacking (e.g., Bässler and Büschges 1998). Two main topics needed to be addressed. 1) How is coordination of motoneuron activity for a multi-segmented locomotor organ generated? 2) Does the basic organization of the central pattern generating networks correspond to the segmentation of the locomotor organs? Can the central neural networks, i.e., the CPG, be regarded as one entity that is somehow reorganized for generating a range of different motor outputs (e.g., see Pearson 2004) or are there “modules” that can be coordinated differentially according to the desired motor output? This article will review recent findings on these two issues from the stick insect walking system and place them in a broader context together with recent data on cat walking and lamprey swimming.

CONTROL OF THE MULTI-JOINTED STICK INSECT

MIDDLE LEG

Each of the six legs of a stick insect is controlled by an individual leg controller, i.e., individual neural networks in the nervous system necessary for generating a motor output for one leg. These are located in the segmental ganglion, i.e., in the prothoracic ganglion for the front legs, in the mesothoracic ganglion for the middle legs, and in the metathoracic ganglion for the hind legs (Bässler 1993; Cruse 1990; Forth and Bässler 1985; Wendler 1977). The interactions of these leg controllers follow certain behavioral rules that generate coordinated gaits for walking (Cruse 1990), but the neural basis of these rules is not known. In contrast to mammalian limbs, arthropod limbs do not move in only one plane, but instead, due to the construction of the limbs, limb movements occur in the horizontal and vertical planes (for recent summary, see Ritzmann et al. 2004). The morphology of the stick insect leg is shown in Fig. 2A. The stick insect middle leg has three main leg joints:
the thoraco-coxal (TC-) joint enables back and forth movements, the coxa-trochanteral (CTr-) joint enables levation and depression of the leg, and the femur-tibia (FTi-) joint enables flexion and extension of the tibia. In the stick insect, there is no trochanter-femur joint because these two segments are fused.

For simplicity, one could compare the FTi-joint with the knee-joint of a vertebrate hind limb and describe the TC- and CTr-joints as an outer and inner part of a joint, respectively, that functionally corresponds to the hip joint of a vertebrate hind limb. The neural networks controlling the individual leg joints of each leg are located within the segmental ganglion of a given leg. By means of tactile stimulation of head or abdomen (Büssler and Wegener 1983; Büschges et al. 2004) as well as by the application of muscarinic agonists such as pilocarpine (Büsclgesch et al. 1995) to deafferented thoracic ganglia, these networks can be activated and generate rhythmic activity in antagonistic motoneuron pools of each leg joint. The activity of antagonistic motoneuron pools of each leg joint is alternating, reflecting the output of central pattern generating networks for each leg joint. Importantly, no reliable cycle-to-cycle coupling seems to be present between the motoneurons controlling different leg joints (Büsclgesch et al. 1995) (Fig. 2), suggesting that the individual joint CPGs can operate rather independently from each other (summary in Büssler and Büschges 1998). Although some premotor interneurons within the CPGs have been identified, the detailed network topology of the CPGs is not known (Büssler 1995).

In recent years, detailed information has accumulated on how sensory signals contribute the coordination of antagonistic motoneuron pools that innervate one leg joint, termed intrajoint control, as well as to the coordination of the motor activity between leg joints, termed interjoint control. Information on this issue was often gathered from preparations in which leg proprioceptors were selectively stimulated, and their influence on rhythmic leg motoneuron activity was monitored when the locomotor system was activated either by tactile stimulation or by application of pharmacological agents (e.g., Büssler 1993; Hess and Büschges 1999). Today, it is clear that signals from leg receptors, reporting movement of a leg segment and load or strain on the cuticle, have access to the CPGs of the individual leg joints and that they can induce transitions in the activity of the individual CPGs (Akay et al. 2001; Hess and Büschges 1999). Examples from the stick insect are given in Fig. 2, B and C. The scheme depicts each joint CPG as a box (symbolized by 2 interneurons with mutual interactions) driving two antagonistic motoneuron pools (box). The first example shows movement and position signals from the FTi-joint affecting the CPG governing the CTr-joint. Sensory signals from the transducer of the knee joint, the femoral chordotonal organ (fCO), that report extension of the tibia, can switch the CPG of the CTr-joint from levator to depressor phase (Bucher et al. 2003; Hess and Büschges 1999) (Fig. 2B). The reverse is true for flexion signals from the FTi-joint. The second example shows the influence of load signals from the trochanteral campaniform sensillae (trCS) on the CPG of the TC-joint. This CPG can be switched to the depressor phase by an increase in load (Fig. 2C) (Akay et al. 2004), while the opposite switch occurs following a decrease in load. Interestingly, in mammalian walking, movement and load signals from the limb induce transitions between phases of motor activity (e.g., Grillner and Rossignol 1978; Hiebert and Pearson 1999; Hiebert et al. 1996). A recent study on the stick insect has indicated that sensory information may act through two independent neural pathways or channels, with one pathway initiating transitions and the second pathway determining the direction of transition (Büssler et al. 2003).

In summary, our results indicate that the leg muscle control system of the stick insect leg contains CPGs for each leg joint that can be active independently. The CPGs receive input from sense organs on the leg that can determine their phase of activity, and thereby, can contribute to the coordination of their actions. Figure 2D summarizes the known sensory-central interactions identified in the stick insect middle leg by arranging them in the sequence for generation of the stepping motor pattern typical for stepping movements in the single middle leg preparation (Fischer et al. 2001). The scheme spans the second half of the swing phase of the leg to the first half of the next swing phase and divides the step into a sequence of four states (1 to 4). It is important to note that the scheme only includes those influences that affect timing of motor activity and does not include the control of motor activity magnitude (cf. Fig. 1 and Büssler and Büschges 1998). The sequence of events in brief. 1) During the swing phase of a stick insect, middle leg levator trochanteris (Lev) and extensor motoneurons (Ext) are active together with protractor coxae motoneurons (Pro). Sensory feedback about extension of the FTi-joint initiates depressor trochanteris (Dep) and terminates levator trochanteris (Lev) motoneuron activity and is thus the first event in initiating stance phase. This causes the leg to be set down (Bucher et al. 2003; Hess and Büschges 1999). 2) Ground contact of the leg and the subsequent increase in load induces a transition in activity in the CPG governing the TC-joint initiating retractor coxae (Ret) activity and terminating Pro activity. This would cause backward movement at the TC-joint when the leg is free to move. Load signals affect knee joint motoneurons by exciting flexor tibiae (Flx) and inhibiting Ext motoneurons (Akay et al. 2001, 2004). 3) During stance, flexion signals from the FTi-joint reinforce flexor activity (Büssler 1986; Knop et al. 2001). 4) At a particular flexed position of the FTi-joint, position signals induce a transition in the FTi-CPG. Flx activity terminates, and Ext activity resumes (Büssler 1986, 1988). Flexion of the FTi-joint can induce transition of activity in the CTr-joint CPG as well, initiating Lev activity and terminating Dep activity (Bucher et al. 2003; Hess and Büschges 1999). As
FIG. 2. Influences of proprioceptive signals from the stick insect middle leg on the timing of activity of the CPGs of the 3 main leg joints. A: schematic representation of the stick insect leg and its main leg joints. B: movement and position signals of the knee joint (FTi-joint) have access to the CPG of the adjacent CTr-joint. CPG of each leg joint is symbolized by 2 interacting neurons in a box according to motoneuron pools driven, e.g., retractor (Ret) and protractor (Pro) motoneurons in the case of the inner hip joint (TC-joint). Each CPG is connected schematically by arrows with 2 antagonistic sets of motoneurons and muscles that they innervate (combined as depicted by boxes; Pro, Ret, Dep, Lev, Flx, Ext). Active elements are shown as filled symbols, inactive elements are depicted as open symbols. Movement signals from the knee-joint can induce transitions in activity of the CPG of the CTr-joint, as exemplified for extension signals switching the CTr-CPG to the depressor phase of activity. C: signals about changes in load affect the activity of the CPG of the TC-joint. These signals can induce a transition in activity of this CPG, e.g., increased load switches the activity of the TC-CPG from protractor to retractor phase of activity. D: diagram summarizing all known sensory influences on the timing of motor activity for intra- and interjoint coordination in single middle leg stepping (for a detailed description, see Akay et al. 2004; Ekeberg et al. 2004). Filled symbols denote active elements/neurons; open symbols denote inactive elements/neurons. Sensory influences on the CPGs are either excitatory (+) or inhibitory (−). Description of the sequence of events is organized in a state-like fashion moving from the 2nd row (1) on the left to the 2nd to last row on the right (4), after which the state of the 1st row would follow again. To exemplify this sequencing of events states, 4 and 1 are repeated at the left and right margin.
a consequence, the leg is lifted off the ground, and the accompanying decrease in load reinforces ongoing Ext activity (Akay et al. 2001) and induces a transition in activity of the TC-joint CPG, leading to activation of the Pro and inactivation the Ret activity during the swing phase (Akay et al. 2004). When the leg is free to move in the horizontal plane, as in forward walking in vivo, position and load signals from the leg contribute to the stance-to-swing transition: When coaxal sensors signal a rather posterior position of the leg, while load on the leg is decreasing, the leg is lifted off of the ground. This influence has so far only been shown on the behavioral level (Cruse 1985). Data from semi-intact walking animals on a double-tread wheel indicate that, in forward stepping position, signals from the leg and load signals are weighted against each other so that a decrease in load can lead to a premature initiation of leg swing. It should be emphasized that the outline of the sequencing of events shown in Fig. 2D does not claim to contain the complete set of sensory influences acting in the control of timing motor activity in the stepping cycle of the stick insect leg, although they have been proven to be sufficient for this task (see next 3 paragraphs). Deficits exist in our understanding of the sensory control of the swing-stance transition in detail. It is known to include a targeting of the leg’s tarsus toward the position of the anterior leg’s tarsus in vivo (Cruse 1985). In addition, there is the question of which sense organs at the coxa report the relevant movement information that is used for initiating the stance-swing transition, such as the hair plates, the hair rows, an internal muscle receptor organ, or any combination of them.

It becomes obvious from the above description that the sensory-central interactions affecting timing of activity in leg motoneurons are very specific. For example, sensory signals reporting movement have only been found to contribute to interjoint coordination between two of three leg joints and in one direction only, i.e., from the knee joint (FTi-joint) to the outer hip joint (CTR-joint) (Hess and Büschges 1999). No influence of movement signals was found for the opposite direction (Akay et al. 2001). In addition, no evidence for movement signals in interjoint timing control has yet been detected between any of the other leg joints (Akay et al. 2001). A similar situation exists for load signals from the leg that contribute to coordination of motoneuron activity (Akay et al. 2001, 2004).

From the number and variety of sensory-central interactions, it is not possible to assess the sufficiency of this information and its explanatory value by a purely qualitative examination of the mechanisms. One tool in physiological research that has proved important for the study of locomotor systems is computer simulation. In the past 10 years, simulations have paralleled and guided electrophysiological studies of locomotor mechanisms in the spinal cord of the lamprey (e.g., Ekeberg and Grillner 1999; Grillner et al. 2000) as well as neurobiological research on rhythmic nonlocomotor systems (e.g., Marder and Prinz 2002). We tested the sufficiency of the sensory-central interactions described above with a three-dimensional (3D) neuro-mechanical simulation of the stick insect based on its morphology (Ekeberg et al. 2004). Implementation of the identified interactions (Fig. 2D) in the 3D neuro-mechanical simulation verified that a simulated neural controller using these principles was able to generate coordinated stepping movements of a middle leg and that its conceptual framework is for example also sufficient to simulate stepping movements of front legs with only minor modifications.

How do these results on stick insect walking pattern generation compare with the known organization of other locomotor systems, especially other walking systems? Two issues need to be discussed. Do general principles emerge for sensory control for walking pattern generation by comparing the results from the stick insect to other legged systems? Is the fine structure of the stick insect walking pattern generating system reflected in other walking systems or other locomotor systems in general?

**Sensory Control of Walking Pattern Generation: Motor Pattern Generation in the Cat Hind Limb**

In a variety of other legged animals, information has been gathered on the sensory control of walking motor patterns, among those are invertebrates, such as the cockroach, crayfish, lobster, and locust, and vertebrates such as the mopuppy, mouse, rat, and humans (for reviews, see Fouad et al. 2002; Orlovsky et al. 1999; Prochazka 1996). Presently, the most complete knowledge of the role of sensory signals in timing motor activity in the stepping cycle that can be compared with the stick insect derive from previous and recent findings on the cat hind leg.

It has been known, since the original work by Brown (1911), that the cat lumbar region of the spinal cord can generate the basic alternating activity in flexor and extensor muscles. Later studies by Grillner and Zangger (1979, 1984) showed that the motor output of the deafferented lumbar spinal cord resembled the motor output for stepping (“fictive locomotion”; recent summaries by Orlovsky et al. 1999; Pearson 2000). The motor output generated expresses a well-coordinated action of the various leg motoneuron pools of hip, knee, ankle, and foot and was thus related to the action of one CPG situated in the lumbar spinal cord (e.g., Pearson and Rossignol 1991; for review, see Orlovsky et al. 1999; Rossignol 1996; but see also Yakovenko et al. 2002). This spinal motor pattern can be drastically modified by sensory feedback that changes its magnitude and timing by signals from movement and force measuring sense organs in the muscles (for review, see Orlovsky et al. 1999; Pearson 2000). At present, the most complete picture exists for sensory signals about position and load from the leg that can contribute to the patterning of motor activity by influencing the timing of the motor output in the stepping cycle. They have been analyzed to an extent that the present knowledge can account for the generation of a complete step cycle in the cat hind leg.

The mechanisms influencing step cycle timing will be reviewed here in the sequence that they are activated during stepping (Fig. 3A). 1) During leg swing, flexor motoneurons activate the leg flexor muscles and move the leg forward. Recent results of Pearson et al. (2003) provide evidence that the transition from leg swing to stance, i.e., from flexor to extensor activity is initiated by movement signals from the hip joint. The receptors have not been identified yet, but receptors in the hip joint or hip extensor muscles are most likely involved (K. G. Pearson, personal communication). 2) After touch down of the hindleg, extensor activity during leg stance is reinforced by position and load signals from group Ia and Ib afferents of ankle extensor muscle spindles and tendon organs (Pearson and
FIG. 3. A: diagram summarizing all known sensory influences on the timing of motor activity for intra- and interjoint coordination in hind leg stepping of the cat. Spinal CPG is depicted by 2 neurons connected schematically with each other by 2 inhibitory synapses (filled circles) and with 2 antagonist sets of motoneurons and muscles that they innervate (combined as depicted by boxes: Flx, Ext). Active elements are shown as filled symbols; inactive elements are depicted as open symbols. Sensory influences on the CPG are either excitatory (¡) or inhibitory (¡). Description of the sequence of events is organized in a state-like fashion moving from the 2nd row (1) on the left to the 2nd to last row on the right (3), after which the state of the 1st row would follow again. To exemplify this sequencing of events, states 3 and 1 are repeated at the left and right margin of the scheme. The 2 lines below the figure give sensory signals and receptors providing them, except for the case in which they have not yet been identified (not ident.). B: comparison of sensory influences identified that influence timing of the motor output for walking movements in the cat and the stick insect: top, sensory signals for stance-to-swing transition; middle, sensory signals for swing to stance transition; bottom, sensory signals in stance control. Sensory parameters are given for the cat (left) and the stick insect (right). Middle: schematical representation is given that holds for both systems. In these schemes, central neural networks generating stance and swing phase motor activity are simplified and lumped together to form 2 states, i.e., stance (St) and swing (Sw). Sensory influences are indicated and identified by arrows that either initiate (+) or terminate (−) 1 of 2 phases of motor output.
Collins 1993; Whelan et al. 1995). 3) The termination of stance and the transition to swing is initiated simultaneously by position signals from the hip joint and load signals from the ankle joint (Duysens and Pearson 1980; Grillner and Rossignol 1978; Hiebert et al. 1996; Pearson et al. 1992; Whelan et al. 1995). Unloading of the ankle extensor muscle reported by group Ib afferents occurs at the time that the contralateral leg initiates its stance phase and results in a decrease of the load signals to the ipsilateral extensor half center. Simultaneously, while the leg approaches its posterior extreme position in the step, the flexor muscles, e.g., of the hip and ankle are further lengthened, which is reported by their group I afferents. The resulting sensory signals lead to an inhibition of the extensor half center, with those from hip flexors being probably the most relevant ones. Both load and position signals are the most significant ones known to contribute to the termination of extensor and initiation of flexor activity for the next swing phase. They seem to be weighted against each other with load being the decisive factor. This is apparent from the fact that prolonged load signals from the leg, evoked by electrical stimulation of group Ib afferents in the ankle extensor, can lead to a marked prolongation of stance and shift of the posterior extreme position (Whelan et al. 1995).

A comparison of the role of sensory signals in the timing of motor activity in the stick insect middle leg and the cat hind leg control systems reveal significant similarities (Fig. 3B). In both systems, movement signals from the leg determine the transition from swing to stance by controlling the phase of central pattern generating networks. In addition, the transition from stance to swing is initiated by sensory signals reporting first, unloading of the leg, and second, position of the leg, by signaling a retracted position of the leg. Finally, in both animals, stance phase activity is reinforced by both load and position signals. From these results, the following general principles emerge for the sensory control of motor output timing during walking. The power stroke in walking (stance phase) is reinforced and timed with respect to the biomechanical demands of the walking system to support the body (load) and with respect to movement of the leg (position). The return stroke (swing phase) is timed primarily with respect to the position of the leg relative to the body.

At present, differences between the two systems are apparent in the extent to which modularity of the central pattern generating networks has been shown. While in the stick insect, evidence suggests the existence of multiple central pattern generating networks, only indirect evidence has been shown for the cat walking system. However, recently published data may shed some new light on this issue.

**Organization of the Central Pattern Generators for Locomotion: New Insights From the Cat and the Lamprey**

How does the modularity of the stick insect walking pattern generating system with CPGs for each leg joint compare with the composition of other locomotor systems? The general scheme of sensory-central interactions outlined in the introduction and Fig. 1 contains one central pattern generating network as the basic kernel. It is now clear, however, that in a variety of legged locomotor systems, the central network can be composed of multiple central pattern generators, each controlling a subunit of the locomotor system, such as a joint, segment, or muscle of a locomotor organ. For example, in the mudpuppy cervical spinal cord, a modular organization has been shown for the central pattern generating networks controlling flexor and extensor motoneuron pools of the forelimb (Cheng et al. 1998), with each hemisegment containing one individual CPG. In the turtle spinal cord, evidence suggests a modular organization of the central pattern generating networks for the control of segmental motoneuron pools of the segments controlling the hind limb (e.g., Stein et al. 1995), generating different types of scratching patterns. Together with the data from the stick insect, it seems that central neural networks governing legged motor systems may exhibit a modular structure. This situation would verify the “unit burst generator” (UBG) concept for locomotor networks formulated by Grillner >20 years ago (Grillner 1981) (Fig. 4). This concept was based on conclusions drawn from data on motor

**Fig. 4.** A: schematic summary of results presented by Cangiano and Grillner (2003) on the modular organization of the lamprey spinal central pattern generating network for swimming. Each hemisegment contains its own pattern generator, L and R, respectively, that is connected with the contralateral hemisegment by mutual inhibition and with the caudal and rostral segments by intersegmental pathways (arrows). According to the apparent role of glutamatergic excitation within the hemisegmental CPGs, each of these networks is presented with 2 interneuron pools exciting each other. B: schematic representation of the unit burst generator (UBG) concept formulated by Grillner (1981). Each synergist muscle group is assumed to be driven by its own rhythm generating network. Individual units controlling functional antagonistic motoneurons of 1 joint are connected with each other by mutual inhibition as well as with the other UBGs in various ways.
pattern generation in the cat hind leg. According to the UBG concept, each group of motoneurons may be controlled by its own central pattern generating network.

Presently, however, direct evidence for modularity is still lacking in the cat spinal cord system where the UBG concept was initially postulated. Except for evidence that suggests that the cat locomotor CPG is formed by two half-centers on each side of the spinal cord inhibiting each other (see also Orlovsky et al. 1999), the detailed organization and circuitry of the CPG for the cat hind limb is not known. Bouyer and Rossignol (2003a,b) analyzed the role of cutaneous input from the cat hind paw on the generation of the stepping motor output. They report that, in spinal cats, denervation of the hind paw caused a permanent deterioration of the motor pattern. While flexor and extensor muscles of hip and knee are still activated (postspinalization) in an alternating fashion during stance and swing, flexor and extensor muscles of the ankle and foot were abnormally co-activated during stance. This is a marked difference compared with the activity of these muscles during intact walking or following postdeafferentation regeneration, because their activity is completely shifted into the same (stance) phase of the step cycle. However, on generating fictive locomotion in the deafferented spinal cord, alternating motor activity is produced, indicating that the abnormal motor output during walking is not the result of a permanent reorganization of that CPG that is activated during fictive locomotion.

These results from the spinal walking cat were unexpected because none of the previously identified sensory-central interactions can explain a simultaneous in-phase activation of ankle and toe extensor and flexor muscles during stance (see Pearson 2000). This may indicate that afferent feedback not only interacts with the presumed single hind limb CPG, but that it may exert a much more powerful influence on the motor output by uncoupling motoneuron activity from CPG drive. Therefore it may exhibit an organization similar to the schemes described above for the stick insect. These results highlight the importance of determining the organization of the cat spinal walking CPG. One approach might be to combine differential, competitive activation of the known powerful sensory influences of movement and load signals from leg joints (hip and ankle joints; Grillner and Rossignol 1978; Hiebert et al. 1996; Whelan et al. 1995) to challenge this CPG. In addition to such approaches, fundamental new insights into the organization of the mammalian hind limb CPG can be expected from recent investigations combining electrophysiological studies of mammalian spinal networks for locomotion with the use of developmental markers for neuron populations in neonatal rodents (Butt and Kiehn 2003).

The number of locomotor systems in which a modular organization has been proven is steadily increasing. In the lamprey spinal cord, evidence for the existence of hemisegmental central pattern generators was recently presented. The undulatory swimming movement of the lamprey is generated by a rostral-to-caudal wave of rhythmic activation of dorsal and ventral myotomal muscles and fin musculature (for description of basic cell types, see Rovainen 1974). The basic motor pattern of the myotomal musculature is based on a CPG that generates alternating left-right activity in motoneuron pools innervating the myotomal musculature on both sides of each segment (recent summaries in Buchanan 2001; Grillner et al. 2000; Orlovsky et al. 1999). Pattern generation of the CPG was thought to rely crucially on mutual glycinergic inhibition between antagonistic centers on both sides of the spinal cord (see Grillner 2003) together with sensory feedback from the intraspinal stretch receptors (edge cells). Their overall sensory activity that is evoked by bending of the cord is able to entrain the activity of the swimming CPG (recent summary in Grillner and Wallén 2002). Generation of a coordinated motor output between segments in the longitudinal direction of the cord is thought to be based on the action of intersegmental projections of the spinal interneurons (Buchanan 1999; Grillner et al. 2000; Matsushima and Grillner 1992) and the interaction with the sensory feedback (Grillner and Wallén 2002).

Cangiano and Grillner (2003) have now shown that each hemisegment of the lamprey spinal cord contains a neural network capable of generating basic rhythmic motor activity (Fig. 3) and thus represents a UBG. They showed this by using different levels of longitudinal lesion of the spinal cord and electrical stimulation of individual hemisegments. While maintaining rhythmicity on both sides of the spinal cord, progressive surgical sagittal lesioning of axons crossing the midline of the spinal cord led to a gradual increase in burst frequency, establishing a continuum between the intact spinal cord and the hemisphinal cord preparation. It is currently assumed that hemisegmental CPGs operate on the basis of interconnected ipsilateral excitatory glutamatergic interneurons that include previously identified morphological classes of excitatory interneurons (e.g., Buchanan and Grillner 1987). Rhythmicity in the hemisphinal cord persists after removal of glycinergic inhibition, and it is currently assumed that inactivation of excitatory interneurons during rhythmic activity arises from their intrinsic properties (Cangiano and Grillner 2003). These results show that each hemisegement is capable of generating rhythmic motor activity and that the contralateral glycinergic inhibition underlies the alternation of activity on both sides of the spinal cord as well as burst frequency reduction. Further questions now arise as to whether coupled CPGs for each pool of segmental motoneurons, i.e., the pools innervating the dorsal, the ventral myotomal muscles, and the dorsal fin motoneurons (Aoki et al. 2001; Shupliakov et al. 1992) exist, and if so, how their activity is coordinated. Finally, what role does sensory feedback play at the level of pattern generation within a given segment.

Apart from the similar modular structure of the segmental spinal CPGs of the walking stick insect and the swimming lamprey, how do these data relate to our present understanding of the stick insect walking system? In the lamprey spinal cord, it is clear that interaction via central pathways plays a key basic role for coordinating the action of the segmental CPGs. In the stick insect leg control system, this prominent action of central pathways does not appear to exist. This may be potentially attributable to the fact that the stick insect walking system is operating at rather slow cycle frequencies and does not require a fast central predictive component for pattern generation on a cycle-to-cycle basis. Pattern generation for walking over uneven ground or climbing on twigs may also be much more dependent on “on-line” sensory feedback action to cope with the nonhomogenous substrate compared with swimming in water. To settle this issue, additional new approaches are needed for the stick insect walking system that allow the investigation of potential central coordinating pathways and mechanisms by “driving” the walking system over a broader range of frequency of operation.
Two conclusions can be drawn about the neural networks controlling multi-jointed locomotor organs. 1) In animal walking, general principles for the control of the stance phase and the step-phase transitions can be proposed from studying the cat and the stick insect. 2) Evidence from systems controlling multi-segmented locomotor organs support the notion that central neural networks contain multiple CPGs corresponding with the segmental structure of the locomotor system. Why is this proposition significant? One striking characteristic of all locomotor systems, including those that operate multi-jointed locomotor organs, is their ability to generate a highly flexible and adaptable motor output, enabling the animal, for example, to walk forward or backward or to turn. We need to know the internal organization of the central pattern generating machinery to be able to develop experimental approaches to study the underlying neural mechanisms responsible. This will allow us eventually to target and analyze those neural mechanisms that allow their task-specific flexibility of motor outputs.

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Invited Review

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