Aquisition and maintenance of the simplest motor skill: investigation of CNS mechanisms

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ABSTRACT

WOLPAW, J. R. Acquisition and maintenance of the simplest motor skill: investigation of CNS mechanisms. *Med. Sci. Sports Exerc.*, Vol. 26, No. 12, pp. 1475–1479, 1994. The spinal stretch reflex (SSR), or tendon jerk, is the simplest behavior of the vertebrate nervous system. It is mediated primarily by a wholly spinal, two-neuron pathway. Recent studies from several laboratories have shown that primates, human and nonhuman, can gradually increase or decrease the size of the SSR when reward depends on such change. Evidence of this training remains in the spinal cord after all supraspinal influence is removed. Thus, the learning of this simple motor skill changes the spinal cord itself. Comparable spinal plasticity probably plays a role in the acquisition of many complex motor skills. Intracellular physiological and anatomical studies are seeking the location and nature of this spinal cord plasticity. Attention focuses on the most probable sites of change, the group Ia afferent synapse on the alpha motoneuron and the motoneuron itself. Results to date indicate that modifications are present at several places in the spinal cord. Current clinical studies are investigating the use of spinal cord adaptive plasticity as a basis for a new therapeutic approach to spasticity and other forms of abnormal spinal reflex function that result from spinal cord injury, stroke, or other neurological disorders. In the future, understanding of spinal reflex plasticity may lead to development of improved training methods for a variety of motor skills.

MEMORY, LEARNING, PLASTICITY, CONDITIONING, TRAINING, MOTOR CONTROL, SPINAL CORD, PRIMATE

Acquisition of a motor skill is typically a gradual process, requiring many repetitions over a long period. Common skills such as walking, talking, or writing require many weeks or months of practice. More specialized skills, such as playing a piano or performing ballet, require years of intensive training. Skill acquisition reflects modifications in the central nervous system (CNS) and the peripheral neuromuscular apparatus, and the need for prolonged practice presumably reflects the characteristics of the learning processes that produce these modifications.

The locations and nature of CNS learning processes remain largely unknown. In the past, investigations of learning and memory have focused on a few CNS structures, such as the hippocampus and the cerebellum. More recently, a large and varied body of evidence has led to increasing recognition that learning processes can occur in many places throughout the CNS and that, as a result, the plasticity responsible for improved performance may be widely distributed. An important factor in this recognition has been the realization that the CNS plasticity that constitutes learning has much in common with plasticity that occurs during nervous system development and during recovery after trauma. Whether occurring during development, in response to trauma, or in the course of learning, CNS plasticity is driven by neuronal activity and depends on comparable processes (18,31). These processes may occur in neurons and synapses throughout the CNS, so that the location of a specific modification depends on the pattern of neuronal and synaptic activity responsible for it.

Most motor performances involve neuronal activity at many levels, including spinal cord, brainstem and cerebellum, basal ganglia and thalamus, and cerebral cortex. Thus, the results of continued practice would be expected to comprise many changes throughout the CNS. However, the complexity and inaccessibility of most CNS pathways, particularly in vertebrates, has prevented definitive localization and description of the modifications that underlie acquisition of motor skills.

OPERANT CONDITIONING OF THE SPINAL STRETCH REFLEX (SSR) PATHWAY

Since 1980, the goal of our laboratory has been to develop and use a new experimental model for defining

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the processes and substrates responsible for acquisition and maintenance of a specific motor skill. To minimize the problems of CNS complexity and inaccessibility, this model is based on the simplest motor behavior of the vertebrate CNS, the initial response to sudden muscle stretch, known as the tendon jerk, M1 response, or the spinal stretch reflex. This behavior is mediated by a wholly spinal, two-neuron pathway, consisting of the Ia afferent fiber from the muscle spindle, its synapse on the alpha motoneuron, and the alpha motoneuron itself (10,12,13,15). Assuming that peripheral axonal conduction velocity does not change, the SSR, unlike more complex motor performances, can be described by a single measure: the size of the response. This measure is expressed most directly as the magnitude in volts of the electromyographic (EMG) signal produced by motor unit excitation. Thus, for the SSR, skill acquisition can be defined as appropriate (i.e., adaptive) modification of SSR size, without change in initial muscle length or background level of motoneuron excitation. Until recently, the SSR and other behaviors mediated by purely spinal pathways were not believed capable of such modification.

The conventional view of the spinal cord has been that it is a hard-wired structure with little or no capacity for the plasticity prominent in supraspinal structures. The SSR in particular is often described in textbooks as the prototype of a predictable, stereotyped response. However, a substantial body of clinical and laboratory data indicates that the spinal cord is capable of considerable plasticity. Much of this evidence concerns the long-term effects of trauma, such as spinal cord transection or damage to supraspinal structures (16,25). It shows that, with the correct impetus in the form of chronically altered descending influence, the spinal cord is capable of enduring change.

This evidence of the potential plasticity of the spinal cord was the impetus for development of an operant conditioning paradigm designed to produce change in the size of the SSR. In this paradigm, an appropriate increase or decrease in SSR size constituted skill acquisition. In the initial design, monkeys were trained to alter the size of the SSR of the biceps brachii muscle in one arm, without change in initial muscle length or background EMG activity (24). For each trial, the animal maintained muscle length and background EMG level in biceps brachii against a steady state extension torque. At an unpredictable time, a brief pulse of additional extension torque extended the elbow and elicited an SSR in biceps brachii. In the control mode, liquid reward always occurred 200 ms later. In the SSR-up or SSR-down mode, reward occurred only if SSR size as measured by EMG was larger (SSR-up) or smaller (SSR-down) than a criterion value. Each animal performed several thousand trials per day. For the initial 1–2 wk, the animal worked under the control mode, in order to define initial, or

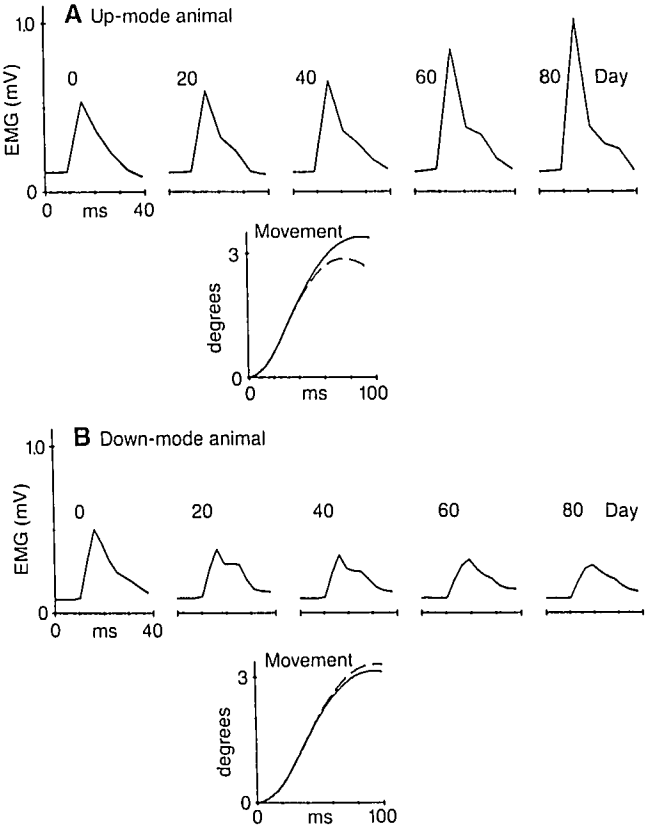

Figure 1—Effects of SSR-up and SSR-down mode exposures on SSR size and on elbow extension. A: Data from an animal exposed to the SSR-up mode for 80 days. The five upper graphs show average daily SSR size for every 20th day starting with imposition of the SSR-up mode. SSR size increases steadily without change in background EMG (represented here by the 12 ms preceding SSR onset). The lower graph shows pulse-induced elbow extension before (solid) and after (dashed) SSR-up exposure. Initial extension, the stimulus that produces the SSR, is the same for both. Starting at 35–40 ms, extension is less after SSR-up exposure than before, presumably because the larger biceps SSR furnishes greater opposition. The 20-ms lag between the SSR and its impact on movement is the time required for muscle contraction after excitation. B: Analogous data from an animal exposed to the SSR-down mode. Steady decrease in SSR size takes place without change in background EMG or in the initial pulse-induced elbow extension. Past 35–40 ms, extension is greater after SSR-down exposure, because the smaller SSR furnishes less opposition. (Modified from ref. 29.)

control, SSR size. Then, it worked under the SSR-up or SSR-down mode for a period that usually lasted 40 d or more. All experimental procedures used in the studies reviewed here were in accord with Department of Health, Education and Welfare Publication No. (NIH) 85-223, *Guide for the Care and Use of Laboratory Animals* and had been reviewed and approved by the Wadsworth Center Animal Welfare Committee.

After imposition of the SSR-up or SSR-down mode, SSR size changed appropriately over at least 40 d. Under the SSR-up mode, it eventually rose an average of more than 50%, whereas under the SSR-down mode, it eventually fell by an average of about 40%. Figure 1 illustrates these gradual changes and also indicates that SSR

change affected limb movement. When the SSR got larger, it provided greater opposition to the sudden stretch, and when it got smaller, it provided less opposition. Consistent with the time needed for muscle activation to produce a mechanical effect, this change in movement began about 20 ms after the SSR as measured by EMG. Additional analyses revealed major features of SSR conditioning (22,29,30,32). First, reversal and redevelopment of SSR size change (prompted by imposition of the opposite mode and reimposition of the original mode, respectively) also occurred gradually over many days. Second, once acquired, mode-appropriate size change survived breaks in performance of at least several weeks. Third, SSR change was focused in the conditioned muscle (i.e., biceps brachii). Lesser changes occurred in the SSRs of its synergists, brachialis and brachioradialis. Fourth, analysis of data from many animals revealed that, although change developed gradually over weeks, it began within the first day with an abrupt change of about 8% in the appropriate direction.

As discussed in detail previously (29), these features strongly suggested that imposition of the SSR-up or SSR-down mode caused a nearly immediate modification in tonic descending influence over the spinal reflex arc. The onset of this altered influence was responsible for the initial 8% change, whereas its continuation over many days gradually modified the spinal cord and thereby produced the progressive additional change in SSR size. Thus, skill acquisition (i.e., achievement of a larger or smaller SSR), seemed to involve plasticity in the spinal cord.

ADAPTIVE PLASTICITY IN SPINAL CORD

To determine whether the gradual acquisition of a larger or smaller SSR did in fact involve spinal cord plasticity, the experimental design was modified to condition the H-reflex (the electrical analog of the SSR) in the triceps surae (TS) muscle of the leg (23,26,28). H-reflex conditioning proved to have features very similar to those of SSR conditioning. As with SSR conditioning, H-reflex increase (HR-up mode) or decrease (HR-down mode) developed gradually over many days. It also seemed to begin with an abrupt change in the first few days. Change was focused on the TS muscle being conditioned. Little or no change occurred in the H-reflex of the contralateral TS muscle. Most importantly, when conditioned animals were deeply anesthetized and the spinal arc of the H-reflex was assessed after thoracic cord transection removed all possible descending control, the conditioned reflex asymmetry was found to persist for at least several days under continued deep anesthesia (after which the still-anesthetized animals were sacrificed by overdose) (27). Thus, acquisition of a larger or smaller H-reflex clearly involved plasticity at the spinal cord level.

Current physiological and anatomical studies of individual TS motoneurons and their synaptic connections are seeking to define the functional and structural nature of this spinal cord plasticity. These studies began with the belief that the most likely site of change was the Ia synaptic connection on the TS motoneuron. This location seemed the logical site for plasticity that would alter H-reflex size appropriately with minimal disruption of other motor behaviors. However, even at this early stage of investigation, two initially surprising facts have become clear. First, the plasticity underlying acquisition of altered H-reflex size involves multiple sites at spinal and supraspinal levels. The most striking evidence for this conclusion is the marked change in reflex size on the contralateral (i.e., unconditioned) side of the spinal cord in anesthetized, transected animals (27). This change was not apparent in the awake behaving animals. Thus, anesthesia and transection uncovered an effect of conditioning that was not otherwise apparent. Second, current intracellular studies of individual TS motoneurons indicate that H-reflex conditioning in response to the HR-down mode is due to changes in fundamental motoneuron properties and suggest that change in Ia synaptic function has only a minor role (5,9).

RELATIONS TO ACQUISITION OF MORE COMPLEX BEHAVIORS AND POTENTIAL CLINICAL APPLICATIONS

Modification of the SSR pathway probably plays a role in acquisition of a variety of motor skills. For example, change in lower limb SSRs occurs gradually in the course of ballet training and correlates with the duration and intensity of training (8). In a particularly pertinent experiment, Meyer-Lohmann et al. (17) found that, in monkeys trained to oppose sudden muscle stretch as rapidly as possible, SSR size increased gradually over many months of performance. The SSR essentially took over from longer latency responses the task of opposing the perturbation.

The two-phase development of SSR change (29) may provide insight into events occurring during acquisition of more complex motor skills. A similar two-phase course is seen with adaptive plasticity in the vestibular ocular reflex (VOR), another behavior mediated by a simple neuronal pathway (14). Clear separation into two courses is not seen in learning curves for more complex skills, which typically show rapid initial progress followed by further improvement at a gradually decreasing rate. It is likely that improvement in more complex performances involves more-or-less simultaneous alterations in many influences and that the continuation of these influences gradually modifies many sites throughout the CNS. Such multiple two-phase sequences would be expected to obscure each other, so that the separate phases of improvement would not be apparent.

Ongoing clinical studies indicate that humans as well as monkeys can modify SSR size (7,19,21). The primary goal of these studies is development of a new therapeutic approach to spasticity and other types of abnormal spinal function that result from spinal cord trauma, stroke, and other neurological disorders. Initial results indicate that patients with partial spinal cord injury can gradually reduce SSR size when exposed to a paradigm such as that used with monkeys. Exploration of possible functional correlates is underway.

THE NECESSITY FOR DISTRIBUTED PLASTICITY

The data reviewed here indicate that operant conditioning of the H-reflex, the simplest possible motor skill, involves changes at multiple sites in the CNS. Detailed understanding of the genesis of this complexity awaits completion of studies now underway. Nevertheless, several considerations suggest that this complexity is both necessary and inevitable.

From the experimenter's point of view, the necessary response to the H-reflex (or SSR) conditioning paradigm is simply a mode-appropriate change in reflex size, which could theoretically be achieved by merely increasing or decreasing the strength of the Ia synapse (e.g., by change in presynaptic inhibition (1–4)). In reality, that is, from the perspective of the CNS, the problem presented by the conditioning paradigm is considerably more complicated. The CNS must adapt to acquire the new skill, i.e., a larger or smaller H-reflex, While still maintaining performance of previously learned skills that depend on the same neural elements. The Ia afferent, the motoneuron, and the synapse between them participate in all behaviors involving the muscles they control or monitor. As a result, any change in these neural elements is likely to affect many motor skills. Additional plasticity is therefore essential if the CNS is to continue to perform all its behaviors satisfactorily. The need for such compensatory plasticity may well underlie the changes that occur on the other, unconditioned side of the spinal cord when the H-reflex on the conditioned side changes in response to the HR-up or HR-down conditioning mode. Thus, when considered in terms of the entire organism and the demands it must satisfy, the fact that H-reflex conditioning entails plasticity at multiple sites is quite explicable. This bilateral plasticity may also be related to cross-education phenomena, in which training of one limb affects the contralateral limb as well (6,11).

Whereas distributed plasticity seems necessary from the perspective of the whole organism, it seems inevitable from the perspective of the individual elements, the neurons and synapses, that comprise the CNS. Each of these elements has a specific repertoire of responses to influences from elsewhere in the nervous system. For example, if excitation of a specific synapse occurs more frequently, transmitter release and/or postsynaptic membrane sensitivity may change in a specific way. The same stereotyped response to increased excitation will occur, whether the origin of the excitation is developmental, traumatic, or adaptive, and whether the ultimate effect of the response is adaptive for the organism. For example, recent data (20) indicate that chronic reduction in Ia synaptic activation leads eventually to an increase in the amplitude of the Ia excitatory postsynaptic potential (EPSP). Thus, although an increase in Ia presynaptic inhibition in response to the HR-down mode might produce an immediate decrease in the H-reflex, it could in the long run produce an increase (or at least no change). This consideration may explain why successful HR-down conditioning is associated with little or no change in the TS Ia EPSP, even though decrease in the EPSP seems at first the most obvious mechanism for decreasing the H-reflex with minimal disruption of other behaviors.

The occurrence of such normal local responses is likely to have two effects on the pattern of plasticity underlying acquisition of a skill. First, the modifications responsible for the new skill itself are likely to be different from and more complex than the theoretically simplest solution. Second, modifications are likely to occur that have no apparent relevance to performance and might actually seem to be counterproductive.

The combination of necessary compensatory plasticity and inevitable local responses ensures that the CNS plasticity underlying acquisition of even the simplest possible motor skill, adaptive change in H-reflex size, involves changes at multiple spinal and supraspinal sites.

This review is based on a presentation in the symposium "Adaptive properties of the sensorimotor system," which was held at the American College of Sports Medicine Annual Meeting in 1993 to honor the contributions of the late Robert S. Hutton, Ph.D. Dr. Hutton provided many important comments during the early stages of the work summarized here. Both his comments and his interest were highly valued and very much appreciated.

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