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The complex structure of a simple memory

Jonathan R. Wolpaw

Operant conditioning of the vertebrate H-reflex, which appears to be closely related to learning that occurs in real life, is accompanied by plasticity at multiple sites. Change occurs in the firing threshold and conduction velocity of the motoneuron, in several different synaptic terminal populations on the motoneuron, and probably in interneurons as well. Change also occurs contralaterally. The corticospinal tract probably has an essential role in producing this plasticity. While certain of these changes, such as that in the firing threshold, are likely to contribute to the rewarded behavior (primary plasticity), others might preserve previously learned behaviors (compensatory plasticity), or are simply activity-driven products of change elsewhere (reactive plasticity). As these data and those from other simple vertebrate and invertebrate models indicate, a complex pattern of plasticity appears to be the necessary and inevitable outcome of even the simplest learning.

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LEARNING CHANGES THE BRAIN, and learning changes behavior; but how the first effect accounts for the second is not clear. The problem requires more than a correlational approach that simply defines processes, such as long-term potentiation, that are essential for learning. It also requires a mechanistic approach that begins from behavioral change and then proceeds to identify its CNS substrates. This approach depends on laboratory models in which the neuronal elements that contribute to a behavior are defined and accessible, since only then is it possible to describe the translation of learning-induced plasticity into behavior. A small number of vertebrate and invertebrate models come close to satisfying these requirements. One of these is the model based on the spinal stretch reflex (SSR).

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The SSR, or tendon jerk, is mediated largely by a two-neuron, monosynaptic pathway that consists of the Ia afferent neuron, its synapse on the alpha motoneuron, and the alpha motoneuron (Fig. 1)[2,4,5]. It is the simplest vertebrate behavior. Because it is influenced by descending activity from supraspinal structures, the SSR can be operantly conditioned. Monkeys, humans, and rats can gradually increase or decrease the SSR or its electrical analog, the H-reflex (Fig. 1)[6–10]. The learning involves plasticity in the spinal cord itself, since evidence of it remains even after all descending activity is abolished[11]. Thus, operant conditioning of this simple behavior provides an opportunity to define the substrates of a vertebrate memory, the mechanisms that create and maintain them, and the manner in which these substrates translate into behavior.

Seven years ago, shortly after SSR and H-reflex conditioning were first described, a *TINS* review from this laboratory offered three hypotheses for the site of the spinal cord plasticity that was responsible[12]. Stated there in order of decreasing probability, they were: the Ia synapse, the postsynaptic region of the motoneuron, and the entire motoneuron. Since then, physiological and anatomical studies of the motoneuron and its inputs have shown these hypotheses to be not so much wrong as naive. The results, described in this new review, are a continuing series of surprises, as they begin to reveal the remarkably complex plasticity that is associated with this ostensibly simple learning.

SSR and H-reflex conditioning in the laboratory

Both the SSR and the H-reflex can be operantly conditioned, and their conditioning appears to be comparable[6–10]. SSR conditioning is readily implemented

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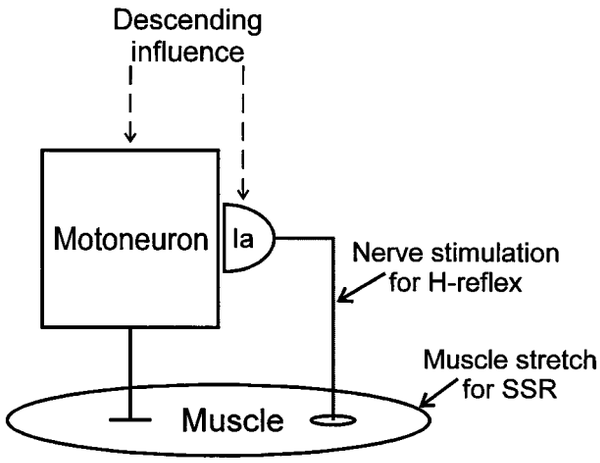

Fig. 1. ***Monosynaptic pathway of the spinal stretch reflex (SSR) and its electrical analog, the H-reflex.*** *The pathway comprises the Ia afferent neuron from the muscle spindle, its synapse on the alpha motoneuron, and the motoneuron itself. When the Ia afferent is excited, it excites spinal motoneurons that innervate the same muscle and its synergists. If the afferent is excited in the normal fashion, that is, by muscle stretch, the muscle's response is the SSR. If it is excited by direct electrical stimulation, the response is the H-reflex[1]. The SSR and the H-reflex are measured by EMG or by their mechanical effects. While their pathway is wholly spinal, both are affected by descending influences on the Ia terminal (exerted presynaptically) and on the motoneuron, and the SSR is also affected by descending control of muscle spindle sensitivity[2,3].*

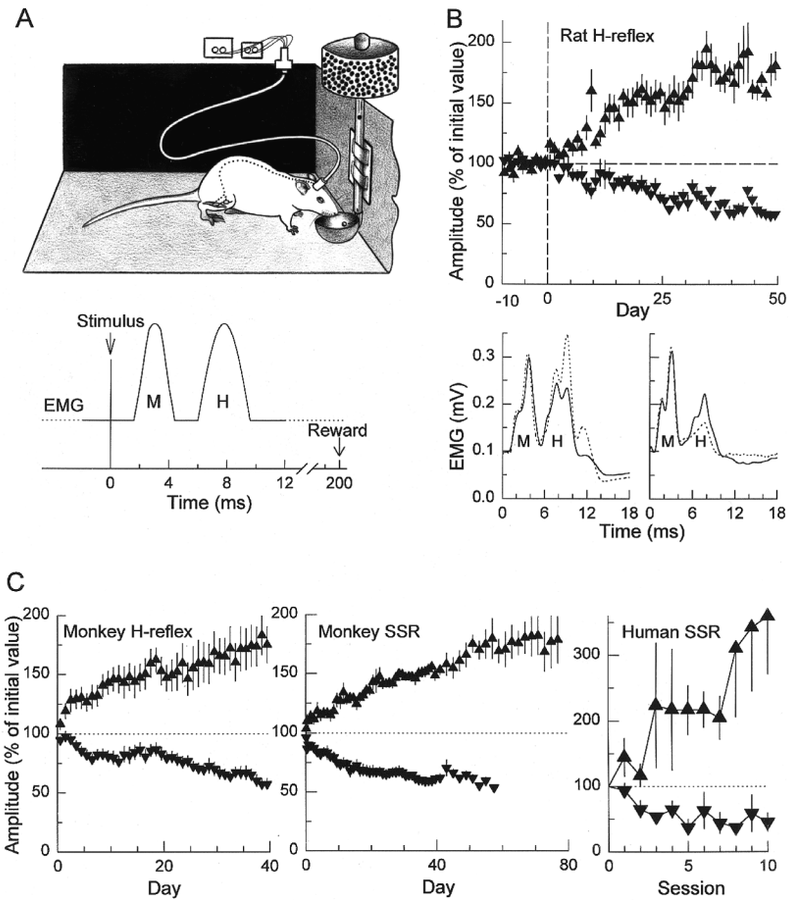

Fig. 2. ***The conditioning protocol and its results.*** **(A)** *The soleus EMG is monitored continuously in a rat with chronically implanted EMG electrodes and a tibial nerve cuff. Whenever its absolute value remains within a specified range for a randomly varying 2.3–2.7 s period, a nerve cuff stimulus elicits a threshold M response (that is, a direct muscle response[1]) and an H-reflex. For the first 10 days, the rat is exposed to the control mode, in which no reward occurs and the H-reflex is simply measured to determine its initial amplitude. For the next 50 days, it is exposed to the HR↑ or HR↓ mode, in which a food-pellet reward occurs if the H-reflex is above (HR↑) or below (HR↓) a criterion value. Background EMG and M response remain constant throughout. Successful conditioning, defined as a change of at least 20% in the correct direction[9,16], occurs in 80–90% of the animals. Their data are shown in* **(B)**. *The top graph shows average daily H-reflexes (±SEM) from 9 HR↑ rats (▲) and 12 HR↓ rats (▼) for the control-mode exposure (that is, days –10 to 0) and for the subsequent HR↑ or HR↓-mode exposure (that is, days 0 to 50). Under the HR↑ mode, the H-reflex rises gradually to about 175% of its initial value, while under the HR↓ mode it falls gradually to about 60%. The bottom graphs show average poststimulus EMG for representative days from an HR↑ rat (left) and an HR↓ rat (right) under the control mode (solid lines) and near the end of HR↑ or HR↓ exposure (broken lines). The H-reflex is much larger after HR↑ conditioning and much smaller after HR↓ conditioning, while background EMG (indicated here by EMG at zero time) and M responses are unchanged. If a rat is switched from the HR↑ to the HR↓ mode or vice versa, the H-reflex change reverses in the same gradual fashion[17].* **(C)** *Average results for up-conditioning (▲) and down-conditioning (▼) of the H-reflex of the triceps surae in monkeys (left), the spinal stretch reflex of the biceps brachii in monkeys (middle), and the SSR of the biceps brachii in humans (right). The courses and final magnitudes of change are similar to those found in the rat.* B is reproduced from Refs 9 and 17 and unpublished data, C from Refs 10,18 and 19.

in humans and might provide a new method for addressing the spinal reflex abnormalities that are associated with a variety of chronic CNS disorders[13–15]. At the same time, H-reflex conditioning is preferable as a laboratory model, because the H-reflex bypasses the muscle spindle and lends itself to long-term recording in freely moving animals. First described in monkeys, it is now being studied in rats.

The conditioning protocol is presented in Fig. 2A. While the rat H-reflex protocol is shown, the primate H-reflex and SSR protocols are equivalent to it and provide comparable results (Fig. 2B,C)[6,9,10,20]. An important feature of the protocol is that the reflex is elicited at an unpredictable time. Because of this, and because the H-reflex is the earliest possible CNS response, the animal can change the amplitude of the H-reflex only by maintaining continual appropriate descending influence over the spinal arc of the reflex. By linking reward to the amplitude of the H-reflex, the protocol operantly conditions the animal to maintain such an influence. The continuation of this descending influence over the period of conditioning changes the spinal cord[11] and increases (HR↑ mode) or decreases (HR↓ mode) the H-reflex. As illustrated in Fig. 2B, the H-reflex of the rat soleus rises to nearly double its initial amplitude under the HR↑ mode, or falls by almost half under the HR↓ mode.

Conditioning of the SSR pathway in real life

While the SSR is by definition a simple behavior, and it (or the H-reflex) is employed as such in the clinical and laboratory protocols, in normal life it is a part of much more complex behaviors. Monosynaptic Ia-afferent input to motoneurons participates in behaviors that range from posture and locomotion to the most sophisticated athletic and technical skills. A diverse body of evidence suggests that SSR plasticity like that produced in the laboratory contributes to motor development in childhood and to the learning of motor skills later in life, and that the plasticity is produced by descending influence.

In the newborn infant, muscle stretch produces SSRs in both agonist and antagonist muscles[21,22]. Antagonist SSRs gradually disappear during childhood, unless perinatal supraspinal damage (for example, cerebral palsy) impairs descending influence[23]. Without normal descending influence, antagonist SSRs can persist into adulthood, and contribute to motor dysfunction (Fig. 3A).

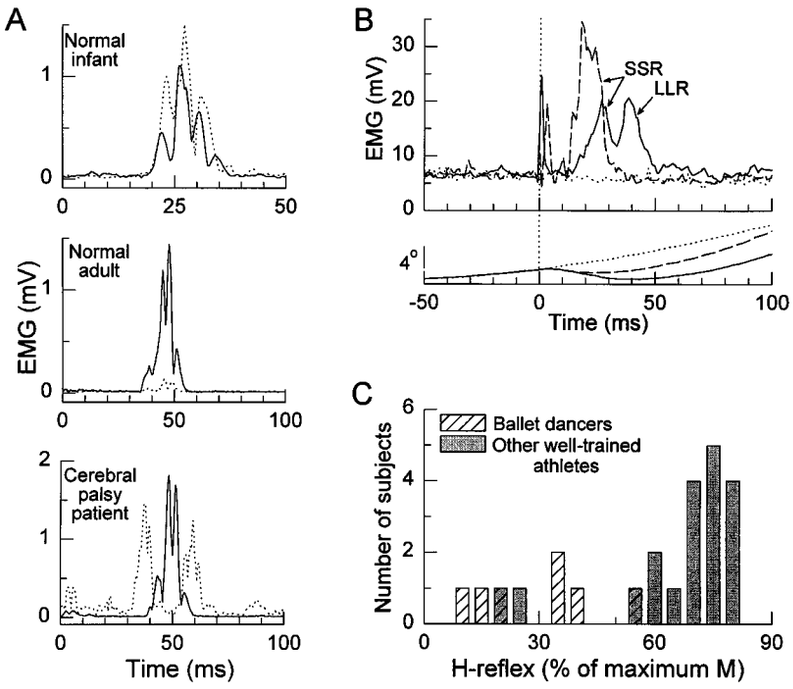

Fig. 3. ***Conditioning of the spinal stretch reflex (SSR) pathway during development and during the acquisition of motor skills.*** **(A)** *EMG responses of soleus (solid lines) and tibialis anterior (dotted lines) muscles to sudden foot dorsiflexion, which stretches the soleus and shortens its antagonist, the tibialis anterior. In a normal infant, this stimulus produces SSRs in both muscles. In a normal adult, an SSR occurs only in the stretched muscle, that is, the soleus; little or no response occurs in the tibialis anterior. In contrast, in an adult with cerebral palsy, in whom perinatal supraspinal injury has impaired the descending influence responsible for the development of normal adult SSRs, the infantile pattern persists: SSRs occur in both soleus and tibialis anterior. (The short latency and unusual form of the tibialis anterior response also suggest the presence of central or peripheral abnormalities, or both.)* **(B)** *Working for reward, monkeys performed an elbow flexion–extension task on which brief perturbations (that is, 10-ms torque pulses) were randomly superimposed. Shown are biceps EMG and elbow angle (flexion is upward) for an unperturbed trial (dotted line), a perturbed trial early in training (solid line), and a perturbed trial late in training (broken line). Early in training, perturbation elicits both an SSR and a long-latency polysynaptic response (that is, LLR). After intermittent training over several years, the SSR is much larger and the LLR has disappeared. The SSR has gradually taken over the role of opposing the perturbation. This is accompanied by improvement in performance: the deflection superimposed by the torque pulse on the smooth course of elbow flexion is smaller and briefer.* **(C)** *Soleus H-reflexes are much smaller in professional ballet dancers than in other well-trained athletes (for example, runners, swimmers, cyclists). (H-reflexes of sedentary subjects are intermediate.)* A from B.M. Myklebust and G.L. Gottlieb (unpublished data comparable to those in Refs 21 and 23), B from Ref. 24, C from Ref. 25.

In adults, SSRs and H-reflexes are correlated with the nature, intensity, and duration of motor training. When monkeys trained to make smooth movements were exposed to random perturbations, the SSRs elicited by the perturbations gradually increased, and the increase accounted for improvement in performance (Fig. 3B)[24]. In professional ballet dancers, H-reflexes and SSRs in the legs (and Group-Ia reciprocal inhibition as well) are much smaller than in other highly trained athletes (Fig. 3C)[25,26]. The decreased direct peripheral influence on motoneurons that is indicated by the smaller reflexes might effectively increase cortical control and allow more precise movement. As these examples illustrate, the conditioning studied in the laboratory appears to represent a phenomenon that plays an integral part in the acquisition and maintenance of motor skills throughout life.

The plasticity that underlies H-reflex conditioning

Physiological and anatomical studies are seeking the site and nature of the plasticity that accompanies H-reflex conditioning. At the beginning, the goal was simply to elucidate the plasticity that explains the behavioral change, that is, a larger or smaller H-reflex. That the problem is more complicated became evident almost immediately.

The first surprise came with the first study, which sought simply to determine whether H-reflex conditioning changes the spinal cord[11]. Nerve volley responses were recorded under anesthesia from monkeys in which conditioning had increased (HR↑ animals) or decreased (HR↓ animals) the H-reflex of the triceps surae in one leg. The reflex asymmetry created by conditioning remained even after transection of the spinal cord had removed descending influence (Fig. 4A). This indicated that conditioning had changed the spinal cord itself. The surprise was that conditioning had an additional, wholly unexpected effect: responses on the contralateral (that is, unconditioned) side were much larger in HR↓ animals than in HR↑ animals (Fig. 4A). This difference was evident only in the acute preparations; it had not been present in the contralateral H-reflexes of the awake behaving animals[16,29]. Thus, anesthesia and cord transection had uncovered a hidden effect of conditioning: conditioning changed the other side of the spinal cord. What this contralateral plasticity might be and how it might relate to the H-reflex on the conditioned side are questions as yet unanswered.

Intracellular study of the motoneurons of the triceps surae brought further surprises[27,30]. Axonal conduction velocity, the motoneuron property that might be least expected to change with conditioning, was lower in motoneurons from the conditioned side of HR↓ animals. In addition, the firing threshold of the motoneuron was shifted positively. As illustrated in Fig. 4B, the threshold change, in combination with the modest decrease found in the amplitude of the Ia EPSP, could explain the decrease in the H-reflex. Furthermore, the positive shift in firing threshold, if present in the axon as well as the cell body, could also explain the lower conduction velocity. A modeling study supported this possibility, indicating that the changes in threshold and conduction velocity could be caused by nearly identical positive shifts in the activation voltage of Na^+ channels in the motoneuron membrane[31]. Altered activation of protein kinase C could be responsible for the hypothesized change in Na^+ channels, but how descending influence might bring this about remains to be determined.

In surprising contrast to the data from HR↓ animals, intracellular physiological data from HR↑ animals gave no explanation for conditioned H-reflex increase[30]. Indeed, the data suggested that H-reflexes on the conditioned side of HR↑ animals should have been slightly smaller than normal. These results introduce additional unexpected complexity on several levels. First, they imply that HR↓ and HR↑ conditioning are not mirror images of each other, but rather have different mechanisms. This implication is consistent with the observation that the rate and magnitude of H-reflex change caused by the HR↑ or HR↓ mode are not affected by previous exposure to the opposite mode[17,32]. Second, the results suggest that the explanation for HR↑ conditioning might lie outside the two-neuron monosynaptic pathway. In fact, Group-Ia or -Ib excitation produced by the nerve stimulation could reach the motoneuron through disynaptic pathways

soon enough to affect the H-reflex[3,33–35]. Such oligosynaptic excitation or inhibition could, respectively, add to or subtract from the monosynaptic Ia EPSP and thereby change H-reflex amplitude.

The *TINS* review of 1990 listed plasticity at the Ia synapse as the most likely explanation for H-reflex change[12]. The rationale was the well-documented influence of presynaptic inhibition on the Ia synapse[3,36–38] and the fact that this mechanism seemed to offer a highly focused method for changing the H-reflex without greatly disturbing other aspects of motoneuron function. In this context, the absence of large changes in the homonymous EPSPs of motoneurons from the conditioned sides of either HR↑ or HR↓ animals was another surprise. On the other hand, while homonymous EPSPs showed little change, heteronymous EPSPs (that is, those elicited by non-triceps surae Ia afferents) were much smaller than normal in both HR↑ and HR↓ animals[30]. Thus, conditioning did appear to affect the Ia synapse, although not as expected.

Electron microscopic analysis of the synaptic coverage of motoneurons of the triceps surae revealed additional aspects of the spinal cord plasticity that is produced by H-reflex conditioning[28]. F terminals (which have flattened vesicles, contain GABA or glycine, or both, and are believed to be predominantly inhibitory[39]) on cell bodies and proximal dendrites were smaller on the conditioned side of HR↑ animals than on the conditioned side of HR↓ animals. F terminals from the unconditioned sides of HR↑ and HR↓ animals and from naive animals were intermediate in size. On the cell bodies, this HR↑/HR↓ difference was accompanied by a difference in the number of active zones per F terminal (Fig. 4C), which implies a comparable functional difference. In addition, C terminals (large terminals with subsynaptic cisterns that are associated with rough endoplasmic reticulum[40,41]) were smaller and more clustered on motoneurons from the conditioned side of HR↑ animals (Fig. 4D). While the implications of the C-terminal difference are unclear, smaller F terminals could be the anatomical substrate of a decrease in disynaptic Group-I inhibition, and thus might underlie the H-reflex increase produced by HR↑ conditioning.

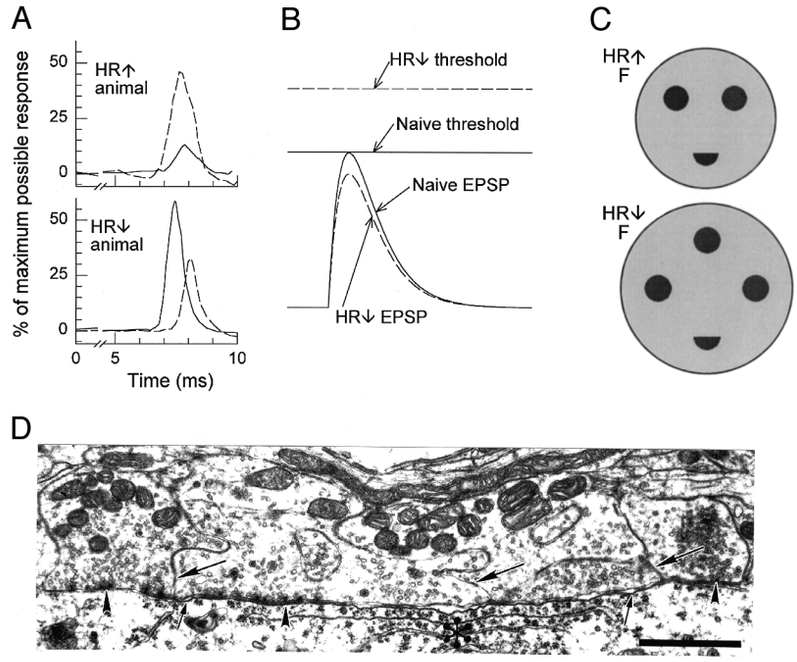

Fig. 4. ***Spinal cord plasticity associated with H-reflex conditioning.*** **(A)** *Monkeys in which the H-reflex of the triceps surae in one leg had been increased (HR↑ animal) or decreased (HR↓ animal) by conditioning were anesthetized and surgically prepared, and the nerve volley responses of the triceps surae to stimulation of the proximal ends of the cut dorsal roots were recorded under continued anesthesia before and for 2–3 days after transection of the thoracic cord had removed descending influence. The reflex asymmetry established by conditioning was still present after transection: nerve volley responses on the conditioned side (broken lines) were larger than those on the unconditioned side (solid lines) in HR↑ animals and smaller in HR↓ animals. In addition, the responses on the unconditioned side were much larger in HR↓ animals than in HR↑ animals. This latter finding was unexpected, since in the awake behaving animals H-reflexes on the unconditioned side changed little over the course of conditioning. It indicated that conditioning had effects on the contralateral spinal cord that affected behavior only after anesthesia and transection had removed descending influence.* **(B)** *Triceps surae motoneurons on the conditioned side of HR↓ monkeys had more positive firing thresholds and slightly smaller Ia EPSPs. Together, these two results could explain why HR↓ motoneurons were less likely to fire in response to nerve stimulation.* **(C)** *The diagram shows the contacts of idealized average F terminals and their active zones on the cell bodies of triceps surae motoneurons on the conditioned sides of HR↑ and HR↓ animals. HR↑ F terminals are smaller and have fewer active zones. Active zone size does not differ. Diameter of the HR↓ F terminal is 2.2 μm.* **(D)** *C terminals on triceps surae motoneurons on the conditioned side were smaller and more clustered in HR↑ animals than in HR↓ animals. The electron micrograph shows a cluster of four small C terminals on a motoneuron from the conditioned side of an HR↑ animal. Large arrows indicate borders between C terminals, small arrows indicate subsynaptic cisterns, arrowheads indicate active zones, and the asterisk indicates rough endoplasmic reticulum. Scale bar, 1 μm.* A from Ref. 11, B from Ref. 27, C and D from Ref. 28.

Supraspinal control of spinal cord plasticity

H-reflex conditioning and the spinal cord plasticity associated with it clearly depend on appropriate descending influence, for it is only supraspinally that the impetus for conditioning – reward delivery – is perceived. In humans and rats, conditioning is still possible after partial injury to the spinal cord[13,42]. At the same time, injury often impairs conditioning and the degree of impairment is correlated with tissue loss. More specifically, as shown in Fig. 5, transection of the dorsal column, which in rats includes the main corticospinal tract, prevents HR↓ conditioning, while transection of the entire ipsilateral lateral column, which includes rubrospinal, vestibulospinal, and reticulospinal tracts, does not prevent it[43]. These results are consistent with data from humans that indicate that strokes that affect the motor cortex and associated subcortical structures usually prevent down-conditioning of the biceps SSR (Ref. 15). Combined with the specificity of SSR and H-reflex conditioning (that is, the fact that change is focused in the muscle that determines reward even when reflexes of other muscles are elicited simultaneously[16,29,44,45]), these results suggest that, while the importance of the ascending tract of the dorsal column remains unclear, the main corticospinal tract is essential for HR↓ conditioning.

Current summary of spinal cord plasticity

Figure 6 summarizes present hypotheses for the ipsilateral plasticity that is associated with H-reflex conditioning. It does not attempt to portray the as yet undefined plasticity that occurs on the contralateral side. While the hypotheses are based on data from monkeys, rats, and humans, it should be recognized that the plasticity could differ substantially across species.

Current evidence suggests plasticity at four sites. A positive shift in the firing threshold of the initial segment and the rest of the axon (and by implication the rest of the motoneuron) is indicated by the intracellular data, is theoretically attributable to a shift in the

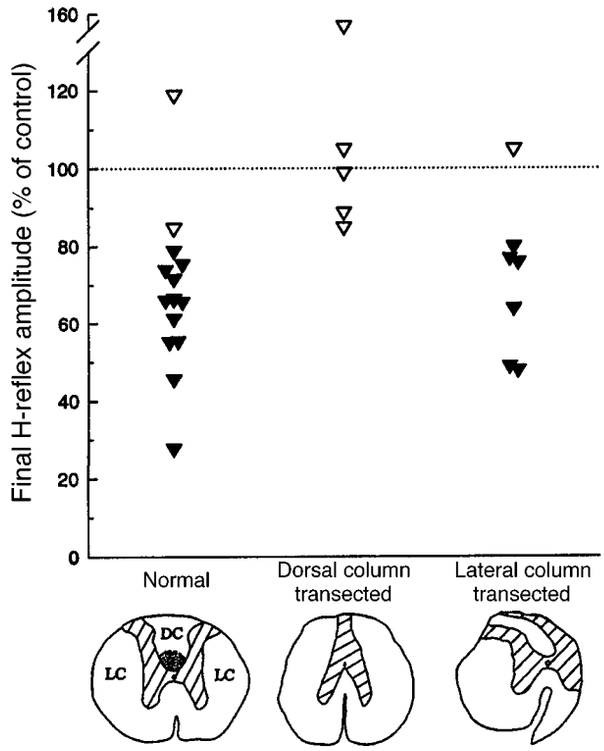

Fig. 5. ***Lesion effects on H-reflex conditioning.*** *Final H-reflex values (in percent of initial values) for normal, dorsal column-transected, and right lateral column-transected rats exposed to HR↓ conditioning of the right soleus muscle are shown. Successful conditioning (that is, decrease to ≤80%), indicated by filled symbols, occurred in 86% of normal or lateral column-transected rats, but not in any dorsal column-transected rats. Shown below are camera-lucida drawings of transverse sections of mid-thoracic spinal cord from a normal rat, a rat with dorsal column transected and a rat with the right lateral column transected. Hatching indicates gray matter. The section from the normal rat has dorsal (DC) and lateral (LC) columns labeled and the main corticospinal tract stippled, and is 2.6 mm wide. For the lesioned rats, the section shown is at the lesion epicenter.* From Ref. 43.

activation voltage of Na^+ channels, and could explain H-reflex decrease under the HR↓ mode (Fig. 4B)[27,31]. A change in disynaptic Group-I input is suggested by the anatomical data (Fig. 4C)[28] (and by the negative intracellular physiological data from HR↑ animals[30]), and could explain the H-reflex increase under the HR↑ mode. Anatomical data also imply a change in the size and grouping of C terminals, which are believed to be of interneuronal origin[28,40]. Change in the Ia afferent synapse is suggested by the intracellular data (that is, the modest decrease in homonymous EPSPs on the conditioned side of HR↓ animals and the large decreases in heteronymous EPSPs in both HR↑ and HR↓ animals[27,30]) and by the high probability that presynaptic inhibition at this synapse contributes to short-term task-dependent adaptation[36–38].

Figure 6 also incorporates the likely role of the corticospinal tract in conditioning[43]. The hypothesized sites of its influence are on spinal interneurons. While direct connections to motoneurons could play a part, these connections are thought to be predominantly excitatory[46–48] and the anatomical data[28] provide no evidence for change in such terminals (that is, F terminals are inhibitory and C terminals are probably of interneuronal origin). Furthermore, it is not known whether direct corticomotoneuronal connections to the lumbar cord exist in the rat.

The origins of complexity

As Figs 4 and 6 indicate, we have as yet only a fragmentary understanding of why the H-reflex is smaller after exposure to the HR↓ mode and larger after exposure to the HR↑ mode. At the same time, we do know that H-reflex conditioning is associated with plasticity at multiple sites in the spinal cord, including sites (for example, on the contralateral side) that do not appear to contribute to the larger or smaller ipsilateral H-reflex[11,27,28,30]. This complex plasticity is comparable to that now appearing in other simple learning models. Plasticity occurs at multiple sites with conditioning of siphon withdrawal in *Aplysia*, eyelid closure in rabbits, and vestibuloocular reflex gain in primates[49–52]. The behavioral changes, however simple, are not due to single changes at single sites.

Although consistent with neural network-based concepts of CNS operation, such complexity was generally not anticipated when these models were first developed. The assumption, or at least the hope, was that simple learning would prove to have simple mechanisms, that single changes at single sites would be found to account for changes in simple behaviors. In fact, complex plasticity appears to be both necessary and inevitable, even for the simplest learning phenomena.

Complex plasticity is necessary

Any learning, even learning as simple as a larger or smaller H-reflex, confronts the CNS with an intricate

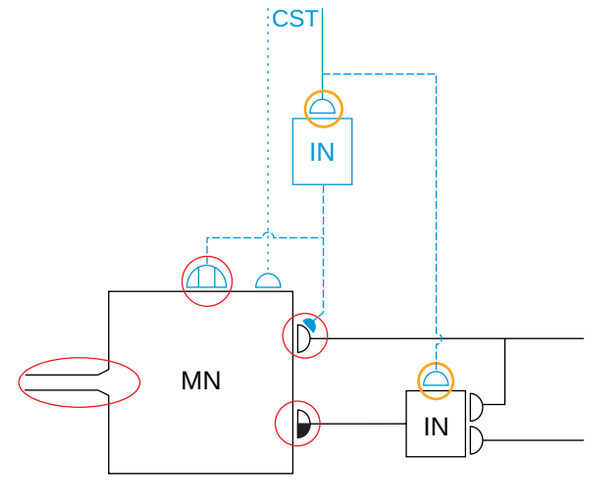

Fig. 6. ***Probable sites of spinal cord plasticity and altered descending influence.*** *MN indicates the motoneuron population of the triceps surae, Ia and Ib indicate Group-I afferent neuron populations, and each IN indicates one or more spinal interneuron populations. Open synaptic terminals are excitatory, solid terminals are inhibitory, half-open terminals could be either, and the subdivided terminal is a cluster of C terminals. Dashed pathways imply the possibility of intervening spinal interneurons, and the dotted pathway is uncertain. The monosynaptic and possibly disynaptic pathway of the H-reflex is black, and the hypothesized sites of operantly conditioned plasticity in it are circled in red. Beginning at the left and proceeding clockwise around the motoneuron, these are: the motoneuron membrane (that is, firing threshold of the initial segment and the rest of the axon), C terminals on the motoneuron, the Ia afferent synaptic connection, and terminals conveying disynaptic group-I inhibition or excitation to the motoneuron. The corticospinal tract (CST) is in blue, and the hypothesized sites of the descending influence that is responsible for the plasticity in the H-reflex pathway are circled in dark yellow. These are: connections on interneurons that mediate presynaptic inhibition of the Ia synapse or on interneurons that supply C terminals to the motoneuron, or both, and connections on interneurons that convey disynaptic Group-I inhibition or excitation to the motoneuron.*

TABLE 1. Plasticity likely to be associated with H-reflex conditioning and other learning phenomena

Plasticity	Definition	Impetus	Possible example
Primary	Responsible for the rewarded behavior	Reward	More positive threshold in HR↓ motoneurons
Compensatory	Maintains previous behavioral repertoire	Behavioral disturbances caused by primary or reactive plasticity	Contralateral spinal cord plasticity
Reactive	Activity-driven product of other plasticity	Altered neuronal activity caused by primary or compensatory plasticity	Absence of large change in Ia EPSP amplitude

problem: to modify a behavior and at the same time preserve other behaviors. The CNS is a multi-tasking system: each of its components participates in many behaviors. This is particularly true for motoneurons and other neurons of the spinal cord, which is the final assembly point for behavior. Thus, the plasticity that is responsible for a rewarded behavior, which might be called 'primary plasticity' (Table 1), is almost certain to disturb a variety of other behaviors. In the case of H-reflex conditioning, the shift in the motoneuron firing threshold seen in HR↓ animals could represent primary plasticity: it could help decrease the H-reflex and thereby increase the probability of a reward. At the same time, it probably has other effects, such as reducing the motoneuron's response to excitatory inputs during walking or climbing. By disturbing these other important behaviors, the threshold change is likely to induce further learning that preserves or restores them. The additional plasticity that underlies this further learning might be labeled 'compensatory'. As indicated in Table 1, compensatory plasticity, like primary plasticity, is identified by its effects on behavior.

The change in the contralateral spinal cord revealed by the nerve volley data (Fig. 4A) could represent compensatory plasticity. This change is evident only after the spinal cord has been isolated by anesthesia and transection. In the awake behaving animal, supraspinal influence and spinal cord function conspire to ensure that behavior on the unconditioned side, at least as assessed by its H-reflex, changes little during conditioning. Nevertheless, as the nerve volley data indicate, the CNS substrates that underlie this unchanged behavior are different after conditioning. The behavior is preserved, but its neuronal bases have been altered.

Complex plasticity is inevitable

The apparent ubiquity in the CNS of the capacity for activity-driven plasticity ensures that change at one site, by modifying the activity that reaches other sites, will eventually cause further change, which might be labeled 'reactive' (Table 1). Like compensatory plasticity, reactive plasticity might bear no obvious relationship to the newly acquired behavior and, when viewed only in the context of that behavior, might even be maladaptive. Furthermore, the fact that some changes that in themselves improve behavior might lead to reactive changes that degrade behavior probably helps to determine the sites and nature of primary and compensatory plasticity.

A recently described example of reactive plasticity is potentially relevant to H-reflex conditioning. Chronic suppression of activity in Ia afferents (produced by tetrodotoxin-filled nerve cuffs) increases the amplitude of Ia EPSPs in the motoneuron: with chronic reduction in activity, the synapse becomes stronger[53]. This suggests that, while tonic increase (HR↓ mode) or decrease (HR↑ mode) in presynaptic inhibition at the Ia terminal could cause a short-term decrease or increase in the H-reflex, it is unlikely to account for the gradual decrease (HR↓ mode) or increase (HR↑ mode) that occurs over the weeks of conditioning. If the Ia synapse reacts to the suppression that is induced by presynaptic inhibition as it does to the suppression that is induced by tetrodotoxin, change in presynaptic inhibition would be in the long run an ineffective response to the conditioning task. That other mechanisms are responsible for the gradual H-reflex change is suggested by the fact that change in Ia EPSPs alone can account for only a small part of the nerve volley asymmetry found in anesthetized transected animals (Fig. 4A,B)[11,27].

Defining the translation of plasticity into behavior

While the behavioral effects of several of the spinal cord changes that are associated with H-reflex conditioning (for example, the threshold change in HR↓ motoneurons) can be predicted with some confidence, the effects of other changes, and the causal connections between changes, remain to be defined. For example, the altered F terminals or C terminals, or both, could conceivably convey to the motoneuron the descending influence responsible for generating the threshold change. Alternatively, the altered F terminals might modify disynaptic Group-I inhibition that affects the H-reflex[30]. Or, these synaptic changes might represent compensatory or reactive plasticity.

Resolution of these questions, and understanding of why the H-reflex becomes larger or smaller, requires a more complete description of the complex pattern of spinal cord plasticity that is associated with conditioning, including the contralateral changes. It also requires description of the interaction that occurs during performance between the spinal cord plasticity and descending influence. It is likely that this descending influence changes over the course of training. Without such change, the contralateral plasticity revealed by the nerve volley study (Fig. 4A) would greatly change the contralateral H-reflex (which does not occur), and the shift in the firing threshold of the motoneuron (Fig. 4B) would probably lead to a drop in background EMG (which also does not occur). For example, an increase in tonic descending excitation could counteract the effect of the threshold shift on tonic motoneuron activity (without necessarily eliminating the effect of the shift on the H-reflex), and thereby maintain background EMG.

While the spinal cord plasticity that is currently under study directly underlies H-reflex change, it is likely that H-reflex conditioning, because it is motivated by an alimentary reward and because it depends on tonic change in descending influence, involves

supraspinal plasticity as well. Plasticity in the sensorimotor cortex is suggested by the changes in somatosensory evoked potentials that accompany H-reflex conditioning[54], as well as by the abundant evidence for such plasticity in many other situations (for example, ablations, specific stimulation paradigms)[55,56]. Cortical change can occur rapidly, and might underlie the change in descending influence that gradually changes the spinal cord. Cerebellar plasticity appears likely on the basis of data from other conditioning models[57] and the observed effects of cerebellar stimulation[58,59]. Further elucidation of the complex spinal cord plasticity and of the descending influence that creates it should guide study of the associated supraspinal plasticity.

The ultimate objective is to define all the major components of the plasticity that is produced by the H-reflex conditioning protocol and to understand their effects on behavior. Because phenomena that are comparable to H-reflex conditioning contribute to normal development and learning (for example, Fig. 3), achievement of this objective should contribute to an understanding of the acquisition and maintenance of more complex behaviors.

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