HIGHLIGHTED TOPIC | Neural Control of Movement

Sensorimotor integration at spinal level as a basis for muscle coordination during voluntary movement in humans

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Nielsen, Jens Bo. Sensorimotor integration at spinal level as a basis for muscle coordination during voluntary movement in humans. J Appl Physiol 96: 1961–1967, 2004; 10.1152/japplphysiol.01073.2003.—Spinal reflexes have traditionally been treated as separate from voluntary movements. However, animal experiments since the 1950s and human experiments since the 1970s have documented that sensory activities in afferents from muscles, skin, and joints are integrated with descending motor commands at the level of common spinal interneurons. Two different roles of this sensorimotor integration at the spinal level may be discerned. First, sensory feedback evoked by the active muscles may help to drive the motoneurons. Second, external stimuli, such as sudden perturbations of a limb, may give rise to “error signals,” which are integrated into the ongoing motor activity and form the basis of corrective responses. When interpreting experimental data, it is important to consider these two different roles. Application of external stimuli may provide little information about how the spinal cord integrates sensory feedback evoked as part of ongoing movements. The complexity of the spinal machinery that is activated by external stimuli also makes the interpretation of data obtained from experiments dealing with artificial external stimuli, such as electrical stimuli, difficult. Nevertheless, such experiments have provided and will continue to provide very valuable information about how the brain and spinal cord ensure coordination of muscle activity during voluntary movement. So far, spinal control mechanisms have only been investigated to a limited extent in relation to sports and occupational activities. Provided that researchers consider the methodological problems of the techniques and that they seek independent validation of the findings, this may be a very fruitful research field in the future.

central motor commands; sensory afferents; applied motor control; spinal cord

I do not intend to provide a comprehensive review of the field but rather to discuss some issues that I find fundamental for understanding the way that the spinal cord machinery is used by the brain to control movement. I will make three different points in the paper. 1) There has been a lot of discussion on the functional role of reflexes over the years, but reflexes are usually not evoked in isolation during normal conditions in human subjects. The sensory feedback and the activity in the spinal pathways evoked by this activity are rather an integrated part of the central motor command reaching the muscles during voluntary movements. 2) The often-used distinction between open-loop control (without sensory feedback) and closed-loop control (with sensory feedback) is artificial. Sensory feedback and lack of sensory feedback are both important sources of information for the brain and spinal cord; in predicted, unperturbed movements, both are integrated parts of the central motor command to the muscle. When perturbations occur, increased and decreased sensory feedbacks act as valuable error signals to the brain. 3) If we are to understand the fundamental principles of sensorimotor interaction at a spinal level and the significance of this interaction for the execution of functional motor tasks, we need to perform more experiments, combining electrophysiological evaluation
of the transmission in identified spinal pathways with precise biomechanical and kinematic analyses of the exerted movements.

STUDYING THE ROLE OF SPINAL INTERNEURONS IN THE CONTROL OF MOVEMENT

Around 50 years of experimental animal research have resulted in a detailed account of the complex organization of the cat lumbar spinal cord (1, 19a). Although this research has been very powerful in identifying and characterizing the interneuronal populations in terms of their input and output organization, it has been far less powerful in demonstrating the functional role of the interneuronal populations in relation to movements. This is an inherent consequence of the experimental approach, which usually requires the animal to be either anesthetized or decerebrated. In only a few studies have direct recordings of the activity of the spinal interneurons been attempted in relation to actual motor behavior. This is partly because of the technical difficulties in obtaining stable recordings during movements and partly because of the difficulties in identifying the interneurons in the intact behaving animal. Recent chronic recordings of interneurons in the monkey cervical spinal cord (25, 36) have made an important step in the way that noninvasive techniques may be used to study the control of spinal interneuronal pathways during movement.

It was the demonstration of disynaptic reciprocal Ia inhibition in human subjects and its modulation during voluntary movement by Tanaka in 1974 (45) that stirred the interest of researchers and opened the field (although partly similar findings had been published earlier; see Refs. 22 and 28). Because the disynaptic reciprocal inhibitory pathway involves only a single interneuron and is highly characteristic by its reciprocal organization, it still represents the most ideal illustration of the way that noninvasive techniques may be used to study the control of spinal interneuronal pathways during movement. Figure 1 illustrates how disynaptic reciprocal inhibition may be demonstrated directly in the cat (A and B) and more indirectly by noninvasive techniques in human subjects (C and D). In the cat, it is possible to record simultaneously from the interneurons in the pathway and the motoneurons to which they project. When group Ia afferents are stimulated, disynaptic inhibition is produced in the motoneurons of its antagonists (Fig. 1B). The interneurons in the pathway may be identified by the monosynaptic excitatory postsynaptic potential produced by the Ia stimulation and the inhibitory postsynaptic potential (IPSP) produced in the target motoneurons by their discharge (Fig. 1B; in addition, the interneurons are also characterized by the existence of inhibition from Renshaw cells).

A similar direct demonstration of disynaptic reciprocal inhibition is naturally not possible in human subjects. However, in human subjects, the inhibition may be demonstrated as a decreased excitability of the spinal motoneurons shortly after the stimulation of the antagonist group Ia afferents. This is illustrated in Fig. 1, C and D. Stimulation of a peripheral nerve (e.g., the tibial nerve) will activate group Ia afferents, which have monosynaptic projections to the spinal motoneurons innervating the same muscle (e.g., the soleus muscle). The stimulation will therefore result in a reflex discharge, which may be recorded in the EMG from the muscle. This reflex is the so-called Hoffmann or H reflex (named after the German neurologist Poul Hoffmann, who described it in 1918), and its size is determined primarily by the amount of transmitter release from the Ia afferents and the excitability of the spinal motoneurons. If the excitability of the spinal motoneurons is therefore decreased by an IPSP elicited by activation of the reciprocal inhibitory pathway, this will be seen as a decrease in the size of the H reflex. In accordance with this, activation of the disynaptic reciprocal inhibitory pathway by stimulation of group Ia afferents from the ankle dorsiflexors depresses the soleus H reflex at a very short latency (Fig. 1C). Both the latency and the low threshold of the inhibition suggest that it is mediated by the reciprocal disynaptic group Ia inhibitory pathway.

Tanaka (45) demonstrated that the inhibition of the soleus H reflex from stimulation of the peroneal nerve became larger when the subjects voluntarily activated the ankle dorsiflexors muscles. In cat, monkey, and human subjects, descending motor pathways have been shown to project in parallel to the spinal motoneurons and the reciprocal Ia inhibitory interneurons projecting to the antagonist motoneurons (19, 20, 24, 35). The most straightforward explanation of Tanaka’s finding was that the transmission in the pathway was facilitated by the voluntary motor command to the ankle dorsiflexors through the parallel activation of spinal motoneurons and interneurons. Tanaka did not take into account that the sensitivity of the H reflex to inhibitory influences depends on its size (6, 7); therefore, much of the apparent increase of inhibition that he observed during dorsiflexion may be explained by the smaller reflexes in that situation compared with at rest (5, 6). Nevertheless, subsequent experiments have confirmed that disynaptic reciprocal inhibition to ankle plantar flexors is indeed increased in relation to at least the dynamic part of a voluntary ankle dorsiflexion (Fig. 2A) and that this is caused by supraspinal influences, since a similar facilitation of the transmission in the pathway may be seen when afferent feedback from the active dorsiflexor muscles is blocked by ischemia or injection of a local anesthetic (30, 34). Facilitation of transmission in the pathway may also be observed before the onset of movement (6). The reciprocal nature of this control has also been demonstrated by the decreased disynaptic reciprocal inhibition to ankle plantar flexors during activation of these muscles (Refs. 6 and 18; Fig. 2B) and opposite changes for the pathway from ankle plantar flexors to ankle dorsiflexors (6, 31). These findings and those of several other findings for other muscles (10) and other types of movements, including walking and bicycling (37, 41), have led to the present view on the control and functional significance of disynaptic Ia reciprocal inhibition (Fig. 3). During voluntary movement, disynaptic reciprocal inhibition of the antagonist muscles is increased to ensure that these remain silent during the movement and that no unwanted stretch reflex activity is evoked; disynaptic reciprocal inhibition onto the active muscle, however, is decreased to facilitate the activation of that muscle.
Although experiments in the cat had certainly pointed in the same direction, based on observations of the parallel sensory and supraspinal projections to spinal motoneurons and Ia inhibitory interneurons, these experiments were not able to make as conclusive a demonstration as for the human experiments. In fact, it is only after the publication of the initial human studies that experiments during fictive locomotion demonstrated that Ia inhibitory interneurons display similar alternating activity patterns, as suggested by human studies (40). In addition, several other pathways contribute to the inactivation of antagonistic muscles during movement (8). However, the disynaptic reciprocal Ia inhibition is the best-studied and best-understood mechanism.

During the past 20 years, numerous studies have used the same fundamental technique as described for disynaptic reciprocal inhibition to study the supraspinal control of transmission in other spinal pathways, including autogenic Ib inhibition (14), recurrent inhibition (38), group II pathways (27), and presynaptic inhibition (8, 17, 33). It is outside the scope of this mini-review to describe all the various interneuronal populations and pathways and discuss their functional significance in relation to voluntary movement. For more information about the various interneuronal populations, the reader may consult the review by Baldissera et al. (1) as well as the monographs by Rothwell (42) and Porter and Lemon (39).

**METHODOLOGICAL PROBLEMS**

The research described above has been followed by a continuous criticism of the techniques, leading to improvements and...
refinements of the existing techniques as well as the development of new supplementing techniques. The importance of maintaining a comparable control reflex size when comparing two different situations as illustrated by Tanaka’s findings (45) in relation to disynaptic reciprocal Ia inhibition during dorsiflexion is only one example of methodological problems that have been clarified and resulted in improved techniques. Other important methodological problems include the following: 1) activity in Ia afferents may lead to prolonged changes in the transmitter release from their synapses (postactivation depression), which may interfere with the determination of the size of both inhibitory and excitatory effects on the H reflex (9, 16); 2) the gain with which the H reflex recruits motoneurons may change during different tasks, which will also interfere with the determination of inhibitory and excitatory effects (21, 33); 3) the H reflex may not be fully monosynaptic but may be influenced to a varying extent by transmission in nonmonosynaptic pathways (2, 26), which may confound the interpretation of the data. All of these problems may be related to the fact that the H reflex measures the effect of activation of a pool of motoneurons. It is therefore generally recommended to confirm findings with the H reflex technique by an independent technique. One such technique is the poststimulus time histogram technique, which may be used to investigate the effect of activation of a spinal pathway on a single motoneuron. In this technique, the discharge probability of a single motor unit is recorded with and without activation of a specific pathway. Increases or decreases in the discharge probability of the unit at specific time lags after the activation of the pathway will then reflect excitatory or inhibitory influences on the motoneuron, and the size of these effects will reflect the transmission through the pathway. When comparing two different situations in which the motor unit is active, information about changes in the transmission in the pathway may thereby be obtained. If data obtained with the H reflex and poststimulus time histogram techniques point in the same direction, the conclusions may be reached on a much more solid ground than if only data from one of the techniques were obtained.

**SHOULD WE CALL IT SENSORY FEEDBACK CONTRIBUTION TO CONTROL OF MOVEMENT RATHER THAN REFLEXES?**

The functional role of each of the various populations of spinal interneurons is different, and their study generally tells us something new about sensorimotor interaction at the spinal level. General conclusions regarding the role of sensorimotor interaction at a spinal level are therefore difficult to make. In the following, I will, however, discuss some topics that are of general relevance for sensorimotor interaction at the spinal level.
Research in both animal and human subjects has shown that convergence between descending supraspinal input and sensory feedback on common spinal interneurons is a cornerstone in the central control of movement. Although the neuronal circuits in the spinal cord certainly may give rise to reflex activity following an adequate stimulus, it should be emphasized that this is not the normal function of the pathways during normal behavior in intact humans. The separation of “spinal reflexes” and “voluntary movement” in separate chapters in many textbooks (Fig. 4A) is not justified based on the present knowledge and understanding of the way that the spinal interneuronal network is organized and functions. It would be more adequate if emphasis was placed on how sensory feedback in specific spinal interneuronal pathways contributes to the activation of the muscles and to their inactivation, when this is required (Fig. 4B). The reflexes certainly have a specific function in primitive invertebrate animals; however, in more complex animals such as humans, it is not possible to discuss in a meaningful way the functional significance of a reflex without considering its integration with the supraspinal motor commands underlying voluntary movements.

SENSORY FEEDBACK CONTRIBUTION TO ONGOING MUSCLE ACTIVITY AND SENSORY FEEDBACK AS AN ERROR SIGNAL

It is important to make a distinction between the sensory activity that is evoked as part of a preprogrammed movement and the sensory activity that is evoked by a sudden, unexpected perturbation of the movement or activation of a sensory receptive field. In the former case, the sensory activity is anticipated by the central nervous system, and it is an essential integrated part of the central motor command reaching the muscles. In the latter case, the sensory activity is an error signal, informing the central nervous system that the movement was not performed according to the plan or that an obstacle was met. In reality, a completely clear distinction between these two modes of sensory feedback does not exist, since the sensory activity evoked during a movement probably never fully corresponds to that expected and therefore could be said also to contain some “error signal.” Such error signals probably help to update the brain and optimize the motor program during movements. Nevertheless, there is at least a quantitative difference between such small deviations from the expected feedback and the much larger deviations evoked by external stimuli.

SENSORY FEEDBACK MECHANISMS CONTRIBUTE TO THE ACTIVATION OF THE MUSCLES DURING ONGOING MOVEMENTS

The evidence that sensory feedback contributes significantly to the muscle activity during movement comes from studies in both the cat and human subjects (35a, 44). In the stance phase of walking, muscle spindle afferents and force-sensitive afferents discharge due to increased gamma drive and increased muscle load, respectively. If this sensory afferent feedback contributes to the activation of the muscles, a sudden drop in

Fig. 3. Parallel control of spinal motoneurons and corresponding Ia inhibitory interneurons. The separation of Ia afferents and descending supraspinal pathways project in parallel to spinal motoneurons and their corresponding Ia inhibitory interneurons. This makes the basis for the observations in Fig. 2. In relation to dorsiflexion, the Ia inhibitory interneurons projecting to soleus motoneurons are thus facilitated by collaterals from the descending projections to the tibialis anterior motoneurons. Conversely, in relation to planar flexion, the Ia inhibitory interneurons projecting to ankle dorsiflexor motoneurons are facilitated by collaterals of descending projections to plantar flexor motoneurons. Because these interneurons also project to the Ia inhibitory interneurons, which project in the opposite direction (i.e., from ankle dorsiflexors to plantar flexors), this explains the decrease of inhibition observed in relation to plantar flexion in Fig. 2.

Fig. 4. Two different views of the organization of reflexes and voluntary movements. In older literature and in many modern textbooks, reflexes and voluntary movements are treated as separate entities (A). In fact, as shown in Figs. 1 and 2, reflexes and voluntary movements are inseparable because sensory afferents and descending supraspinal pathways converge on the same interneurons (B). Rather than a discussion of the functional significance of reflexes, which is quite common in many publications, it is more reasonable to discuss the role of sensory modulation of the voluntary movements.
activity should result in a decrement in the EMG activity recorded from the active muscles. This was also what Sinkjær et al. (44) observed when the ankle plantar flexor muscles were suddenly unloaded in the middle of the stance phase. The unload was performed by a portable mechanical device, which could suddenly superimpose a plantar flexion movement on the ongoing ankle joint trajectory or prevent the ongoing dorsiflexion movement in the middle of stance. In both cases, a very clear drop in the EMG activity recorded from the soleus muscles was observed at a latency of ~60 ms after the onset of the unload. Control experiments with local anesthesia were performed to exclude that the observed drop in EMG activity could be caused by activation of afferents from the antagonist muscle, ankle joint afferents, or cutaneous afferents. The study by Sinkjær et al. thus demonstrated that length and/or load-sensitive afferents from the ankle plantar flexors contribute to the activation of the soleus muscle during the stance phase of walking through feedback to spinal interneuronal pathways. Convergence on the interneurons in these pathways from the sensory afferents and descending supraspinal fibers determines the synaptic drive to the spinal motoneurons; thus removal of either one, i.e., by unloading/shortening of the muscle leading to decreased sensory afferent feedback (44) or inhibition of the cortical function by transcranial magnetic stimulation leading to decreased corticospinal drive (36a), results in a significant drop in the muscle activity.

EXTERNALLY EVOKED CHANGES IN SENSORY FEEDBACK ACT AS ERROR SIGNALS

Whenever an external stimulus causes the sensory feedback to deviate from that expected by the central motor program, the sensory feedback may serve as an error signal. For example, this occurs when a subject stumbles over an obstacle or when instabilities of the ground lead to perturbation of the supporting foot. In both cases, corrective reactions are elicited at relatively short latency (usually ~70–120 ms). It is important to realize that both increased and decreased sensory feedback act as error signals. Lack of sensory feedback in a situation where sensory activity is expected is as much as an error signal as the increased sensory activity caused by stimulation of the sensory receptors. Note that in the study by Sinkjær et al. (44) the normal contribution of the positive feedback mechanism is inferred from the drop in EMG activity caused by the external perturbation. However, the decrease in sensory activity that it reflects acts as an error signal for later corrective reactions.

Responses evoked by activation of sensory receptors in muscles and skin have been studied in a long range of studies during various types of movement (4, 11, 12, 43, 47, 48; see also Ref. 3). Such studies have provided important information about the central modulation of the responses evoked by sudden external perturbations and have helped to emphasize the importance of the sensorimotor interaction in the spinal cord as well as supraspinal sites for the elicitation of appropriate corrective reactions.

It is not straightforward to make inferences about the contribution of sensory activity to the ongoing movement based on such studies. The afferents may not normally be active in the phase where they are activated by the external stimulus (particularly in the case of cutaneous afferents). Observations of a large or small reflex response in that phase of the movement would thus say very little about the normal (unperturbed) function of the afferent feedback. On the other hand, if an external stimulus is applied at a time when the sensory afferents are already very active, the evoked responses may be small instead of large due to occlusion in the pathway. Data from both humans and cats also suggest that the central gating of the desynchronized and relatively low-rate sensory activity, characteristic of the normal afferent feedback and the sudden (artificial) highly synchronized afferent feedback evoked by an external stimulation (13, 29), may be very different.

SHOULD WE ABANDON THE “CLOSED LOOP-OPEN LOOP” CONCEPT?

From available data on sensorimotor interaction in the spinal cord, I do not find it reasonable to distinguish between the “open-loop” (without sensory feedback) and “closed-loop” modes of motor control, although this distinction is often advanced in motor control textbooks. Sensory feedback is manifest already 50 ms after the onset of movement (46), and no movements are therefore so quick that they can be executed before sensory feedback has reached the spinal cord. Even if it is granted that the first 50 ms of all movements have to be performed in an open-loop mode, my point is that the sensory feedback, which occurs at 50 ms after onset of movement (and later), is “anticipated” by the central nervous system and “buils” into the central motor program. Furthermore, even in the resting situation, sensory feedback is constantly informing the central nervous system about the position of joints and limbs; this information is necessary for the central nervous system to ensure the correct movement of a limb from one position to another. The loop is thus in reality not “open.”

FUNCTIONAL RELEVANCE OF DATA OBTAINED BY NONINVASIVE ELECTROPHYSIOLOGICAL EXPERIMENTS IN HUMANS

Electrophysiological experiments such as those described in this mini-review have only to a limited extent been applied to functional every-day motor tasks; in many studies, only a rather rudimentary biomechanical or kinematic analysis of the exerted movement has been performed. This is because these studies have focused on characterizing and defining the central pathways under study rather than making any functional deductions. This is in stark contrast to the majority of research on applied motor control, which focuses on functional application and in which detailed biomechanical and kinematic analyses of the movement are the rule. The drawback of these latter studies is that there is very little chance that phenomenological descriptions on their own will provide us with any fundamental understanding of how movements are initiated and controlled, how the execution of movement is optimized, and what goes wrong when movements fail to reach their goal. Clearly, there is a great need that the “neurophysiological tradition” and the “biomechanical/kinematic tradition” are combined. Such a combined approach has the potential of providing us with a fundamental understanding of the functional outcome of sensory-motor integration in identified spinal pathways, and it may help us to understand how the central nervous system controls the types of movements involved in sports and occupational activities.
I hope with this mini-review to have stirred the interest for performing such experiments.

REFERENCES