The Role of Spinal Cord in Motor Control: reflexes, patterning and final motor production

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The spinal cord has an unambiguous position in motor control, containing the final common pathway to the musculoskeletal system. It is also among the evolutionarily most ancient structures, with homologues of vertebrate spinal cord in lower chordates such as amphioxi or lancelets. The precise role and operations of spinal cord circuitry continue to be areas of dispute and occasional controversy. Some of the very earliest experimental physiologists (e.g., Whytt, Legalois, and Marshall Hall[18]) had already shown that the spinal cord, isolated from the rest of the CNS, could organise semi-purposive goal-directed behaviours. As a result of these fundamental observations, three areas of discussion and controversy have dominated the investigation of spinal motor control almost from the outset:[1] What are the relative roles and relationships between the brain proper and this potentially semi-autonomous spinal cord circuitry?[2] What are the relative roles of peripheral inputs and central spinal circuitry in organising the spinal generated behaviours?[3] How modular and generalisable is the organisation underlying spinal generated behaviours and is this organisation used in executing skilled voluntary behaviours? Following Hall and others, Sherrington and colleagues used decerebrate mammalian preparations, adopted the neuron doctrine, promulgated the idea of the synapse and established the motor unit description, while Brown worked on central generation of pattern.[29] Together they set the stage for the exquisite neurophysiology, and other developments and idea swings that have followed over the past century.[17,18]

What do the spinal segmental reflexes contribute to movement?

The spinal cord circuitry is the 'fastest responder' for motor corrections and adjustments besides the corrections managed by the muscle properties themselves. It is involved in regulating these limb biomechanical, muscle and reflex properties. Spinal cord organisation is intimately matched to the body. At the most fundamental level the motor pools mirror musculature, and through development proprioceptive projection patterns are also precisely topographically organised, prior to any active use of these circuits. The precision and repeatability of the projections has allowed identification of various sensorimotor interneuron circuits in detail, first physiologically, and more recently with cellular and molecular genetics methods.[12] The understanding of spinal connectivity, interactions and descending targets together can also suggest novel therapeutic strategies.[1,13] The monosynaptic reflex arc, and motoneuron control circuits comprising Ia, Ib interneurons and Renshaw cells are now the stuff of basic physiology and medical texts (see Figure 1). Less well appreciated is the subtlety and precise wiring structures actually needed. What is presented in textbooks as a uni-articular single-joint feedback system for position control as in Figure 1A, in the working spinal controls must regulate properties of a complex limb with multi-articular muscles of diverse actions. Though the basic story is correct, the devil is in the details.[24]

Motoneuron pool control of the muscle

Fundamental to limb control is the process of regulating muscle contraction. For vertebrates, high safety factor end-plate synapses guarantee 1 for 1 following of motoneuron drive by motor unit muscle fibres. Well graded contractions can only arise from a progressive recruitment of the motor pool population. This process is quite well understood in broad terms: the Henneman size principle operates throughout the motor pool. The size principle is extremely robust and has withheld severe scrutiny.[4] Small motoneurons that are attached to slow, small twitch non-fatiguing fibres have high input resistance (based on both their size and their cellular membrane properties). As a result, these are thus brought to threshold first by common synaptic drive. Larger fatigue-resistant, and still larger fast-fatigable fibres are innervated by proportionately larger and lower input resistance motoneurons, and thus are recruited later by the distributed common drive. Fibre types of muscles are dynamically determined properties. They depend on motor-

A. Simplified Reciprocal Reflex Circuit Organisation
(Sherrington, Lundberg, Jankowska and others).

B. Basic Half-Centre Circuit Organisation (Brown, Lundberg).

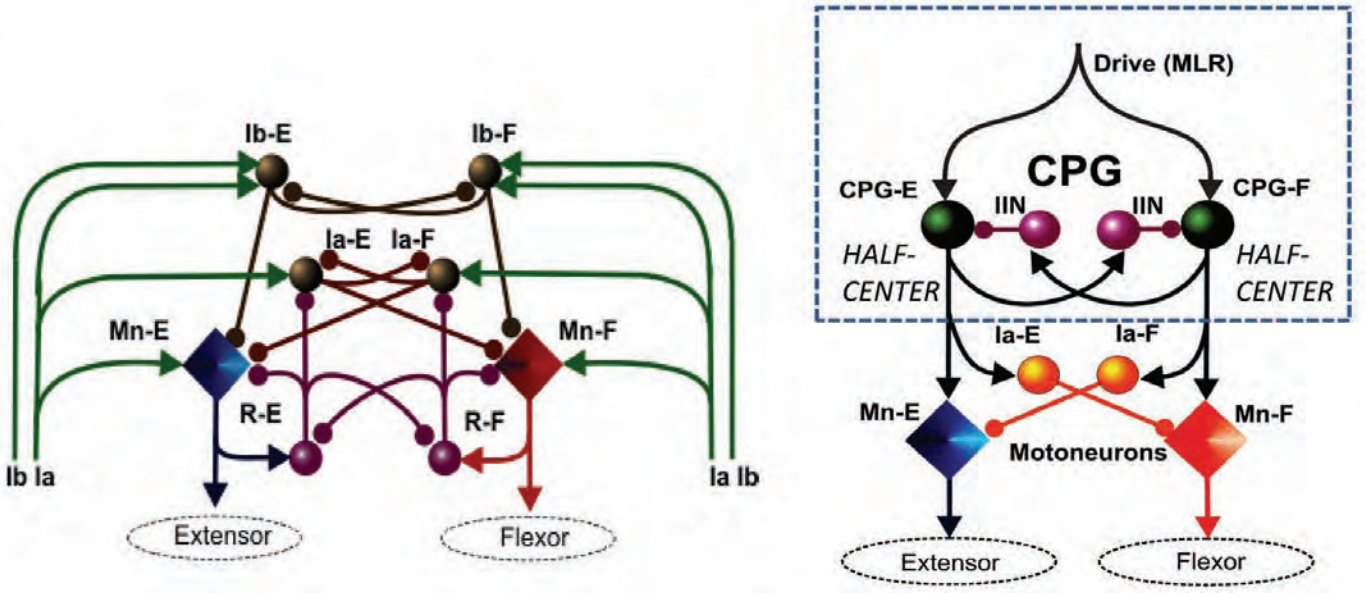

Figure 1:
Reflex circuitry and the half-centre concepts. A. The basic reflex circuitry now identified comprises the Ia afferents (muscle spindle, length and velocity sensing, Ia), the Ia interneurons Ia-E and Ia-F, the Ib afferents (Golgi tendon organ, muscle force sensing, Ib), the Ib interneurons Ib-E and Ib-F and the Renshaw cells (recurrent inhibition of motor pools, R-E and R-F). These are arranged to manage agonist and antagonist muscles and their interactions and are generally drawn in the kind of simplified schematic shown. The schematic shows two things: Firstly, length and force feedback are in competition, for example in control of an extensor on the left. Secondly, synergist and antagonist circuits interact and inhibit one another. Together these two sets of interactions regulate the spring-like properties of muscles and joints, and manage their spinal control. If regulation goes awry spasticity and clonus can result. However, in real limbs the anatomical and mechanical organisation does not permit the level of simplicity of this textbook scheme, and it is not correct to infer that individual joints are managed in this way in isolation from one another. More likely, these pathways are structured to regulate multi-joint and whole limb properties and are organised and integrated into multi-joint controls and modules. B. The basic half-centre central pattern generator (CPG) concept of Brown. Extensor (CPG-E) and Flexor (CPG-F) Half-centres and their associated inhibitory interneurons (IIN) act to inhibit one another. When activated by neuromodulation, and/or directly driven from the mesencephalic locomotor region (MLR) the two half centres interact to create an alternating dynamics and oscillation. These half-centres then drive the appropriate motor pools and muscles (Mn-E, Mn-F) and modulate interneurons in the reflex pathways (Ia-E and Ia-F).

unit firing patterns received, and hence in part on the size principle. Motoneurons act as linear summing junctions for their inputs to a first approximation. However, they also possess persistent inward current (PIC) mechanisms that alter their recruitment drive responses, primarily after initial recruitment, allowing persistent firing with reduced synaptic drive. Exactly how these active mechanisms operate in normal motor control is still murky, though they likely contribute to spastic post-injury spinal behaviour.[14] Renshaw cells, through recurrent inhibition act to focus drive, vary recruitment gain and likely act to desynchronise motoneuron action potentials, perhaps particularly important in PIC conditions. Despite the importance of muscle fatigue processes in both performance and pathology, the spinal cord mechanisms that manage fatigue at spinal and voluntary control levels remain only poorly understood.[8] Motor unit rotation is believed to perhaps contribute.

Feedback regulation of muscles and mechanics

The classic monosynaptic stretch reflexes and interneuron systems in Figure 1A have considerable delays. Such delays would be intolerable to a design engineer. Modeling how the spinal feedback pathways might operate has spawned a range of motor control theories, including the Merton follow-up servo, and alpha and lambda variants of equilibrium control.[27,18] What now seems most clear is that the spinal feedback circuitry is set up to regulate and coordinate the mechanical properties of muscle and joints: like the shocks in a car, the springy stiffness and damping properties (the mechanical 'impedance') of muscles and joints must be set appropriately for context. For example, a mogul skier, a soccer player and a driver will all need different mechanical springiness at the knee. Due to seminal contributions of Rack and Westbury, and Nichols and Houk, it is now understood that the Ia and Ib feedback pathways, from spindles and Golgi tendon organs (GTO) respectively, partly linearise muscle responses and disturbance rejection.[24] Spindle and GTO pathways act in opposition. It is not physically possible to arbitrarily control both force and position simultaneously, and the two opposing controls of force and position/velocity act in concert to vary the impedance responses of muscle and joint so as to adapt them to task context.

Because most muscles are not uniarticular, the segmental spinal feedback regulations act to regulate multi-joint or whole limb impedance. Biarticular muscles are likely contributors to within-limb energy exchanges that are mechanically efficient in locomotion, and regulating multi-joint impedance in locomotion is likely a key spinal function. Further, segmental feedback patterns spanning multiple joints must be precisely balanced to avoid instabilities in the limb as a whole which could be both pathological and physically damaging. All of these pathways and interneuron systems are targets of corticospinal and other regulations, both directly and through presynaptic 'primary afferent depolarisation' (PAD) mechanisms. In this fashion, classically, the spinal cord has been thought to form a general purpose motor control substrate, available for the execution of a rich variety of behaviours under direct and full control by descending pathways.

The semi-autonomous spinal system – Generation of behaviours and patterns locally in the spinal cord

Both Sherrington and Brown recognised that headless newts, frogs and decerebrate cats could generate purposive behaviour closely resembling natural movement. They differed primarily in how they considered it to be generated. Sherrington more strongly favoured a reflex chaining like framework in which limb state and sensory inputs determined the control action and unfolding of reflex behaviour. Brown favoured a centrally driven pattern and popularised the half-centre model of central rhythm generation (see Figure 1B). Today a synthesis of these perspectives is thought to be closer to the truth. The spinal circuits are now believed to partly anticipate future states, so as to cope with the neural delays, to be able to generate pattern, both in feedforward and in more flexible fashions, and to respond to the

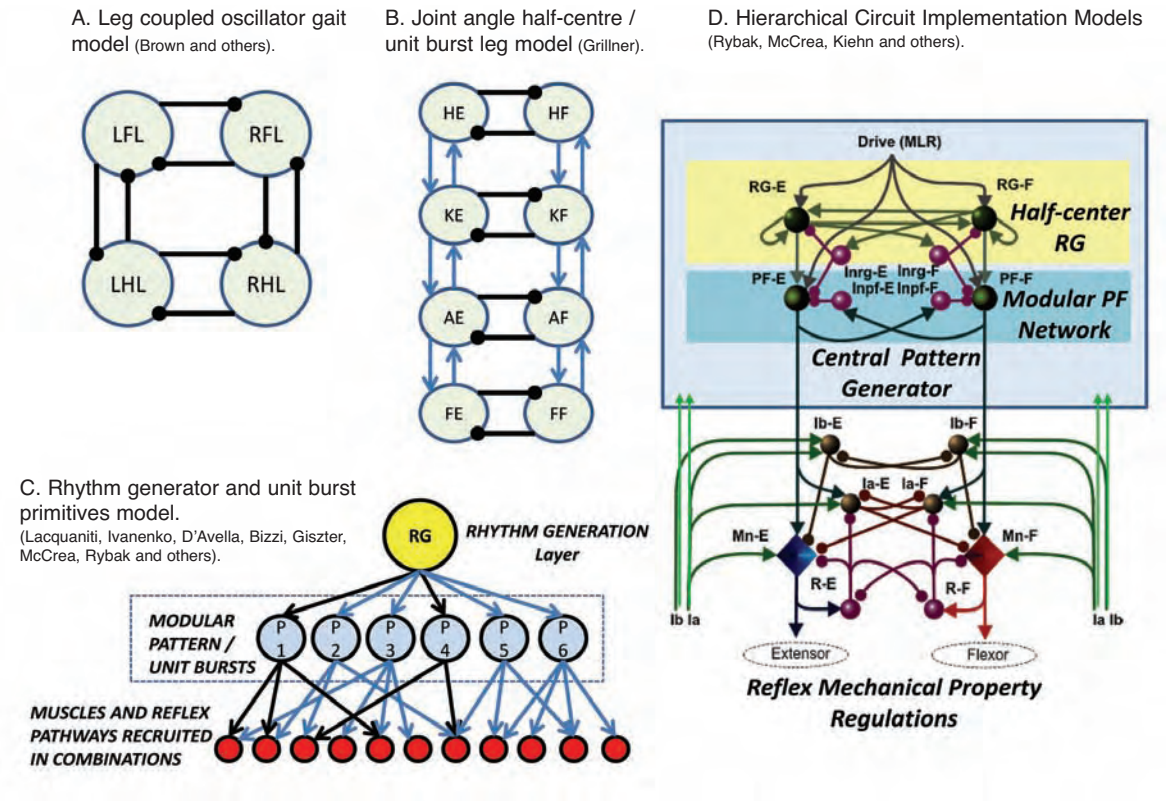

Figure 2:
Spinal circuits can manage basic patterns of gait and limb control in isolation. From the basic understanding of pathways and pattern generation current research is elaborating an understanding of how spinal circuits support movement. A. The half-centre oscillator formulation of Brown can be applied to the four legs of a quadruped – the four oscillators can synthesise a range of gaits, and form a well-regarded model of quadrupedal locomotion. (LFL – left forelimb/upper-limb, RFL– right forelimb/upper-limb, LHL – left hindlimb/lower limb, RHL – right hindlimb/lower limb), B. The half-centre oscillator framework was extended conceptually to reciprocating unit bursts acting around joints by Grillner and colleagues in order to manage leg degrees of freedom and more complex rhythmic motions in a decentralised dynamic network (HE/HF Hip extensor/flexor half-centres or unit burst generators; KE/KF Knee extensor/flexor half-centres; AE/AF Ankle extensor/flexor half-centres; FE/FF Foot extensor/flexor haf-centres). The unit burst notion is also adopted in the synergy/primitive framework, but not tied to specific joints. C. Current data support a hierarchy of a rhythm generator system which presumably involves half-centres (see D), recruiting a collection of discrete modular synergies or primitives in a pattern formation layer (P1-P6). The primitives each individually control different groups of muscles and low-level reflexes, lumped together as biomechanical units or building blocks for movement. These hierarchical spinal functional units are likely to be the ideal targets of physical therapies and interventions such as epidural stimulation to activate intrinsic spinal rhythmic capacities, and may represent evolved structures common across individuals. D. As more detailed circuit structures are garnered from physiology and developmental molecular genetics a synthetic effort is underway to develop and understand the detailed wiring diagrams of spinal cord circuitry that support the functional modularity and units in A-C. PF-E and PF-F represent pattern formation modules in this scheme. This type of detailed modeling and physiology of spinal movement construction systems may enable better understanding of rehabilitation and new therapies after spinal cord or segmental spinal circuit damage.

mechanics through feedback mechanisms to adjust sequences and the associated phase and frequency of rhythmic motions.

Pattern generation – sensory versus central control of behaviours

It has been established that the basic patterns of locomotion can be generated in the isolated mammalian spinal cord, devoid of both patterned descending and sensory feedback. Spinal locomotion thus fulfils the classic operational definitions of 'central pattern generation[20]' (CPG). Spinal central pattern generation is established in animals ranging from the jawless fishes such as lamprey to the mammals.[12,20] Half centre mechanisms (Figure 1B), network mechanisms, and intrinsic neuronal properties together support the rhythmic pattern formation. Descending neuromodulation strengthens and varies pattern generator dynamics and overall state. Pattern generators arise in mammals in utero, and are progressively elaborated. By birth a rat can crawl effectively, and a few hours after birth a wildebeest can walk with its parents and herd. Some rats with complete mid-thoracic spinal transection at birth succeed in developing effective quadrupedal weight bearing coordination strategies despite the transection.[10] There is evidence of similar CPG mechanisms in human infants.[6] However, a major controversy has been the extent to which these mechanisms are players in subsequent voluntary bipedal locomotor tasks, and the degree of persistence of a CPG into human adulthood. Recent data from various laboratories support a role and persistence of pattern generator circuitry in human development, normal function and post injury processes and therapy.[6,7,8]

Spinal structure – Modularity in pattern formation and reflex organisation

Beside the basic observation of rhythmic pattern generating and purposive reflex behaviours such as scratching and defensive motions, data have also accumulated supporting a modular composition of spinal generated and rhythmic behaviours. In able-bodied human locomotion, animal locomotion and other behaviours, the compact modular descriptions of the muscle activity patterns and adjustments prove useful (see Figure 2 for examples). Classic pattern generator views have emphasised coupled oscillators and perhaps joint level oscillators as a compositional basis of pattern (Figure 2A and B). However, a range of studies of intact and fictive (paralysed) decerebrate animals, and spinalised animals, now support a spinal hierarchical structure for pattern generation and other spinal behaviours (Figure 2C). McCrea and Rybak have demonstrated the need for separated rhythm generation and pattern formation layers using classical neurophysiology and computational models.[21] The pattern generators schedule both reflex gain changes, and unitary muscle bursts to accomplish locomotion. Elements of pattern (unit bursts) in this framework can be likened to building blocks. Building blocks, unit burst synergies or primitives, support both reflex and other behaviours in spinal cord, and can be identified independent of rhythmic pattern, in flexible reflexes and other adjustments.[11] Together with McCrea and Rybak's analysis, work has established single unit bursts of fixed muscle composition as the fundamental elements of movement composition by spinal cord,

rather than more complex sequenced time-varying patterns. These act rather like notes in a musical score to construct behaviours. It is suggested that by sequencing (the 'score') and combining (the 'chords') these unitary elements, much of the basic structure of motor patterns can be accounted for. Interneurons that specifically act to drive muscles in these synergies or primitives have been found in the frog spinal cord,[15] and might form some of the spinal 'piano keys' for descending pathways. Skilled acts likely augment this basic 'instrument' (see below). The primitive burst structures in the frog are likely to be conserved across species, and similar modular patterns exist in mammals[6] (see Figure 2C and D). It continues to be controversial how these synergies or primitives identified in other species relate to human movement but a role seems clear.[6] In stroke recovery and post stroke motor patterns some authors[2,3] have published data supporting a common modular basis for the intact and injured pattern, and they have represented recovery as an elaboration and differentiation of control of the synergies. Post stroke, some lower limb stepping synergies may collapse and two synergies be active together, for example. If this can be precisely understood, then rehabilitation could then be better tailored to the patient, and therapy targeted to aid control of specific synergies that are deficient. This could lead to a more 'natural' set of motor compensations, that are more easily integrated into an individual's existing motor repertoire and other activities of daily living. This perspective of synergy and primitive contributions in voluntary skills remains controversial. However, early spinal mediated infant behaviours such as grasp reflex, Babinski and so on emerge post-injury in adults. The structural circuit support for these patterns is not 'dissolved' through development of adult behaviours, and their synergies appear to be conserved throughout life.

Descending control of the spinal cord and its local behaviours – working through or working round?

The most primitive mammalian spinal cords have corticospinal projections focused on the dorsal horns. One interpretation is that early corticospinal control simply modulated feedback pathways and thereby adjusted or co-opted how spinal motor circuitry responded. The corticospinal projections have moved to deeper laminae and added corticomotoneuronal synapses throughout mammalian evolution, and the likelihood is that descending controls can thus exert control over reflexes, spinal modules, rhythm generation, and muscle feedback regulation, or could bypass these altogether. Which of these control strategies are optimal or normal in humans, and in different skills and individuals? This will likely determine how these mechanisms act post-injury, and whether spinal circuits act as aids or detriments to recovery of function. How much are the spinal cord mechanisms 'bypassed' in skilled voluntary motor acts and supplanted by direct controls and long-loop reflexes? Much of our current understanding is for the upper limb. Work of Scott and colleagues[26] and Wolpert, Franklin and colleagues[5,31] shows that implementations of fast task-dependent optimal feedback controls may occur primarily at the level of long-loop transcortical reflex effects (latency ~50-60ms in upper limb), rather than by using direct alterations of the fastest responses of segmental levels (latency ~25-35 ms in upper limb). The notion of 'downloading' all task details into spinal cord and allowing the cord to reconfigure the fastest reflexes (i.e., the segmental reflex) on a momentary basis seems to be wrong. The fast segmental reflex systems appear to operate with a preset pattern in voluntary tasks, one of which is largely unaltered by the detailed unfolding of events occurring in individual trials, and unresponsive to specific changes in the task that happen 'on-line'. Segmental responses are thus most likely to be anticipated by the 'internal models' that are used to organise the more flexible long-loop responses, and more flexible on-line corrections of movement. Adjustments of the fastest and purely segmental components of reflexes to better match them to repeated voluntary tasks and skills appear to only be accomplished on much longer time scales using long term plasticity mechanisms outlined in the next section.

Spinal plasticity and its local and descending modulation

It is now well established that in addition to the strongly conserved structures in the spinal cord of mammals, there is also considerable plasticity. This plasticity arises locally in the spinal cord and is also imposed through descending controls, even in mature individuals. These controls alter spinal mechanisms to better match persistent task demands and have the potential to radically alter the way the feedback systems of the spinal cord function after sufficient training. Seminal work on the H-reflex from Wolpaw and colleagues shows that the gains of the (electrical stimulation elicited) H-reflex can be voluntarily conditioned and altered up and down on long time scales.[30] These types of changes are likely to contribute to adjusting the segmental motor reflex gains optimally for frequently used skills 'on average'. They involve a complex of descending controls and intrinsic spinal plastic adjustments in response to these inputs.[30] As a concrete example, Hultborn and colleagues showed that professional dancers in the Royal Danish Ballet had a significantly diminished Achilles H-reflex compared to other well-trained athletes and control subjects.[25] Thus, although momentary flexible adjustment of rapid low-level segmental reflexes to task context may not be routinely possible, long-term adjustments of rapid low-level segmental reflexes in response to repeated practice of skilled activities are likely to happen under control of descending systems.

The spinal cord itself also shows plasticity in isolation, and this is seen for both protective reflexes and pattern generation. Nociceptive reflex thresholds and protective reflex execution speeds can be altered in the isolated spinal cord with repeat practice in both lower tetrapods and mammals. Perhaps more interestingly, the pattern generators for locomotion, though surgically isolated from the brain in cats and rats, can gradually improve weight bearing, and recover quite detailed and normal appearing kinematics following repetitive (mass) training.[7,27] These data suggest the spinal cord itself may have specifically embedded objectives for its intrinsic plasticity [and see reference 10]. These could potentially be exploited in post-injury therapies. Recent efforts along these lines are very promising. Use of combined training and epidural stimulation after SCI can lead to significant improvements.[7,8,14] Further, coordinated plastic changes in both cortex and spinal cord can be promoted using therapies with appropriate stimulation regimes.[21,22] However, independent spinal plastic changes operating out of the context of descending controls might also sometimes conflict with functional needs and contribute to pathology. It will be essential to manage spinal plasticity carefully, in order to successfully coordinate it with descending plasticity, so as to promote appropriate functional changes through a rehabilitative scheme.[1,8,22,30]

Conclusions

Spinal mechanisms form the fundamental foundations for motor development and skill formation. The spinal circuitry and intrinsic behaviours cannot be ignored by the brain in developing motor skills or managing a developing pathology. Structure in the spinal cord supports a range of protective and movement generating mechanisms, with potential building blocks for movement and control. These are seen in newborn human movements as well as pathologies. However, despite considerable advances in understanding the spinal cord since the time of Sherrington, the relationships of such intrinsic spinal segmental mechanisms to adult skill development and recovery of function after injury remain controversial. It is likely that the newborn's motor infrastructure may bootstrap subsequent skill development and be subsumed into these skills through ontogeny. However, to the extent such infrastructure is simply suppressed or bypassed in adult behaviour, it also has the potential to emerge and run covert or overt interference in motor control when this occurs in the context of pathology or injury. ◆

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