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RESEARCH ARTICLE

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Corticospinal tract transection prevents operantly conditioned H-reflex increase in rats

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Abstract Operant conditioning of the H-reflex, the electrical analog of the spinal stretch reflex, in freely moving rats is a relatively simple model for studying long-term supraspinal control over spinal cord function. Motivated by food reward, rats can gradually increase (i.e., up-condition) or decrease (i.e., down-condition) the soleus H-reflex. Earlier work showed that corticospinal tract transection prevents acquisition and maintenance of H-reflex down-conditioning while transection of other major spinal cord tracts does not. This study explores the effects on acquisition of up-conditioning of the right soleus H-reflex of mid-thoracic transection of: the right lateral column (LC, five rats) (containing the rubrospinal, vestibulospinal, and reticulospinal tracts); the entire dorsal column (DC, six rats) [containing the main corticospinal tract (CST) and the dorsal ascending tract (DA)]; the CST alone (five rats); or the DA alone (seven rats). After initial (i.e., control) H-reflex amplitude was determined, the rat was exposed for 50 days to the up-conditioning mode in which reward was given when the H-reflex was above a criterion value. H-reflex amplitude at the end of up-conditioning was compared to initial H-reflex amplitude. An increase ≥20% was defined as successful up-conditioning. In intact rats, H-reflex amplitude at the end of up-conditioning averaged 164% (±10%, SE), and 81% were successful. In the present study, LC and DA rats were similar to intact rats in final H-reflex amplitude and percent successful. In contrast, results for DC and CST rats were significantly different from those of intact rats. In the six DC rats, final H-reflex amplitude averaged 105% (±3)% of control and none was successful; and in the five CST rats, final H-reflex amplitude averaged 94% (±3)% and none was successful. The results indicate that the main CST, located in the dorsal column, is essential for H-reflex up-conditioning as it is for down-conditioning, while the dorsal column ascending tract and the ipsilateral lateral column (containing the main rubrospinal, vestibulospinal, and reticulospinal tracts) do not appear to be essential.

Keywords Spinal cord injury · Dorsal column · Lateral column · Plasticity · Learning

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Introduction

Descending activity from the brain gradually changes the spinal cord during development, during skill acquisition throughout life, and after spinal cord injury or with other supraspinal disorders (Wolpaw and Tennissen 2001); yet the pathways and the processes through which this activity induces and maintains spinal cord plasticity are not known. These mechanisms are an important component of motor function; and their understanding could lead to novel methods for inducing, guiding, and assessing recovery after injury.

The spinal stretch reflex (SSR), the simplest behavior of the vertebrate CNS, is mediated by a wholly spinal and largely monosynaptic pathway, consisting of the primary afferent neuron, the α-motoneuron, and the synapse between them (Brown 1984; Matthews 1972). Operant conditioning of the SSR or its electrical analogue, the H-reflex, has been demonstrated in monkeys (Wolpaw 1987, Wolpaw et al. 1983), humans (Evatt et al. 1989; Wolf and Segal 1990, 1996; Wolf et al. 1995), and rats (Chen and Wolpaw 1995). Motivated by a paradigm in which reward depends on reflex amplitude, both primates and rats can gradually increase or decrease the SSR or the H-reflex.

H-reflex conditioning depends on descending influence from the brain to the spinal cord. Contusion injury of the thoracic spinal cord impairs conditioning of the soleus H-reflex, and the degree of impairment correlates with the percentage of white matter lost (Chen et al. 1996, 1999). Current studies are defining the roles of

specific spinal cord tracts in H-reflex conditioning. Work to date (Chen and Wolpaw 1997, 2002; Chen et al. 2000) indicates that the main corticospinal tract (CST), located in the dorsal column (DC), is essential for both acquisition and maintenance of down-conditioning, while the lateral column (LC) (containing rubrospinal, vestibulospinal, and reticulospinal tracts and several ascending tracts (Holstege and Kuypers 1987; Kennedy 1990; Kuypers 1981; Tracey 1995)) and the dorsal column ascending tract (DA) are not essential. The present study explored the role of specific spinal cord tracts in up-conditioning. Rats with LC, DC, CST, or DA transection were exposed to the up-conditioning protocol and the effects on H-reflex amplitude were compared to the effects observed in intact rats exposed to up-conditioning.

Materials and methods

All animal procedures conformed to the "Guide for the Care and Use of Laboratory Animals" of the Institute of Laboratory Animal Resources, Commission on Life Sciences, National Research Council (National Academy Press, Washington, DC, 1996). They had been reviewed and approved by the Institutional Animal Care and Use Committee of the Wadsworth Center. The protocols for chronic electrode implantation in freely moving rats, H-reflex conditioning, and spinal cord tract transection have been described in detail previously (Chen and Wolpaw 1995, 1997, 2002; Chen et al. 1996, 1999, 2001b) and are summarized here.

Subjects were female Sprague-Dawley rats (200–300 g at the beginning of the study). Under general anesthesia (ketamine HCl, 80 mg/kg, i.p.; xylazine, 10 mg/kg, i.p.) each rat was implanted with chronic stimulating and recording electrodes in the right leg. To obtain soleus EMG activity, a pair of fine-wire electrodes were inserted into the right soleus muscle. To elicit the H-reflex, a silicone rubber nerve stimulating cuff was placed on the right posterior tibial nerve. The Teflon-coated wires from these implants went subcutaneously to a connector plug on the skull. Data collection began at least 30 days after implantation. During collection, the animal lived in a standard cage with a 40-cm flexible cable attached to the skull plug. This cable, which permitted the animal to move freely around the cage, conveyed the wires from the electrodes to an electrical commutator above the cage. They then passed to an EMG amplifier and a nerve cuff stimulation unit. A computer system monitored soleus EMG continuously and controlled the nerve cuff stimulus. If the absolute value (i.e., equal to the full-wave rectified value) of background (i.e., ongoing) EMG stayed within a specified range for a randomly varying 2.3- to 2.7-s period, a 0.5-ms stimulus pulse was given by the nerve cuff. Pulse amplitude was first set slightly above M-response threshold and was thenceforth automatically adjusted to maintain stable M-response amplitude throughout data collection. In the control mode, the computer simply measured each absolute value for 50 ms after stimulation and determined H-reflex amplitude. In the HRup conditioning mode, it provided a reward (a 20-mg food pellet) 200 ms after the stimulus if EMG amplitude in the H-reflex interval (5.5–9.0 ms after the stimulus in a typical rat) exceeded a criterion value. During its normal activity, the animal typically fulfilled the background EMG requirement, and thus received the nerve cuff stimulus 2500–7500 times/day. H-reflex amplitude was calculated as average EMG amplitude for the H-reflex interval minus average background EMG amplitude. It was expressed in units of average background EMG amplitude.

Spinal cord pathway transection was performed by electrocautery (Chen and Wolpaw 1997; Chen et al. 2001b). The animal was anesthetized as for electrode implantation and a one-vertebra dorsal laminectomy was performed at T8 or T9 with minimal disturbance of the dural envelope. The rat was placed in a stereotaxic frame and the cord was visualized under a dissection microscope. The cauterizer was activated in brief pulses to minimize thermal damage to adjacent tissue. For LC rats, the lateral half of the right side of the spinal cord was transected. For DC rats, transection extended 0.4 mm to either side of the midline and 1.1 mm into the spinal cord from the dorsal surface. For CST rats, the tip of the cautery was positioned 1.0 mm left of the midpoint of the dorsal surface of the spinal cord, pointed medially at an angle of 45° from vertical, and advanced 1.7 mm. This was calculated to produce a transection track that was 1.5 mm long and about 0.5 mm wide in the transverse plane and involved the dorsal horn of the left side and the dorsal column CST of both sides. As previously noted, this is the main CST in the rat (Chung et al. 1987; Cliffer and Giesler 1989; Patterson et al. 1989, 1990; Smith and Bennett 1987; Tracey 1995). For DA rats, transection extended 0.4 mm to either side of the midline and 0.7 mm into the spinal cord from the dorsal surface.

Following transection, the site was rinsed with normal saline and covered with Durafilm to minimize connective tissue adhesions to the dura, and the muscle and skin were sutured in layers. DC, CST, and DA transections were bilateral because a transection that was both complete and exclusively ipsilateral was not technically feasible, and because, at T8–9, the main CST and the DA are mainly or exclusively ipsilateral to the leg they innervate (Tracey 1995) so that the effects on H-reflex conditioning of ipsilateral and bilateral transections should be comparable. LC transection was ipsilateral because we wished to avoid the disability likely to be associated with a bilateral LC transection (which would have destroyed about two-thirds of the white matter), and because, at T8–9, major LC descending tracts (i.e., rubrospinal, vestibulospinal, and reticulospinal tracts) are mainly or exclusively ipsilateral to the leg they innervate (Tracey 1995) so that the effects on H-reflex conditioning of ipsilateral and bilateral transections should be comparable.

Immediately after the transection procedure, the rat was placed under a heating lamp and received an analgesic (Demerol, 0.2 mg, i.m.). Once awake, it was given a second dose of analgesic, returned to its cage and allowed to eat and drink freely. Until spontaneous voiding returned, the bladder was expressed at least twice per day, and antibiotics Gentocin (gentamicin sulfate; 0.25 mg, b.i.d., i.m.) and Flo-Cillin (penicillin G benzathine and penicillin G procaine; 15,000 units, q.o.d., i.m.) and lactated Ringer's solution (5 ml, b.i.d., s.c.) were administered. For the first 5 days after transection, the animal was given a soft mash of water-soaked rat chow with added vitamin C (about 8 mg/kg/day, in order to keep urine acidic to avoid urinary tract infection). Body weight was measured every day and a high-calorie dietary supplement (Nutri-Cal; 2–4 ml/day, p.o.) was given until body weight regained its pre-lesion level. At least 10 g of apple was given each day from before transection until the end of the study. Starting the day after transection, open-field locomotion was assessed according to the rating scale of Basso et al. (1995) (i.e., the BBB test) for each rat (except for three DC and three LC rats) every day for the first 3 days and then every other day until locomotion had returned to normal (i.e., until the BBB scores for both hindlimbs were 21).

Figure 2A shows the experimental protocol. To permit injury-induced changes in reflex excitability to stabilize (Malmsten 1983; Chen et al. 2001b), HRup conditioning began 47–103 days after spinal cord tract transection. To determine which spinal cord tracts are essential for HRup conditioning, we transected a specific tract and collected H-reflex data first under the control mode for at least 10 days and then under the HRup conditioning mode for 50 days (except for one LC rat and one CST rat in which the head plug was lost after 33 HRup days). We then compared H-reflex amplitude at the end of up-conditioning (i.e., the final 10 days of HRup exposure) to control H-reflex amplitude (i.e., the final 10 days of control-mode exposure) to determine whether the specific transection affected the H-reflex increase that usually occurs in intact rats exposed to HRup conditioning. Differences in H-reflex increase among the five groups [i.e., 43 intact rats from other studies (Chen and Wolpaw 1995, 1996; Chen et al. 1999; Carp et al. 2001), LC rats, DC rats, CST rats, and DA rats] were assessed by ANOVA

with post hoc pairwise comparisons by the Newman-Keuls test. Differences between groups in the percentage of rats in which HRup conditioning was successful (defined as in Chen and Wolpaw (1995) as an increase of ≥20% in H-reflex amplitude) were assessed by Fisher's exact test.

At the end of the study, each rat was given an overdose of sodium pentobarbital (i.p.) and perfused through the heart with saline followed by 4% paraformaldehyde in 0.1 M phosphate buffer (pH 7.3). The placement of the EMG electrodes and the nerve cuff and the integrity of the tibial nerve were verified and the soleus muscles of both sides were removed and weighed. The spinal cord was removed and blocks encompassing the lesion were embedded in paraffin. Transverse 10- to 20-µm-thick serial sections were cut and stained with Luxol fast blue (for myelinated fibers) and 0.1% cresyl violet (for Nissl substance). Camera lucida drawings were made at a magnification of 50. Remaining white matter was identified at a magnification of 200 by the presence of normal Luxol fast blue staining. Figure 1 shows camera lucida drawings of T8–T9 transverse sections from two LC, two DC, two CST, and two DA rats and an intact rat. The tracings were enlarged photographically and then traced on a digitizing pad (Summagraphics Co.) using Sigmascan (Jandel Scientific). The tissue remaining at the rostrocaudal epicenter of the transection was measured according to the method of Olby and Blakemore (1996). For DC, CST, and DA rats, the area of DC, CST, or DA remaining was measured as percent of the area of that structure 2–5 mm rostral to the rostral limit of the lesion. [In accordance with Olby and Blakemore (1996), the structure at a level rostral to the rostral limit of the lesion was found to be comparable in area to the structure in intact rats.] For LC rats, the area of right LC remaining was measured as percent of the left LC. (Nearly identical values were obtained when LC area was calculated as percent of the right LC rostral to the rostral limit of the lesion.) Thus, for example, a value of 15% indicates that, at the transection epicenter, 85% of the LC was destroyed. The border between the LC and the ventral column was defined according to Paxinos and Watson (1986). The CST was distinguished in the dorsal column from the rest of the DC (i.e., the DA) by its obvious darker blue staining (Fig. 1, photomicrograph).

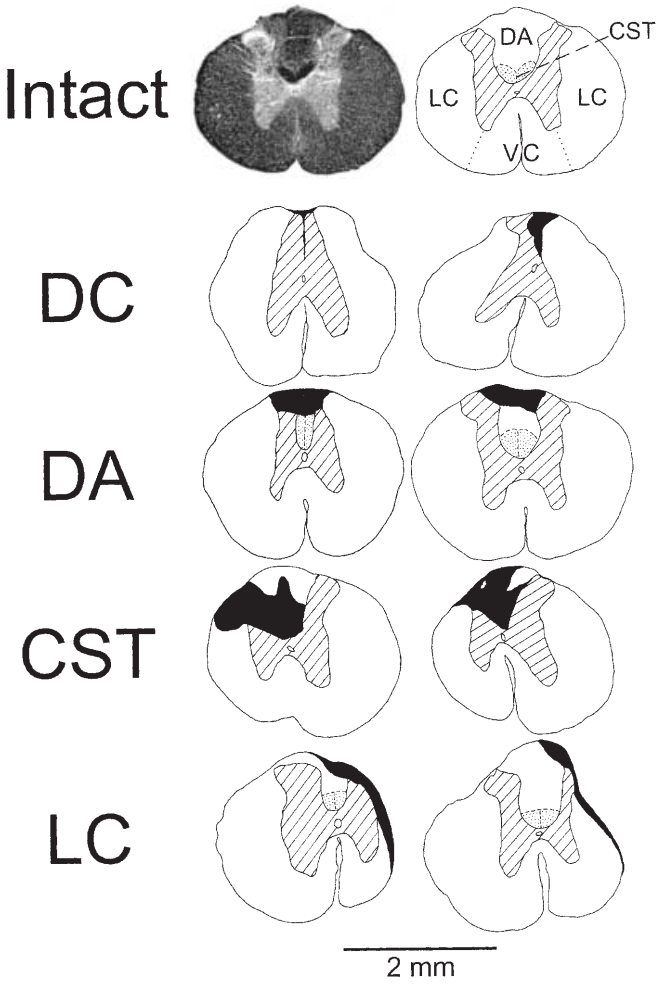

Fig. 1 *Row 1* Photomicrograph (*left*) and camera lucida drawing [*right*; with the gray matter *hatched*, the main corticospinal tract (*CST*) *stippled* and the dorsal ascending tract (*DA*) *clear*, and the lateral and ventral columns labeled (*LC* and *VC*, respectively)] of transverse sections T8–T9 of spinal cord from an intact (i.e., untransected) rat. Note that the main CST area can be easily distinguished from the rest of the dorsal column by its darker staining in the photomicrograph. *Rows 2–5* Representative camera lucida drawings of transverse sections of T8–T9 spinal cord (two for each transection group) from rats with transection of the entire dorsal column (DC rats), the dorsal ascending tract (DA rats), the dorsal column corticospinal tract (CST rats), or the right lateral column (LC rats). *Hatching* indicates gray matter, *stippled areas* are the main corticospinal tract, and *black areas* are necrotic debris, cystic cavities, or fibrous septa

Results

Spinal cord tract transections

As illustrated in Fig. 1, tissue damage at the lesion epicenter was largely confined to the targeted area (except for CST rats, in which the contralateral cautery approach made some damage to the left dorsal horn and/or dorsal LC inevitable). In the LC rats, 21 (±11)% (mean ± SD, range: 9–35%) of the right LC remained. Two LC rats also showed slight loss of the right DA (83% and 84% remaining). In the DC rats, only 2 (±4)% (range: 0–9%) of the DC remained. In all the CST rats, the CST was completely destroyed. Most CST rats also showed some loss of the right DA, with 45 (±29)% (range: 4–72%) remaining. In the DA rats, 27 (±25)% (range: 0–62%) of the right DA remained, while the CST remained completely intact. (CST and DA rats also showed variable damage to the left DA and/or LC.)

HRup conditioning

Figure 2B displays final H-reflex amplitudes for the LC, DC, CST, and DA rats exposed to the HRup mode conditioning, and compares them to data from 43 intact rats similarly exposed (data from Carp et al. 2001; Chen and Wolpaw 1995, 1996, 1997; Wolpaw and Chen 2001). In the intact group, final H-reflex amplitude averaged 164% (±10% SEM) of the control-mode H-reflex, and 35 of 43 rats (81%) were successful [i.e., H-reflex increase to ≥120% of its initial value (Chen and Wolpaw 1995); solid symbols in Fig. 1B]. Results for the DA and LC groups were similar to those in the intact group: final H-reflex amplitude for LC rats averaged 179% (±26% SEM) and four of five (80%) were successful, and final

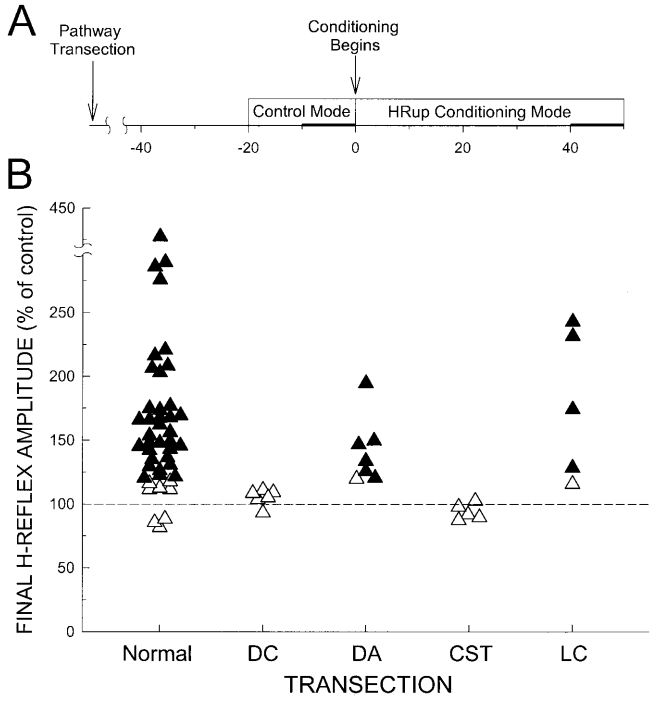

Fig. 2 **A** Experimental protocol. Rats underwent tract transection, and after a period of at least 30 days were exposed for 10–20 days to the control mode, in which the H-reflex was simply measured to determine its initial amplitude. They were then exposed for 50 days to the HRup conditioning mode, in which food reward was given when H-reflex amplitude was above a criterion value. Background EMG, M-response amplitude, and trials/day remained stable throughout data collection. **B** Average H-reflex amplitude for each rat for the final 10 days of HRup conditioning (days 41–50 in **A**) as percent of average H-reflex amplitude for the final 10 days of control-mode exposure (days –10 to 0 in **A**) for all intact, LC, DC, CST, and DA rats exposed to HRup conditioning. *Filled symbols* indicate that HRup conditioning was successful, i.e., increase to ≥120% of initial H-reflex amplitude (Chen and Wolpaw 1995). (Data for intact rats are from Carp et al. 2001; Chen and Wolpaw 1995, 1996, 1997.) As detailed in the text, LC and DA rats achieved H-reflex increases comparable to those of intact rats, while DC and CST rats did not increase the H-reflex

H-reflex amplitude for DA rats averaged 141% (±10% SEM) and six of seven (86%) were successful. There were no significant differences between the intact group and either the DA or LC groups in final H-reflex amplitude or in percentage of rats that exhibited successful conditioning (P>0.9 vs intact group for all comparisons).

In contrast, final H-reflex amplitude for DC rats averaged 105% (±3% SEM) and none of six (0%) was successful, and final H-reflex amplitude for CST rats averaged 94% (±3% SEM) of control and none of five (0%) was successful. Both the DC and CST groups differed from the intact group in both final H-reflex value (P<0.05) and number successful (P<0.001). Over the entire period of data collection in all rats, background EMG and M-response amplitude, which were controlled as indicated in "Materials and methods," remained stable. These results imply that the dorsal column CST (i.e., the main CST) is essential for HRup conditioning, and that the LC and DA are not essential.

Specificity of transection effects on HRup conditioning

As described above, while all DC and CST rats had complete or nearly complete destruction of the targeted tract, LC and DA rats varied considerably in the completeness of their transections. However, in neither group did the amount of the tract remaining correlate significantly with the amount of H-reflex increase (P>0.25 for DA rats and P>0.55 for LC rats). Indeed, in the three DA rats with only 0–5% of DA remaining, final H-reflex amplitude averaged 154% (±22% SEM), while in the four DA rats with 39–62% of DA remaining final H-reflex amplitude averaged 132% (±6% SEM). In the two LC rats with 9–13% of LC remaining, final H-reflex amplitude averaged 174% (±58% SEM), while in the three LC rats with 21–35% of LC remaining final H-reflex amplitude averaged 182% (±33% SEM).

Also as described above, tract transections often destroyed some tissue in addition to the targeted tract. Thus, in order to assess further the dependence of conditioning-induced H-reflex increase on specific tracts, we performed multiple linear regression analysis of final H-reflex amplitude on the extent of CST, DA, and/or LC transection in all 23 rats. Final H-reflex amplitude varied significantly with damage to the entire CST (r^2=0.26, P=0.005) or to the right CST alone (r^2=0.30, P=0.003) independent of damage to other areas. Final H-reflex amplitude did not vary significantly with damage to the right LC (r^2=0.05, P=0.16), the right DA (r^2=0.00, P=0.86), or the entire DA (r^2=0.00, P=0.99). In addition, final H-reflex amplitude did not vary significantly with the extent of damage to the pooled DA and LC (expressed as a percent of the total non-CST white matter; r^2=0.01, P=0.6). This analysis is consistent with the conclusion that the CST, and the CST alone, is essential for HRup conditioning.

Potential influence on HRup conditioning of nonspecific effects of tract transections

As in previous studies (Chen and Wolpaw 1997; Chen et al. 2001b), rats showed a transient hindlimb paralysis immediately after transection (both hindlimbs for DC, CST, and DA rats and right only for LC rats). This deficit abated over several days. For all rats, locomotion about the cage appeared normal or nearly normal within 3–10 days. Final H-reflex amplitude at the end of HRup conditioning did not vary significantly with the number of days it took the right hindlimb BBB score to return to the normal value of 21 (r^2=0.03, P=0.51 by linear regression). Spontaneous voiding of the bladder, which was absent immediately after injury, returned over 0–5 days. There was no significant relationship between final H-reflex amplitude and the time until return of bladder function (r^2=0.10, P=0.14). Final H-reflex amplitude did not vary significantly with the number of days between transection and the onset of HRup conditioning (r^2=0.07, P=0.23).

Body weight fell 3–11% in the 1st week after transection, regaining its pre-transection level in 1–6 weeks. For all rats, weight increased from 281 g (±24 g SD) at the time of transection to 358 g (±37 g SD) at the time of perfusion. There was no significant relationship between final H-reflex amplitude and weight gained between transection and the end of HRup conditioning (r^2=0.06, P=0.26). Soleus muscle weights (measured as percent of body weight) were symmetrical and did not differ significantly from those of intact rats.

Inclusion of any of the factors described above in the multiple regression analysis described in the preceding section did not alter the significant and unique dependence of successful HRup conditioning on the CST.

Discussion

Under the HRup conditioning mode, LC and DA rats achieved H-reflex increases comparable to those achieved by intact rats, but DC and CST rats did not. None of the DC and CST achieved successful up-conditioning. In the rat spinal cord, the major occupants of the dorsal column at the level of our transections are the main CST (occupying the ventralmost part of the DC) and the rostrally projecting axons of primary afferents and spinal neurons that together comprise the DA (occupying the more dorsally located remainder of the DC) (Tracey 1995). Thus, the primary implication of the present results is that the dorsal column main CST is essential for HRup conditioning, and that DA and the ipsilateral LC are not. This conclusion is further supported by regression analysis indicating that loss of up-conditioning was strongly correlated with damage to CST and was not correlated with damage to other white matter.

Effects of the tract transections alone on H-reflex amplitude do not appear able to explain these results. In rats not exposed to the conditioning protocol, neither DC nor CST transection had any persistent effect on H-reflex amplitude over the course of several months after lesion (Chen et al. 2001b). Thus, the failure to increase the H-reflex in DC and CST rats cannot be ascribed to a hypothetical transection-induced H-reflex decrease. On the other hand, DA or LC transection produced a modest increase in H-reflex amplitude that was evident 3–6 weeks after transection and lasted at least several months (Chen et al. 2001b). To avoid the complication of these medium-term effects on HRup conditioning in the present study, we began HRup exposure at least 47 days after transection, well after any DA or LC transection-induced increase in H-reflex amplitude should have occurred and stabilized (Chen et al. 2001b). That the H-reflex amplitude had already stabilized in these rats is also indicated by the lack of correlation between control-mode H-reflex amplitude and time after DA or LC transection (r^2=0.09 and 0.01, respectively, and P>0.5 for both by linear regression). Thus, the success of HRup conditioning in DA and LC rats cannot be ascribed to lesion-induced H-reflex increase.

Some ascending axons course through the darkly stained region that defines the CST near its border with the DA (Smith and Bennett 1987). These fibers represent only a small percentage of the total number of fibers in the CST. Assuming that these ascending fibers have functions similar to comparable fibers in the DA itself (the transection of which had no effect on HRup conditioning), it is unlikely that this small ascending projection within the CST contributes significantly to the loss of HRup conditioning after CST transection. Confirmation of this conclusion will require assessment of HRup conditioning in rats after pyramidal tract or sensorimotor cortex lesions.

Pathways in addition to the main CST may influence H-reflex conditioning. While the results imply that the rubrospinal, vestibulospinal, and reticulospinal tracts are not essential for HRup conditioning, these tracts are largely but not exclusively ipsilateral at mid-thoracic levels (Kennedy 1990; Kuypers 1981; Tracey 1995), so that the effects of bilateral LC lesions should be evaluated. The importance for H-reflex conditioning of the ventral column, which contains a minor projection of the CST (Brosamle and Schwab 1997), also remains to be determined.

While physiological, anatomical, and behavioral data (Carp and Wolpaw 1994, 1995; Chen and Wolpaw 1996; Feng-Chen and Wolpaw 1996; Wolpaw and Chen 2001; Wolpaw et al. 1986) suggest that H-reflex up-conditioning and down-conditioning are not mirror images of each other, but rather have different mechanisms, they appear to be similarly dependent for their acquisition on the CST, and similarly independent of the LC and DA. The results of the present study, along with the previous demonstration of the importance of the CST in HRdown conditioning (Chen and Wolpaw 1997, 2002; Chen et al. 2000), describe a CST role – long-term adaptive control over spinal reflex strength – that seems distinctly different from the immediate CST control over distal fine motor activity previously recognized (Cheney et al. 1991; Darian-Smith et al. 1999; Davidoff 1990; Porter and Lemon 1993). The demonstration of this effect in the rat lumbosacral spinal cord, which is thought to contain very few direct CST-to-motoneuron connections, suggests that this long-term CST control operates through spinal cord interneurons. Furthermore, the close similarities between H-reflex conditioning in monkeys and rats (Wolpaw 1997), the evidence that strokes involving sensorimotor cortex prevent SSR conditioning in humans (Segal 1997), and the evidence that conditioning changes interneuronal synaptic terminals on primate motoneurons (Feng-Chen and Wolpaw 1996) suggest that the CST exerts comparable long-term adaptive reflex control in primates and that this control is effected through spinal cord interneurons rather than through direct motoneuron connections.

The results of CST transection imply that the contralateral sensorimotor cortex – the primary source of the CST (Miller 1987; Li et al. 1990) – is essential for H-reflex conditioning. Studies of the effects of ablation of

this cortical area are needed to confirm this, because other cortical areas do make minor contributions to the CST (Miller 1987; Li et al. 1990). These ablation studies could in turn further demonstrate the importance of the CST. The importance of ipsilateral sensorimotor cortex is also worthy of exploration, especially in view of the evidence that H-reflex conditioning is associated with contralateral, as well as ipsilateral, spinal cord plasticity (Wolpaw and Lee 1989) and that strokes involving sensorimotor cortex on one side affect stretch reflexes on both sides (Thilmann et al. 1990). The evidence that rubrospinal tract transection does not impair up-conditioning or down-conditioning implies that cerebellar output to spinal cord is not essential. On the other hand, initial data (Chen et al. 2001a) on the effects of cerebellar nuclear ablation on down-conditioning suggest that cerebellar-cortical connections are important.

While conditioned H-reflex change can persist for days after spinal cord transection (Wolpaw and Lee 1989) and some aspects of the spinal cord plasticity associated with up-conditioning or down-conditioning have been described (Wolpaw 1997 for review), the long-term maintenance of H-reflex change (i.e., over weeks and months) may require continued descending influence (Wolpaw et al. 1986; Chen and Wolpaw 1996; Chen et al. 2000). Recent studies indicate that, in rats that have decreased the H-reflex in response to the HRdown mode, CST transection leads to loss of the decrease over about 10 days, while LC or DA transection has no effect (i.e., the H-reflex remains small) (Chen and Wolpaw 2002). The effects of tract transections on maintenance of conditioned H-reflex increase are not yet clear. Initial data suggest that neither LC, DA, nor CST transection leads to loss of a conditioned H-reflex increase (Chen et al. 2000). Confirmation of this preliminary result would add to the evidence for mechanistic differences between H-reflex up-conditioning and down-conditioning.

Resolution of these issues should enhance understanding of H-reflex conditioning specifically and of long-term supraspinal control of spinal cord function generally. This knowledge should help clarify the reflex abnormalities that occur with spinal cord injury and could provide a basis for the design of new therapeutic interventions to induce and guide spinal cord plasticity after injury.

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