

# Correction of the Spinal Generator Work

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## Abstract

The study of the spinal cord is an important field of activity in neurology and neurobiology. Its functional activity is necessary for the normal functioning of a living organism. This article presents data on the work of nerve impulse generators in the spinal cord.

**Keywords:** spinal cord, neurons, nerve impulse generator

## Peripheral Feedback

Neurons of segmental reflex arcs of the spinal cord are interneurons of the generator of spinal reflexes. It is obvious that with such organization of afferent inputs, a change in the state of the generator is accompanied by a corresponding change in segmental reflexes. In turn, the afferent impulses coming from the moving limbs should influence the work of both the interneurons of the generator and the motor neurons.

Tonic restructuring of segmental reflexes. In acute experiments, the introduction of dopamine (DOFA) or 5-hydroxytryptophan (5-HTP) in spinal cats results in the inhibition of short-latency effects of stimulation of afferent fibers (AFR). The excitatory and inhibitory actions of the AFR on motoneurons and on neurons of ascending tracts are suppressed, as well as the conduction from the AFR to the terminals of primary afferents; in other words, the posterior root potentials caused by the stimulation of the AFR are reduced. However, alongside the reduction of early responses from motoneurons, the spinal centers acquire the ability to generate prolonged late discharges in efferent nerves. In response to stimulation of ipsilateral AFR, late activity with a hidden period of about 200 ms and a duration ranging from several hundred milliseconds to several seconds appears in the flexor nerves. Typically, there are late discharges in contralateral extensor nerves simultaneously with the late activity in ipsilateral flexor nerves. However, this organization of late discharges is not always observed. Sometimes, in response to irritation of the AFR, late discharges occur in both ipsilateral and contralateral flexor nerves. The appearance of late discharges is accompanied by a late wave of depolarization in primary afferents, primarily affecting the terminals of type 1a fibers. The only difference in the actions of DOFA and 5-HTP is that the latter, in addition to the effects described above, exerts an excitatory influence on both flexor and extensor motoneurons. In this case, there is an increase in the monosynaptic reflex, and a background discharge in the ventral roots is often observed. There are grounds to believe that similar tonic changes in segmental reflexes occur with

descending activation of spinal locomotor centers. In immobilized mesencephalic animals, stimulation of the mesencephalic locomotor region (MLR), which does not lead to the appearance of fictive locomotion, is accompanied by inhibition of short-latency inhibition of the testing monosynaptic reflex from the ankle extensor nerves during conditioning stimulation of cutaneous or high-threshold muscle afferents. Stimulation of the MLR also facilitates the appearance of late discharges in motor nerves in response to stimulation of the AFR. In thalamic immobilized animals capable of fictive locomotion, the early excitatory action of the AFR on motoneurons is reduced in the resting period compared to spinal animals, and in response to AFR stimulation, late long-lasting discharges appear in the motor nerves. The latter may transition into rhythmic patterns.

The reason for this tonic inhibition of short-latency effects of AFR stimulation is currently unclear. There are two pathways that facilitate transmission from the AFR to motoneurons. The first pathway is short-latency, and the second is long-latency. The latter is responsible for late activation of motoneurons and is inhibited by the short-latency pathway. Descending inhibitory noradrenergic terminals end on the neurons conducting short-latency transmission. The introduction of dopamine (DOFA), by increasing the release of norepinephrine from these terminals, leads to inhibition of conduction along the short-latency pathway and, due to disinhibition, facilitates the emergence of late discharges in response to AFR stimulation.

The previous discussion focused on the state of segmental reflexes in animals (thalamic, mesencephalic, or spinal) that are capable of locomotion but are at rest. At the same time, it is reasonable to assume that the transition of the generator into a mode of rhythmic activity may be accompanied by additional tonic changes in segmental reflexes. In studies conducted on immobilized decerebrated cats, it was found that the appearance of fictive locomotion is accompanied by tonic amplification

(compared to rest) of many evoked segmental reactions, which is largely explained by sustained hyperpolarization of the terminals of primary afferents. Thus, these data suggest that the activation of the locomotor generator is accompanied by a kind of opening to afferent signals.

**Phase-dependent reflexes.** During locomotion in chronic spinal cats, tactile or electrical stimulation of the dorsal surface of the paw produces various short-latency responses depending on the phase of locomotion. In the swing phase, such stimulation is accompanied by short-latency activation of all flexor muscles of that limb. In the contralateral limb, there is an enhancement of extensor activity. In the stance phase, the same stimulation elicits short-latency activation of extensor muscles. The reflex reversal point coincides with the transition from one phase of locomotion to another.

A similar pattern of phase dependence of reflexes induced by electrical stimulation of skin fibers has been observed during fictive locomotion in decerebrated and spinal cats. Judging by the responses in the motor nerves, the reflexive action of cutaneous afferents on flexor or extensor motoneurons is maximal during their respective activity. Intracellular recordings from motoneurons during fictive locomotion in immobilized spinal cats have shown that the amplitude of the local postsynaptic potentials (PSPs) evoked by weak electrical stimulation of the dorsal surface of the paw or direct stimulation of skin nerve fibers depends on the phase of the "step cycle." In flexor motoneurons, the PSPs are significantly larger in amplitude during the flexion phase. In the motor neurons of the extensors, the amplitude of the PSPs is higher during extensor activity.

The fact that the same stimulus during the flexion phase produces a reflexive response in the flexor nerve, while during the extension phase it produces a response in the extensor nerve (reflex reversal), appears to be related to the ability of the same afferent signal to reach both the flexor and extensor half-centers. In this case, during the operation of the generator, the conduction of afferent impulses through the active half-center to motoneurons will be facilitated, while through the inhibited half-center it will be suppressed.

It can also be assumed that at a low level of spinal generator activity, when fictive locomotion is not yet observed, there is an absence of dominance of one half-center over another. It is likely that there is an enhancement of both mutual inhibition between the half-centers and cross-inhibition of motoneurons, which may be related to the previously described tonic inhibition of early segmental reflexes that occurs in the resting state. In this case, the same inter- neurons of the half-center and the corresponding motoneurons, upon receiving afferent impulses, would experience not only excitatory but also inhibitory influences from the neurons of the other half-center, which are activated by the same afferent source; consequently, the resulting early reflex response would be reduced in amplitude. Clearly, with such a mechanism in place, there is no need to postulate a short-latency pathway from the AFR to the motoneurons that is inhibited by descending monoaminergic systems.

The reflexive action of 1a afferents also depends on the phase of locomotion. During fictive locomotion in spinal cats, the amplitude of monosynaptic local postsynaptic potentials (PSPs) was found to be higher during the depolarization wave in the motoneuron. In addition to the increased amplitude of monosynaptic PSPs in the motoneuron during its activity in response to stimulation of group 1a fibers, polysynaptic PSPs are also observed, which disappear during hyperpolarization of the motoneuron. It can be assumed that this dependence of the amplitude of monosynaptic PSPs is related to their reduction during hyperpolarization of the motoneuron, as it has been established that the latter acts as an inhibitory postsynaptic potential.

When analyzing the phase dependence of reflexes, it is essential to consider not only the organization of afferent inputs and the state of postsynaptic neurons in relation to them but also the condition of the central terminals of afferent fibers. During the activity of the locomotor generator, alongside tonic changes towards hyperpolarization, the central terminals of afferents also experience phase-dependent changes in polarization. These changes manifest as periodic depolarization waves that occur in sync with the generator's rhythm and take place against a backdrop of sustained hyperpolarization. At moderate intensities of fictive locomotion, there is a gradual increase in depolarization at the afferent endings during the flexion phase, while in the extension phase, there is a gradual return to the baseline level. These tonic and phase-dependent changes occur in the central endings of both cutaneous and muscular afferents.

The described cyclic depolarization changes in primary afferents likely underlie certain features of the phase dependence of segmental reflexes. During fictive locomotion in decerebrated cats, the polysynaptic efferent discharge at the beginning of the flexion phase is higher than at the end, when there is a maximum negative wave of depolarization in the primary afferents. Conversely, parameters of the extension phase are most significantly altered when afferents are stimulated in the second half of that phase. This conclusion is further supported by data showing that during fictive locomotion in spinal animals (both in acute experiments following the administration of dopamine (DOFA) and in chronic experiments), the local postsynaptic potentials (PSPs) in the flexor motoneurons evoked by stimulation of the skin of the limb are higher at the beginning of the flexion phase. In the extensor motoneurons, similar stimulation results in PSPs composed of an early component followed by a subsequent late component. Notably, at the end of the extension phase, the late component of the PSP is greater than at its beginning.

Consequently, under natural conditions, via modulation of presynaptic inhibition, the spinal locomotor generator can actively perform tonic and phase-dependent selection of incoming afferent information.

Reflex control of the phase of the step cycle is integral to understanding locomotion. The duration of the step cycle is influenced by the speed of movement; specifically, as locomotion speed increases, the duration of the step cycle decreases. This reduction in duration primarily occurs due to a shortening of the stance phase, while the duration of the swing phase changes little with increasing locomotion speed. These findings suggest that the transition from the extension phase to the flexion phase of the limb is a critical point in the step cycle, and that signals from limb receptors play a significant role in facilitating this transition.

In spinal dogs, the swing phase can be initiated by proprioceptors located in the proximal part of the limb. A sharp passive extension of the hip induces the flexion phase, while the extension of other joints does not elicit such an effect. Subsequent research indicated that the position of the hip joint remains constant during the stance phase at various locomotion speeds. If the limb is held in the extension phase during locomotion, its rhythmic movements cease, whereas the other limbs continue to perform stepping movements. In the held limb, there is an increased activity of the extensors. By allowing the held limb to slowly extend at the hip joint while maintaining a specific position, a transition to the flexion phase can be observed. This effect is remarkably consistent and is independent of the angles at the knee and ankle joints, being solely determined by the angle at the hip joint. However, it remains unclear which signals from the hip receptors (muscle or joint receptors) are responsible for this switching mechanism.

Additionally, locomotor movements of the limb can also be interrupted by stretching the ankle extensors, which is accompanied by an increase in

the activity of the extensors. In this scenario, the flexion phase can only commence after the cessation of this stretching. This highlights the importance of both proprioceptive feedback and joint positions in the reflex control of locomotion phases, illustrating how intricate the regulatory mechanisms of stepping are in response to different positional and stretch stimuli.

Experiments with electrical stimulation have demonstrated that two types of afferent inputs—thick cutaneous fibers innervating the distal parts of the limb skin and, likely, tendon afferents of the extensors—are particularly effective in preventing the transition from the stance phase to the swing phase. Low-threshold stimulation of distal cutaneous nerves or direct stimulation of the plantar skin during the extension phase not only prolongs but also enhances this phase. Conversely, applying the same stimulus during the flexion phase results in its shortening and a faster transition to the extension phase. On the other hand, stimulation of thin afferent fibers leads to an elongation of flexor activity and a shortening of extensor activity when the stimulus is applied in the corresponding phase.

There are compelling reasons to suggest that the transition from the flexion phase to the extension phase is also determined by afferent information, as the position of the limb at the end of the swing phase does not depend on its position at the beginning.

Additionally, it is important to note that cyclic modulation of depolarization in the central terminals of primary afferents, as influenced by the locomotor generator, may play a significant role in the reflex control of the phase of the step cycle. Over a wide range of variations in the intensity and frequency of locomotion, this modulation occurs such that presynaptic inhibition is minimized precisely at the end of the extension phase and the beginning of the flexion phase. This indicates a finely tuned mechanism of reflex control that optimizes the transitions between different phases of the step cycle, ensuring smooth and coordinated locomotion.

**Facilitatory Reflexes.** The load on the muscles during locomotion depends on the speed of movement, the terrain, the phase of the step cycle, and many other factors. At the same time, for stable locomotion, it is necessary for these influences to be compensated. Unexpected changes in muscle load should not significantly affect the speed of its contraction, which is related to the speed of the animal's movement. Facilitatory reflexes perform this role. These reflexes cause the recruitment of new motoneurons that were previously inactive or slightly increase the firing frequency of already active motoneurons.

As partially mentioned above, during locomotion in thalamic and mesencephalic cats, resistance to limb extension is accompanied by an increase in the activity of extensor muscles. However, the receptors responsible for this facilitatory effect have not yet been definitively identified. The most likely candidates are muscle spindle receptors, as the blockade of conduction through gamma fibers is accompanied by a significant decrease in extensor activity during the stance phase. Although, as stated above, the activity of tendon receptors may also enhance the extensor phase.

Another well-known facilitatory reflex is the extensor thrust. Stimulation of the receptors on the plantar surface of the foot is associated with a strong increase in extensor activity. This effect is bilateral. This reflex is important during the gallop of the animal. During galloping and other fast movements, it seems that the factor compensating for the load is solely the elasticity of the muscles, as the central delay of reflexes is too great for peripheral feedback to compensate for changes in load.

After the crossing of the nerves leading to the plantar surface of the foot, no significant changes in gait were observed. Minor disturbances in foot

positioning during locomotion were attributed to denervation of the foot muscles. These reflexes are not essential for locomotion; they merely enhance the activity of the extensors. When studying the activity of extensors during locomotion before and after anesthesia of the foot, no differences were found.

**Position-Dependent Reflexes.** In acute spinal cats, after the administration of DOPA or clonidine, noxious stimulation of the skin or electrical stimulation of cutaneous and high-threshold muscle afferents induces late prolonged activity in the ipsilateral flexor muscles. On the contralateral side, depending on the position of the limb, similar activity is observed either in the flexor or extensor muscles. If the contralateral limb is positioned to effectively support body weight (such as when it is on the ground or flexed), such stimulation activates the extensors. Conversely, if the limb is in a position that does not support weight effectively (for example, at the end of the extension phase when the limb is fully extended and pulled back), it flexes and then extends again.

Selective deafferentation of the hip joint does not change the response pattern. The response pattern remains unchanged even after denervation or cutting of the tendons of a number of hind limb muscles. However, after deafferentation of the contralateral hind limb from the fourth lumbar to the first sacral segment, only the crossed extensor reflex is elicited in response to stimulation. A similar pattern is observed after cutting only the seventh contralateral dorsal root. With intact afferentation of the contralateral limb, strong stretching of the ankle flexors is sufficient to inhibit responses in the extensors, despite all joints being in a flexed position. After cutting the tendons of the ankle and knee flexors, extension of the limb inhibits the crossed extensor reflex.

Thus, the signals coming from many flexor muscles of the limb determine the type of crossed response. It is likely that the stretching of the flexor muscles is associated with an increase in activity of the flexor half-center and the corresponding motoneurons, which underlies the inhibition of the crossed extensor reflex. It should be noted that the described reversal of responses is sometimes observed with stimulation of ipsilateral afferents.

**Other Complex Reflexes.** In chronic spinal cats, a phenomenon known as the placing reaction has been observed. Tactile or electrical stimulation of the dorsal surface of the foot causes the limb to flex, followed by extension and placement on the ground in a position more rostral than its original placement. A similar reaction can be seen when a chronic spinal cat locomotes on a treadmill. However, as noted earlier, the nature of the response during locomotion depends on the phase of the step cycle. The response to stimulation disappears after anesthesia of the skin in that area. It is evident that the physiological significance of the placing reaction lies in stepping over obstacles while the animal is moving.

Chronic spinal cats are also capable of maintaining balance. If the center of gravity shifts to one side, the limb that experiences increased load flexes and is then positioned more laterally.

In acute experiments with unilateral tetanic stimulation of the afferent fibers in spinal cats treated with DOPA, a very complex structure of rhythmic discharge can be observed in the motor nerves. Immediately after the onset of stimulation, the rhythmic organization appears as if the animal is trying to shake off the stimulus. Rhythmic discharges are seen on the side of stimulation, while the opposite limb displays tonic activity in the extensor nerves. Subsequently, the animal seems to "run away" from the stimulus. Rhythmic discharges are observed in the nerves of both hind limbs and are organized in a synchronous pattern. Hence, even in the absence of phase-dependent peripheral input, spinal centers, under the influence of tonic afferent input, can, in a sense, program a behavioral response.

Activity of Limb Receptors during Locomotion and Their Physiological Role. It has been shown that during locomotion in thalamic and mesencephalic cats, primary and secondary endings of muscle spindles are activated during the contraction of the corresponding muscles. More vigorous locomotion corresponds to stronger activation of the receptors. This activation is based on  $\alpha$ - $\gamma$ -coactivation. Although spindle receptor activity has been detected during the phase of passive stretch in mesencephalic cats, the prevailing view in the literature is that during this phase, spindle receptors, if activated, do so to a lesser extent compared to the phase of active contraction.

In addition to spindle receptors, the activity of Golgi tendon receptors has also been studied during the induced locomotion of mesencephalic cats. Similar to spindle receptors, they are activated during muscle contraction. The behavior of other limb receptors during locomotion in both thalamic and mesencephalic animals has not been extensively investigated.

In recent years, several researchers have reported data on the activity of various limb receptors during locomotion in freely moving intact animals. It was found that primary muscle endings are activated during both passive muscle stretching and active muscle contraction, with some primary endings being more vigorously activated during passive stretching. There are also primary endings that discharge with a higher frequency during active muscle contraction. Typically, there is a pause in the activity of primary endings during the peak contraction velocity of the muscle. The greatest variability in responses from cycle to cycle is observed during muscle contraction.

The secondary endings of muscle spindles during locomotion in intact animals exhibit similar activity patterns as the primary endings. The only difference between the activity of primary and secondary endings is that the latter can discharge at greater frequencies.

Golgi tendon receptors during locomotion in intact animals show activity that correlates well with the work of the corresponding muscles. These receptors are primarily activated during muscle contraction, although a slight amount of activity is also observed during passive muscle stretching.

The responses of joint receptors during locomotion in intact animals are highly variable and depend complexly on the angle of the joint. Their responses are likely affected by the load on the joint, the tension of the joint capsule from the muscles, and various other factors.

During natural locomotion, hair follicle receptors typically exhibit activity that correlates strongly with limb movements, even when their receptive fields do not contact surrounding objects. In contrast, light touch receptors are only activated when their receptive fields come into contact with external objects.

The described pattern of activity in primary endings may underlie the facilitation of reflexes, as it is during the phase of active muscle contraction that the reflexive influence of Ia-afferents on motoneurons is enhanced. Furthermore, during locomotion, Ia interneurons are activated in phase with the motoneurons of the muscle from which they receive afferent input. Clearly, the increase in activity of Ia interneurons due to the impulses received from primary endings will be accompanied by enhanced reciprocal inhibition, which could lead to changes in the phase of the step cycle. Considering the phases of activation of the respective motoneurons and Ia interneurons, it is reasonable to conclude that during locomotion, the influence of input from primary endings during passive muscle stretching will be reduced. Nevertheless, this input may still play a role. For instance, it appears that the incoming impulses from flexor muscles may be correlated with the spatial dependence of reflexes described above.

There are some controversies regarding the role of Golgi tendon receptors during locomotion. The impulses received from these receptors enhance the activity of the corresponding motoneurons. Golgi tendon receptors are primarily responsible for causing flexion at the very beginning of the support phase during locomotion due to autogenic inhibition of the synergistic muscles. The occurrence of flexion is triggered by the contact of the limb with the surface, which is accompanied by the elongation of the contracting extensor muscles.

The physiological significance of the information conveyed by secondary endings and high-threshold muscle fibers, alongside the role of joint and skin receptors during locomotion, remains somewhat unclear. The nature of afferent inputs regarding to neurons in half-centers, it can be inferred that high-threshold muscle and cutaneous fibers primarily exert an excitatory influence on the interneurons of the flexor half-center. Conversely, low-threshold cutaneous afferents mainly exert an excitatory effect on the interneurons of the extensor half-center. This is further supported by findings from electrical stimulation of various nerves during locomotion.

When assessing the role of afferentation in locomotion, it is essential to consider not only the organization of afferent inputs, the state of segmental neurons, and the central endings of afferents but also the fact that there will be complex interactions at the entry points to the spinal cord. These interactions entail depolarization of the central terminals of primary afferents, which may originate from both peripheral and central sources. Action potentials generated in central terminals under the influence of depolarization may also play an important role in shaping the incoming afferent information. These impulses, traveling antidromically, can block the transmission of impulses from receptors to the spinal cord at sufficiently high frequencies due to the phenomenon of collision.

### **Fast-Conducting Descending Systems**

Numerous studies have shown that impulses transmitted through fast-conducting descending systems (corticospinal, rubrospinal, reticulospinal, and vestibulospinal) have a powerful impact on the activity of specific groups of interneurons and motoneurons in the spinal cord. There is also reason to believe that some spinal interneurons involved in the generation of locomotor rhythmicity are activated by these descending systems. Indeed, the areas where these descending pathways terminate partially overlap with the zones containing interneurons that are rhythmically active during locomotion.

Irritation of the ipsilateral lateral and ventral funiculi elicited monosynaptic focal potentials in regions where interneurons that activated during late discharges were located. Some of these neurons were excited monosynaptically by descending bursts. Thus, the impulses transmitted along the fibers of fast-conducting descending systems influence the activity of at least some spinal interneurons and motoneurons involved in generating locomotor rhythmicity, and therefore may modify the fundamental locomotor program established by spinal centers.

The activity of rubrospinal, reticulospinal, and vestibulospinal neurons, whose axons reach the lumbar region of the spinal cord, has been investigated during locomotion in thalamic and mesencephalic cats. The movements of the hind limb were correlated with the activity of ipsilateral reticulospinal and vestibulospinal neurons and contralateral rubrospinal neurons. The activity of vestibulospinal neurons from the Deiters nucleus was specifically studied. The impulse activity of reticulospinal neurons was recorded from medial areas of the pons and medulla oblongata.

Most neurons in these three descending systems exhibited background activity at rest. The onset of locomotion (whether spontaneous or induced)

was usually accompanied by a significant increase in the firing rate of the neurons. Additionally, the activity of most cells showed clear modulation in rhythm with the movement of the hind limb. These modulating neurons could reach maximum activity during different phases of the step cycle. Most vestibulospinal neurons were active at the beginning of the stance phase, while most rubrospinal and reticulospinal neurons exhibited maximum activity during the swing phase.

Experiments involving electrical stimulation of various descending systems during locomotion demonstrated that while the effects of stimulating a particular descending structure are determined by its organization, they are significantly dependent on the phase of the step cycle. Indeed, it is well known that stimulation of the lateral vestibular nucleus has an excitatory effect on extensor motoneurons, whereas stimulation of the medial reticular formation, red nucleus, and pyramidal tract excites flexor motoneurons and inhibits extensors. Similar effects are observed when stimulating these structures in the absence of locomotion in mesencephalic and thalamic cats. However, during locomotion, stimulation of the Deiters nucleus with a short series of stimuli enhances extensor activity only in the phase of the step in which they are active. In the absence of extensor activity, the same series of stimuli has no effect. The pyramidal tract, red nucleus, and medial reticular formation, in turn, only enhance flexor activity during their active phase.

It is important to note that stimulation of descending systems, despite its powerful influence on motoneuron activity, does not change the duration of the stance and swing phases. The frequency of locomotion is altered only with very strong stimulation of the descending structures.

These results indicate that during locomotion in mesencephalic cats, the maximum activity of a particular descending system coincides with the activity of the muscles it excites, and at this time, the excitatory effect is at its peak.

During spontaneous fictive locomotion in decorticated cats, modulation of the activity of neurons in the reticular formation, lateral vestibular nucleus, and red nucleus was also observed. Among the neurons in the reticular formation, whose axons reached the lumbar region of the spinal cord, some showed varying degrees of correlation with efferent discharges in the nerves of the hind limbs. Some neurons increased their activity during discharges in flexor nerves, while the responses of others displayed the opposite behavior. Often, different types of "binding" to efferent discharges were observed in neighboring neurons. The tonic activity of reticulospinal neurons also depended on the presence or absence of fictive locomotion. Some neurons increased their activity while others decreased it during fictive locomotion. The spontaneous activity of red nucleus neurons typically increased during fictive locomotion. All cells were rhythmically active during this state, and in this context, the emergence of a discharge in the flexor nerve was generally accompanied by a decrease in the frequency of impulse activity of the neuron. In actual spontaneous locomotion of decorticated cats, red nucleus neurons behaved similarly to those in immobilized animals. It is also noteworthy that the response of a neuron could predict the onset of fictive locomotion.

An obvious question arises: is periodic activity in the descending systems the source of locomotor rhythmicity, and if not, what modulates their activity? Based on the literature, it seems more likely that the modulation of the activity of the descending systems is secondary and has a spinal origin. Indeed, locomotion can be observed in spinal animals. The delay in the stepping limbs of a mesencephalic cat halts the modulation of activity in the descending pathways. As demonstrated in decorticated cats, red nucleus neurons are inhibited during the flexion phase, indicating that this pathway does not trigger discharges in the flexor nerve. Additionally,

distinct fictive locomotion can be observed in immobilized decorticated cats, while periodic activity in the descending pathways is not detected.

In thalamic and mesencephalic cats, removal of the cerebellum leads to almost complete disappearance of the modulation of rubro-, reticulo-, and vestibulospinal neuron activity in rhythm with locomotor movements. After cerebellectomy, during locomotion, neurons in these descending systems only tonically increase or decrease their impulse activity. The removal of the cerebellum is also associated with changes in the background activity of neurons in these tracts. For instance, neurons in the Deiters nucleus increase their activity, while reticulospinal and rubrospinal neurons decrease their activity, which is likely related to the increased activity of extensor muscles following cerebellectomy.

The activity of neurons in the projection zone of the hind limb cortex of the cerebellum and its nuclei was studied both during locomotion in thalamic and mesencephalic cats on a treadmill and during fictive locomotion in decorticated animals. It was shown that some of the investigated neurons exhibit distinct modulation of activity in rhythm with locomotor movements or rhythmic discharges in the efferent nerves.

The source of modulation of the activity of cerebellar neurons appears to be cyclic ascending influences. These influences reach the cerebellum via fibers of various spinal-cerebellar tracts. Neurons in the dorsal spinocerebellar tract (DSCT) transmit signals to the cerebellum regarding the characteristics of limb movements during locomotion. Following deafferentation, the cyclic activity of neurons in this tract disappears. In contrast, the periodic activity of neurons in the ventral spinocerebellar tract (VSCT) during locomotion in mesencephalic cats on a treadmill does not disappear after deafferentation of the hind limbs. Although the possibility of incoming phase-related afferent impulses from the moving forelimbs via long propriospinal descending pathways to the VSCT neurons was not excluded, these results led to the conclusion that the neurons in the VSCT convey information to the cerebellum not only about limb movements but also about the state of spinal neurons. This conclusion was supported by results obtained during fictive locomotion in decorticated cats. In the excised dorsal and dorsolateral funiculi, cyclic activity was not observed during fictive locomotion. In contrast, clear periodic impulses were present in the fibers of the ventrolateral funiculus, where fibers of the VSCT course.

It is known that afferent impulses reach the cerebellum not only through the fibers of the ventral and dorsal spinocerebellar tracts but also via the spinoreticulocerebellar and spino-olivocerebellar tracts. During fictive locomotion in decorticated cats, there was a distinct modulation of ascending activity in rhythm with the efferent discharges in the excised ventral funiculus, which lacks direct spinocerebellar fibers. The modulation of descending impulses, which partially occurs after cerebellectomy during both locomotion in thalamic and mesencephalic cats on a treadmill and during fictive locomotion in decorticated animals, is likely related to the activity of indirect spinocerebellar and other ascending pathways. However, it is unknown which brainstem structures are responsible for such modulation in the absence of the cerebellum.

Although current understanding of the processes occurring in the cerebellum during locomotion is largely speculative, it is reasonable to believe that the disconnection of the cerebellum and the reduction of phase-dependent corrective activity in the descending systems underlie the disruption of coordination in locomotor movements of the limbs in animals following cerebellectomy. Partial disruption of coordination may be associated with increased extensor tone after the removal of the cerebellum.

During locomotion in thalamic and mesencephalic cats, the responses of rubrospinal, reticulospinal, and vestibulospinal neurons to stimulation of vestibular receptors in the labyrinth (animal tilts in the frontal plane) are suppressed. After cerebellectomy, the dynamic component of the response of Deiters' nucleus neurons to vestibular stimulation disappears, leaving only a static reaction, which is also suppressed during locomotion. These results indicate a partial disconnection of the vestibular system during locomotion. This is likely related to the impracticality of reflexive reactions to all head displacements occurring during animal locomotion. Moreover during locomotion, spinal centers partially take over the function of maintaining balance.

### Inter-Segmental Coordination

Cats, like many other quadrupedal animals, exhibit two main types of gaits during natural locomotion: alternating and synchronous. In the alternating type (e.g., pacing, walking, trotting), the corresponding limbs (hind and fore) operate in an out-of-phase manner. The synchronous type (various forms of galloping) is characterized by the synchronous movement of the hind limbs (and sometimes the forelimbs).

Detailed studies conducted on decerebrated and intact cats have shown that, despite the diversity of gaits, there are only two programs of interaction realized between homologous (limbs of the same body region) and homolateral (front and hind limbs on the same side) limbs — the out-of-phase and in-phase programs. In the out-of-phase program, flexion of one limb corresponds to the extension of another. In the in-phase program, both limbs operate in the same manner (either flexing or extending). The transition from one type of limb coupling to another occurs suddenly within one or two stride cycles.

It has been suggested that the various types of gaits are based on corresponding combinations of interaction programs from the generators of homologous and homolateral limbs. In alternating locomotion (pacing, walking, trotting), homologous limbs work out of phase. Homolateral limbs may interact according to either the out-of-phase or in-phase program. In the first case, either pacing or trotting occurs; in the second case, it is a lateral walk.

During synchronous locomotion, the movements of the hind limbs, and to a lesser extent the forelimbs, occur in phase. In some types of galloping (transverse, rotational, semi-pair), and sometimes during jumps, the coupling of movements of homolateral limbs is asymmetric. On one side, it follows the in-phase program, while on the other side, it follows the out-of-phase program. In paired galloping and typically during jumps, the homolateral interaction is symmetric and occurs according to the out-of-phase program.

Gaits in which the interaction of homolateral limbs is symmetrical are characterized by a more pronounced synchronization of limb movements. This is likely explained by the fact that, in these cases, the interaction programs of homologous and homolateral limbs reinforce each other. This is particularly evident during lateral walking, walking, and trotting. In contrast, asymmetric types of synchronous gaits (transverse, rotational, and semi-pair gallops) are characterized by less clear synchronization of the limbs, which is likely due to the competition between the interaction programs of homologous and homolateral limbs.

There is sufficient reason to believe that the implementation of the interaction programs of homologous and homolateral limbs occurs at the spinal cord level. In high-spinal cats, coordinated movements of all four limbs can be observed after the administration of dopamine (DOPA). In this case, the same types of coupling between homologous and homolateral limbs are observed as in decerebrated and intact animals. During fictive locomotion in spinal cats (in the absence of cyclic afferent

impulses), the rhythmic discharges in the motor nerves of the hind limbs are well-coordinated. Further research has shown that during fictive locomotion, just as in real locomotion, only two interaction programs are possible between the centers of the hind limbs—alternating and synchronous. The type of interaction is determined by the activity of flexor half-centers. At low levels of activation, the flexor half-centers operate out of phase. However, an increase in the level of activation is accompanied by a transition to a synchronous interaction program between the flexor half-centers. The extensor half-centers usually do not define the type of interaction. The synchronization of the extensor half-centers occurs secondarily through alternating interaction with the homolateral flexor half-center. The activity of the extensor half-centers of both limbs can partially overlap in time during alternating fictive locomotion.

The nature of the interaction between the hind limbs has a specific physiological significance. During the animal's standing position, the extensor centers on both sides are usually active. Simultaneous activity of the extensor half-centers of the limbs on one side is necessary to maintain balance during slow walking, as the flexion of one limb should only begin after the other limb of the same side has been placed on the ground. For this purpose, the mechanism of interaction between the limbs of one side must allow for simultaneous bilateral activity of the extensor half-centers. Conversely, the flexor half-centers should not be activated simultaneously during slow locomotion, as this would lead to a loss of balance; they must operate out of phase.

The mechanism of interaction among the spinal generators of the hind limbs can be described as follows. The flexor half-centers of both limbs exert both inhibitory and excitatory influences on each other. At low activation levels, inhibitory influences prevail, resulting in alternating rhythmic patterns. However, at high activation levels, mutual excitatory influences predominate, leading to synchronous rhythmic patterns. It is likely that the extensor half-centers exert only excitatory influences on each other. However, this influence is weak at low activation levels of the spinal locomotor centers. Strong activation of the spinal locomotor centers significantly enhances this mutual excitatory influence. In this case, the synchronous type of limb interaction can be determined by the activity of the extensor half-centers. Indeed, after the administration of DOPA to decerebrated and spinal animals, synchronous rhythmic patterns are defined by the activity of the extensor half-centers. DOPA is known to enhance firing in extensor nerves while reducing the amplitude of discharge in flexor nerves, thus exerting a preferential excitatory effect on the extensor half-centers.

As of now, the central mechanisms of interaction of the forelimbs during locomotion have not been studied. However, it can be inferred that they are analogous to the mechanisms of interaction in the locomotor centers of the hind limbs. The movements of the forelimbs during locomotion also occur either out of phase or in phase. In decerebrated rabbits with additional spinalization at the thoracic segments, fictive locomotion of the forelimbs can be observed, organized in either synchronous or alternating types. Research shows that during induced locomotion, the centers of the forelimbs and hind limbs are not equal. In mesencephalic cats, during treadmill locomotion, the hind limbs typically initiate walking, with the forelimbs joining after several stride cycles. Spontaneous locomotion in mesencephalic cats is not observed. However, after additional spinalization in the thoracic segments, the forelimbs spontaneously move along the treadmill.

It is likely that when connections between the centers of the forelimbs and hind limbs are intact, the latter dominate; they possess a greater degree of automatism and tonically inhibit the centers of the forelimbs in the

absence of locomotion. This tonic inhibition decreases with the activation of the locomotor centers of the hind limbs. This perspective is also supported by the fact that when the forelimbs are not in contact with the treadmill, they do not perform stepping movements, while the hind limbs walk on the treadmill. On the other hand, when the hind limbs are suspended, they perform stepping movements if the forelimbs are walking on the treadmill. Finally, in high-spinal cats, after the administration of DOPA, the locomotor movements of the forelimbs are not always well coordinated, despite the well-coordinated movements of the hind limbs.

It appears that the coordination of the forelimbs and hind limbs during locomotion involves long descending and ascending propriospinal pathways. However, there is currently a lack of data regarding the activity of neurons in these pathways during locomotion. Literature only indirectly allows us to assess their role in locomotion. Long propriospinal reflexes are facilitated upon activation of spinal locomotor centers. Facilitation of ascending polysynaptic reflexes has been observed in curarized mesencephalic cats during stimulation of the medial longitudinal fasciculus (MLF) and in high-spinal cats following the administration of DOPA.

In addition to tonic facilitation, long propriospinal reflexes are phase-dependent during locomotion. Stimulation of the forelimb nerves elicits excitatory postsynaptic potentials (EPSPs) in the motoneurons of the flexor muscles of the hind limbs during the flexion phase. During the extension phase, similar stimulation elicits EPSPs in the motoneurons of the extensors. Conversely, during the hyperpolarization phase, particularly in the motoneurons of the flexors, distinct inhibitory postsynaptic potentials (IPSPs) can be detected in response to stimulation.

The phase dependence of propriospinal reflexes is likely determined by the organization of long propriospinal reflex pathways. Stimulation of the forelimb nerves in the absence of locomotion typically results in mixed responses in the motoneurons of the hind limbs, which are not organized reciprocally. Mixed reactions without reciprocity are observed in lumbar motoneurons and during direct stimulation of long propriospinal ipsilateral fibers that traverse in the lateral and ventral funiculi. There is also some evidence to suggest that long ascending propriospinal reflexes are organized in a similar manner. It should also be noted that ipsilateral propriospinal reflexes are generally more powerful than contralateral ones.

Based on the above data, it can be hypothesized that through long propriospinal pathways, each half-center of the forelimb is connected to each half-center of the ipsilateral hind limb via both excitatory and inhibitory connections. In this case, mutual excitation is reinforced between the two active half-centers. Conversely, when the half-centers work out of phase, the inhibitory influence of the active half-center on the inactive one is enhanced. Such an organization of connections adequately explains the aforementioned phase dependence and the reversal of long propriospinal reflexes. The existence of such a mechanism may also account for the fact that in the interaction of homolateral centers, there are only two stable states, one of which realizes an alternating program and the other a synchronous program of interaction.

Peripheral feedback plays a significant role in interlimb coordination. This is particularly evident in locomotion of mesencephalic or spinal animals walking on a split treadmill. Despite the differences in the speeds of movement of both belts, the durations of the stepping cycles for the "fast" and "slow" limbs are equal. The distances covered by the "fast" and "slow" limbs from the moment of contact with the belt to the beginning of the swing phase are also the same. Equalization of stepping cycle durations occurs primarily through changes in the duration of the extension (E) phase. However, if the speeds of movement of the different

belts differ to such an extent that equalization of stepping cycle durations becomes impossible, the limb on the faster belt performs two stepping movements while the "slow" limb performs only one. In this case, the durations of the stepping cycles are not equal, with the "fast" limb completing one step during the swing phase and another during the stance phase of the "slow" limb.

This suggests that afferent information influences the duration of specific phases within the stepping cycle. Ultimately, the coordination of limb movements is achieved through interaction among the generators. Supporting this conclusion is the fact that fictive locomotion of different hind limbs can occur in a 1:2 rhythm.

It is evident that supraspinal structures play an important role in interlimb coordination, as they receive information about both the activity of the generators and the movements of different limbs. It is likely that the absence of supraspinal coordinating influences accounts for the observation that in high-spinal cats, during locomotion after the administration of DOPA, well-coordinated movements of the forelimbs are not always evident.

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