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Operant Conditioning of Reciprocal Inhibition in Rat Soleus Muscle

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Chen, Xiang Yang, Lu Chen, Yi Chen, and Jonathan R. Wolpaw. Operant conditioning of reciprocal inhibition in rat soleus muscle. *J Neurophysiol* 96: 2144–2150, 2006. First published June 28, 2006; doi:10.1152/jn.00253.2006. Operant conditioning of the H-reflex, the electrical analog of the spinal stretch reflex (SSR), induces activity-dependent plasticity in the spinal cord and might be used to improve locomotion after spinal cord injury. To further assess the potential clinical significance of spinal reflex conditioning, this study asks whether another well-defined spinal reflex pathway, the disynaptic pathway underlying reciprocal inhibition (RI), can also be operantly conditioned. Sprague-Dawley rats were implanted with electromyographic (EMG) electrodes in right soleus (SOL) and tibialis anterior (TA) muscles and a stimulating cuff on the common peroneal (CP) nerve. When background EMG in both muscles remained in defined ranges, CP stimulation elicited the TA H-reflex and SOL RI. After collection of control data for 20 days, each rat was exposed for 50 days to up-conditioning (RIup mode) or down-conditioning (RIdown mode) in which food reward occurred if SOL RI evoked by CP stimulation was more (RIup mode) or less (RIdown mode) than a criterion. TA and SOL background EMG and TA M response remained stable. In every rat, RI conditioning was successful (i.e., change ≥20% in the correct direction). In the RIup rats, final SOL RI averaged 171 ± 28% (mean ± SE) of control, and final TA H-reflex averaged 114 ± 14%. In the RIdown rats, final SOL RI averaged 37 ± 13% of control, and final TA H-reflex averaged 60 ± 18%. Final SOL RI and TA H-reflex sizes were significantly correlated. Thus like the SSR and the H-reflex, RI can be operantly conditioned; and conditioning one reflex can affect another reflex as well.

INTRODUCTION

Operant conditioning of the spinal stretch reflex (SSR), or its electrical analog the H-reflex, is a simple model for studying the brain's induction and maintenance of activity-dependent plasticity in the spinal cord. When exposed to an operant conditioning protocol, monkeys, humans, rats, and mice can gradually increase or decrease the SSR or the H-reflex (Carp et al. 2005; Chen and Wolpaw 1995; Evatt et al. 1989; Wolpaw 1987; Wolpaw et al. 1983; reviewed in Wolpaw 1997, 2001; Wolpaw and Tennissen 2001).

As adaptive behaviors acquired through practice, these operantly conditioned reflex changes qualify as simple motor skills (Compact OED 1993) (Chen et al. 2005b). They involve persistent anatomical and physiological changes in the spinal cord itself (Carp and Wolpaw 1994, 1995; Carp et al. 2001; Feng-Chen and Wolpaw 1996; Pillai et al. 2004; Wang et al. 2004, 2006; Wolpaw and Lee 1989). The main corticospinal tract (CST) is essential for H-reflex conditioning, whereas other major descending pathways are not (Chen and Wolpaw 1997, 2002; Chen et al. 2002, 2003). Recent data show that H-reflex conditioning can modify locomotor function in normal rats (Chen et al. 2005b) and can be used to improve locomotion after a partial spinal cord injury (Chen et al. 2005a). Thus spinal reflex conditioning could be a new method for inducing and guiding spinal plasticity and could help to improve motor function after spinal cord injury or in other motor disorders.

Up to the present, spinal reflex conditioning has been demonstrated only for the SSR and the H-reflex. This study explores the generality of this conditioning phenomenon by asking whether another well-defined spinal reflex pathway can also be operantly conditioned. It explores operant conditioning of the reciprocal inhibition (RI) of soleus (SOL) produced by the disynaptic pathway consisting of the Ia afferent from the antagonist muscle [i.e., the tibialis anterior (TA)], the Ia inhibitory interneuron, and the agonist (i.e., SOL) alpha motoneuron (Ashby and Wiens 1989; Baldissera et al. 1981; Friesen and Stent 1978; Fu et al. 1978; Sherrington 1913). The results broaden the range of spinal reflex conditioning phenomena and encourage their further development as a new rehabilitation methodology.

METHODS

Animal preparation

Subjects were 10 male Sprague-Dawley rats weighing 250–350 g at the beginning of the study. All procedures satisfied 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, D.C., 1996) and had been reviewed and approved by the Institutional Animal Care and Use Committee of the Wadsworth Center.

The methods for construction and implantation of the chronic nerve stimulating cuff and the EMG recording electrodes were comparable to those previously described for study of H-reflex conditioning (Chen and Wolpaw 1995, 1997, 2002, 2005; X. Y. Chen et al. 2002, 2003; Y. Chen et al. 2005b; Wolpaw and Chen 2006). Each rat was implanted under general anesthesia [ketamine HCl (80 mg/kg) and xylazine (10 mg/kg), intraperitoneal]. To record EMG activity, pairs of multistranded (10 × 50 gauge) stainless-steel fine-wire electrodes with the final 0.5 cm stripped were implanted in the right soleus (SOL) and right tibialis anterior (TA) muscles. To elicit reciprocal inhibition (RI) of the SOL, the silicone rubber nerve cuff (with inside diameter about twice that of the nerve) containing a pair of stainless-steel multi-stranded fine-wire electrodes was placed on the right common peroneal (CP) nerve at the knee ~3.5 cm below its origin from the sciatic and was closed by a suture that encircled the cuff. The

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Teflon-coated wires from the muscles and the nerve cuff passed subcutaneously to a connector plug mounted on the skull with stainless steel screws and dental cement. Immediately after surgery, the rat was placed under a heating lamp and given an analgesic [Demerol (0.2 mg im)]. Once awake, it received a second dose of analgesic and was returned to its cage and allowed to eat and drink freely.

Data collection

Data collection began ≥23 days after surgery [41± 15 (SD) day (range: 23–71)]. During data collection, the rat lived in a standard rat cage with a 40-cm flexible cable attached to the skull plug. The cable, which allowed the animal to move freely in the cage, conveyed the wires from the electrodes to a commutator above the cage which connected to EMG amplifiers and a nerve-cuff stimulation unit. The rat had free access to water throughout. During operant conditioning of SOL RI, it received most of its food by performing the task described in the following text. Animal well-being was carefully checked several times each day, and body weight was measured weekly. Laboratory lights were dimmed from 2100 to 0600 hours daily.

A computer-based data-acquisition system continuously monitored SOL and TA background (i.e., ongoing) EMG and controlled the nerve-cuff stimulus, 24 h/day, 7 day/wk, for the entire period of the experiment. It sampled ongoing EMG from both SOL and TA at 5 kHz and stored its absolute value (equivalent to full-wave rectification). If the absolute values of background EMG from both muscles remained within predefined ranges (based on the rat's typical EMG levels as it moved about the cage) for a randomly varying 2.3- to 2.7-s period, the computer saved the most recent 100 ms (i.e., the background EMG interval) and delivered a stimulus pulse (typically 0.5 ms in duration) to the CP nerve cuff and elicited an M response and an H-reflex from TA and RI from SOL (i.e., a transient decrease in SOL background EMG). The computer collected and saved EMG for another 200 ms. The prestimulus 100 ms and poststimulus 200 ms recording comprised a single trial. Pulse amplitude and duration were initially set for each rat to produce a maximum TA H-reflex. The maximum TA H-reflex was usually accompanied by a small TA M response. There was no EMG or visible movement evidence of a withdrawal response. For each rat, pulse duration (usually 0.5 ms; occasionally 0.1 ms when the 0.5-ms pulse produced a stimulus artifact that impinged on the M response) remained fixed throughout data collection. Pulse amplitude was adjusted by the computer after each trial to maintain the TA M response [i.e., average amplitude of TA EMG in the M response interval (typically 2.0–4.5 ms after stimulation)] unchanged throughout data collection. This ensured that the effective strength of the CP stimulus was stable throughout data collection despite any changes that occurred in nerve cuff electrode impedance or in other factors (Chen and Wolpaw 1995; Wolpaw 1987). The randomly varying 2.3- to 2.7-s background EMG requirement prevented the rat from knowing exactly when a trial would occur and, combined with the poststimulus interval and processing, ensured that the shortest possible interstimulus interval was 2.75 s.

Under the control mode, the computer simply measured the absolute value of TA and SOL EMG for 200 ms after the stimulus. Under the up-conditioning (i.e., RIup) mode or down conditioning (RIdown) mode, the computer gave a food-pellet reward 200 ms after CP stimulation if SOL EMG amplitude in the RI interval (typically 7.0–17.0 ms after CP stimulation) was smaller (RIup mode) or larger (RIdown mode) than a criterion value. For each rat, the reward criterion was adjusted daily to give a reward percentage that ensured sufficient food [e.g., ~1,000 pellets (20 g) per day for a young male rat weighing 500 g]. In the course of its normal activity, the rat usually satisfied the background EMG requirement, and thus received CP stimulation, 3,200–9,900 times per day. Depending on the rat, the number of rewards/d constituted 10–30% of the trials. [In rats, as in monkeys (Wolpaw et al. 1993), the speed and final magnitude of conditioned H-reflex change does not correlate with the number of trials/day or the number of rewards/day. Thus for example, rats that average 4,000 trials/day do as well as rats that average 8,000.] The nerve stimulation itself does not affect H-reflex size over the prolonged course of data collection: in rats exposed to the control mode for 60 days, soleus H-reflex size did not change (Chen et al. 2006). For each rat, data were collected first under the control mode for ≥10 days and then under the RIup mode (RIup rats) or RIdown mode (RIdown rats) for 50 more days. The 10 rats were randomly divided into two groups of 5 rats each, an RIup group and an RIdown group. The groups were comparable in body weight and in TA and SOL background EMG.

Data analysis

SOL and TA background EMG amplitudes were calculated as average absolute value of EMG during the 100 ms prior to CP nerve stimulation. TA M response size was calculated as average absolute value of EMG in the M response interval (typically 2.0–4.5 ms after stimulation) minus average background EMG amplitude. TA H-reflex size was calculated as average absolute value of EMG in the TA H-reflex interval (typically 6.0–10.0 ms after CP stimulation) minus average TA background EMG amplitude and was expressed in units of average TA background EMG. SOL RI size was calculated as average absolute value of EMG in the SOL RI interval (typically 7.0–17.0 ms after CP stimulation) minus average SOL background EMG amplitude and was expressed in units of average SOL background EMG amplitude. (Thus RI size was a negative value, and it became more negative with successful RIup conditioning and less negative with successful RIdown conditioning.)

For each rat, average daily values of TA and SOL background EMG, TA M response, TA H-reflex, and SOL RI were determined. Each rat's initial (i.e., control) values were the average values for the 10 days immediately before onset of the 50-day RIup- or RIdown-mode exposure, and its final values were the average values for the final 10 days (i.e., days 41–50) of these 50 days. (In 1 RIdown rat, the nerve stimulating cuff failed 41 days after conditioning, and days 32–41 provided the final values). To evaluate for each rat the final effect of RI conditioning on RI or on the H-reflex, the average of the values for the final 10 days was expressed as percent of the average of the values for the 10 control days immediately before conditioning began.

In all rats, SOL and TA background EMG and TA M response size remained stable throughout data collection. To assess for each rat group the effects of RIup- or RIdown-mode exposure on SOL RI size, a paired *t*-test was used to compare the average values of the final 10 control-mode days to the average values of the final 10 days of conditioning.

Animal perfusion and anatomical study

At the end of study, the rat received an overdose of sodium pentobarbital (intraperitoneally) and was perfused through the heart with saline followed by 3% paraformaldehyde and 1% glutaraldehyde in 0.1 M phosphate buffer (pH 7.3). The EMG electrodes, nerve cuff, and CP nerve were examined, and the SOL and TA muscles of both sides were removed and weighed.

RESULTS

Animals remained healthy and active throughout data collection. Body weight increased from 384–498 g at the time of implantation surgery to 515–733 g at the time of perfusion. Both the percentage weight gains and absolute weight gains were comparable for the RIup and RIdown groups [40 ± 18% and 165 ± 67 g for RIup rats and 34 ± 15% and 152 ± 57 g

for RIdown rats; (means ± SD); $P = 0.58$ and $P = 0.74$ between RIup and RIdown by *t*-test, respectively). There was no significant difference between RIup and RIdown rats in SOL and TA muscle weights; and there was no significant difference in either group between SOL and TA muscle weights for the implanted (right) leg and the unimplanted (left) leg. In all rats, the cuff was located where it had been implanted and was covered by connective tissue, and the CP nerve was well preserved inside the cuff. That the CP nerve remained intact structurally and functionally was further indicated by the bilateral symmetry in SOL and TA muscle weights and also by the fact that the pulse amplitude needed to elicit the target M response remained stable throughout data collection.

In all rats, a TA H-reflex was present (e.g., Fig. 1). Under the control mode, it averaged 0.75 ± 10 (SE) of TA background EMG level, somewhat smaller than the SOL H-reflex, which averaged 1.04 ± 10 of SOL background EMG level in 135 rats previously studied (Chen and Wolpaw 1995, 1997, 2002; Chen et al. 2002, 2003; and unpublished data). As expected for a disynaptic pathway, SOL RI began at ~7 ms, ~1 ms later than the typical SOL H-reflex. SOL RI peaked at about 10 ms and ended at ~17 ms (e.g., Fig. 1). Most of the rats showed in SOL a small response that was concurrent with the TA M response (e.g., Fig. 1*A*) and did not change over the course of study. It probably reflected pickup by the SOL electrodes of the TA M response and/or was a small SOL M response produced by proximal spread of the CP nerve stimulation to the branch point of the sciatic where it divides into the CP and posterior tibial nerves. In none of the rats was SOL excitation at H-reflex latency evident.

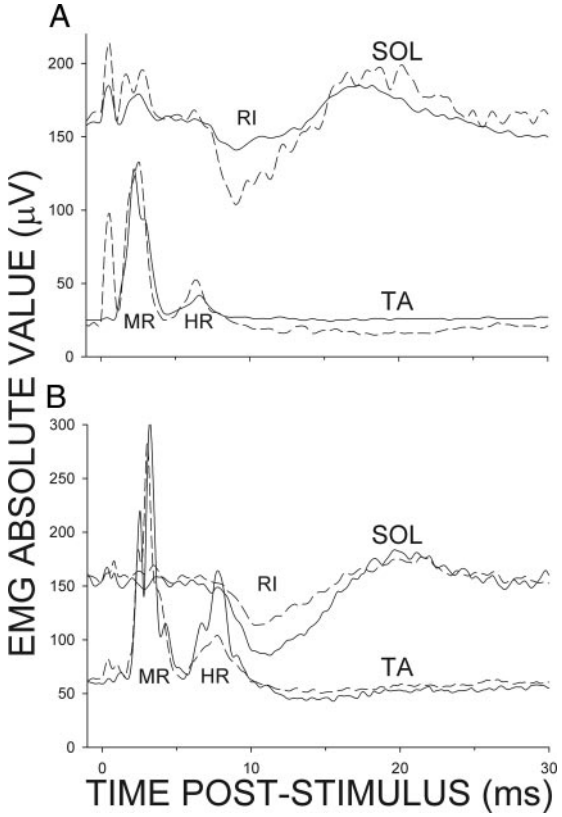

FIG. 1. Effects of reciprocal inhibition up or down (RIup or RIdown) conditioning. Average absolute value (equivalent to full-wave rectification) of peristimulus electromyography (EMG) for representative days from a RIup (*A*) and a RIdown (*B*) rat for 1 day before conditioning (—) and 1 day near the end of RIup or RIdown conditioning (- - -). After conditioning, soleus (SOL) RI and the tibialis anterior (TA) H-reflexes are larger in the RIup rat and smaller in the RIdown rat, whereas SOL and TA background EMG (EMG at *time 0*) and TA M response do not change in either rat. In *A,* small stimulus artifacts are present, and small responses are evident at M response latency in the SOL EMG (see text).

Every rat responded appropriately to the RIup or RIdown mode: RI increased in all the RIup rats and decreased in all the RIdown rats. Figure 2 shows SOL RI values for all RIup and RIdown animals at the end of RIup or RIdown exposure (i.e., days 41–50). Each rat met the standard criterion for successful conditioning, a change of ≥20% in the correct direction (Chen and Wolpaw 1995; Wolpaw et al. 1993). To confirm for each rat the significance of this change, the rat's daily average RI values for the final 10 days before conditioning were compared with those for the final 10 days of conditioning. Every RIup rat's RI values were significantly increased at the end of up-conditioning, and every RIdown rat's RI values were significantly decreased at the end of down-conditioning ($P = 0.001$ for each rat by *t*-test). In the five RIup rats, final (i.e., days 41–50) RI averaged 171± 28% (range: 121–270%) of control. In the five RIdown rats, final RI averaged 37 ± 13% (range: 11–78%) of control. In the five RIup rats, the average RI (in units of background) was −0.16 ± 0.04 (range: −0.08 to −0.28) before RIup conditioning and −0.26 ± 0.05 (range: −0.14 to −0.41) at the end of RIup conditioning. This RI increase was statistically significant ($P = 0.02$ by paired *t*-test). In the five RIdown rats, the average RI was −0.22 ± 0.03 (range: −0.15 to −0.31) before RIdown conditioning and −0.08(±0.04) (range −0.02 to −0.22) at the end of RIdown conditioning. This RI decrease was also statistically significant ($P = 0.02$). Neither RIup nor RIdown conditioning had a marked effect on RI latency, form, or duration. In addition, no significant relationship was found for either the RIup rats or the RIdown rats between number of trials/d and the magnitude of RI change.

In 6 of the 10 successful RI rats, the mode-appropriate change in RI was accompanied by a change in the same direction in the TA H-reflex that also met the criterion for successful conditioning. That is, in two of the five RIup rats and four of the five RIdown rats, the TA H-reflex changed by ≥20% in the same direction as SOL RI (i.e., TA H-reflex increase in RIup rats and decrease in RIdown rats). In the remaining 4 rats, the TA H-reflex remained within 20% of its control value. Final TA H-reflex in the five RIup rats averaged 114 ± 14% (range: 91–161%) of control, and final TA H-reflex in the five RIdown rats averaged 59 ± 18% (range: 12–119%) of control.

Figure 1 illustrates the effects of conditioning with SOL and TA data for representative days before conditioning and near the end of conditioning from an RIup rat and an RIdown rat. SOL and TA background EMG and the TA M response remain stable throughout data collection. In contrast, SOL RI is much larger after RIup exposure and much smaller after RIdown exposure. In addition, the TA H-reflex is larger after RIup exposure and smaller after RIdown exposure.

Figure 3 shows average SOL RI size and background EMG (▲, ▼) and average TA H-reflex size, M response size, and background EMG (△, ▽) for all RIup animals (△, ▲) and RIdown animals (▽, ▼) for each 5-day period during the last 10 days in the control mode and the subsequent 50 days in the

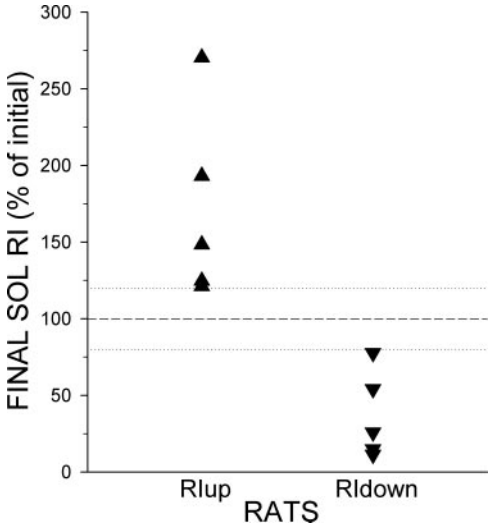

FIG. 2. Final SOL RI (i.e., average value for the final 10 days as percent of average value for the 10 control days immediately before conditioning began) for RIup and RIdown rats. ···, ≥20% criterion for successful RIup or RIdown conditioning (Chen and Wolpaw 1995; Wolpaw et al. 1993).

RIup or RIdown mode. SOL RI markedly increases (RIup rats) or decreases (RIdown rats) over 30–40 days. Concurrently, the TA H-reflex increases slightly in the RIup rats and decreases substantially in the RIdown rats. SOL and TA background EMG and TA M response remain stable throughout.

Figure 4 plots final SOL RI versus final TA H-reflex for the five RIdown animals (▼) and the five RIup animals (▲). There is a significant positive correlation between final SOL RI and final TA H-reflex size ($R = 0.71$, $P = 0.02$). To further explore the correlation between TA H-reflex and SOL RI, we analyzed its evolution over the 50-day conditioning period. Table 1 shows the correlation coefficient and P value for each 10-day period. The correlation becomes significant by days 11–20 and remains at about the same level through days 41–50. When this analysis was performed separately for RIup and RIdown rats, no significant correlation was found for any 10-day period between SOL RI and TA H-reflex size ($P > 0.1$ for every 10-day period for the 5 RIup rats, $P > 0.3$ for every 10-day period for the 5 RIdown rats). Thus there was no indication that H-reflex change was more likely to occur in rats with larger RI changes.

DISCUSSION

Reciprocal Ia inhibition between agonist and antagonist muscles is mediated by the Ia inhibitory interneuron (Boorman et al. 1996; Capaday 1997; Crone and Nielsen 1994; Jankowska 1992; Morita et al. 2001). After the monosynaptic pathway of the SSR and H-reflex, it is perhaps the best-characterized spinal cord reflex pathway (Ashby and Wiens 1989; Baldissera et al. 1981; Boorman et al. 1996; Capaday 1997; Crone 1993; Crone and Nielsen 1994; Friesen 1994; Friesen and Stent 1978; Fu et al. 1978; Jankowska 1992; Kido et al. 2004; Morita et al. 2001; Perkel and Mulloney 1974; Sherrington 1913). It is influenced by corticospinal and other descending pathways and is capable of short-term plasticity induced by appropriate sensory stimulation (D. Chen et al. 2001; Crone and Nielsen 1994; Crone et al. 2004; Nielsen et al. 1995; Perez et al. 2003). By implanting rats with a nerve cuff on the common peroneal nerve and EMG electrodes in both agonist (TA) and antagonist (SOL) muscles and applying a conditioning protocol analogous to that used for SSR and H-reflex conditioning, the present study explored operant conditioning of the RI pathway.

The results are clear: in response to the RIup or RIdown conditioning mode, rats gradually increased or decreased, respectively, RI magnitude, without change in SOL or TA background motoneuron tone as measured by background EMG and without change in effective stimulus strength as measured by TA M response size. In all rats, the occurrence and direction (i.e., increase or decrease) of change in RI matched the reward contingency (i.e., RIup or RIdown), and thus appeared to be a specific adaptive response to the specific reward criterion. RI conditioning in rats appears to be similar in course and final magnitude to SSR and H-reflex conditioning in rats, mice, and primates (Carp et al. 2005; Chen and Wolpaw 1995; X. Y. Chen et al. 2001; Evatt et al. 1989; Wolpaw et al. 1983, 1993). In addition, the magnitude of RI increase or decrease did vary widely among rats. Similar variation occurs with H-reflex conditioning in rats and in monkeys (Chen and Wolpaw 1995; Wolpaw 1987), probably due to a variety of

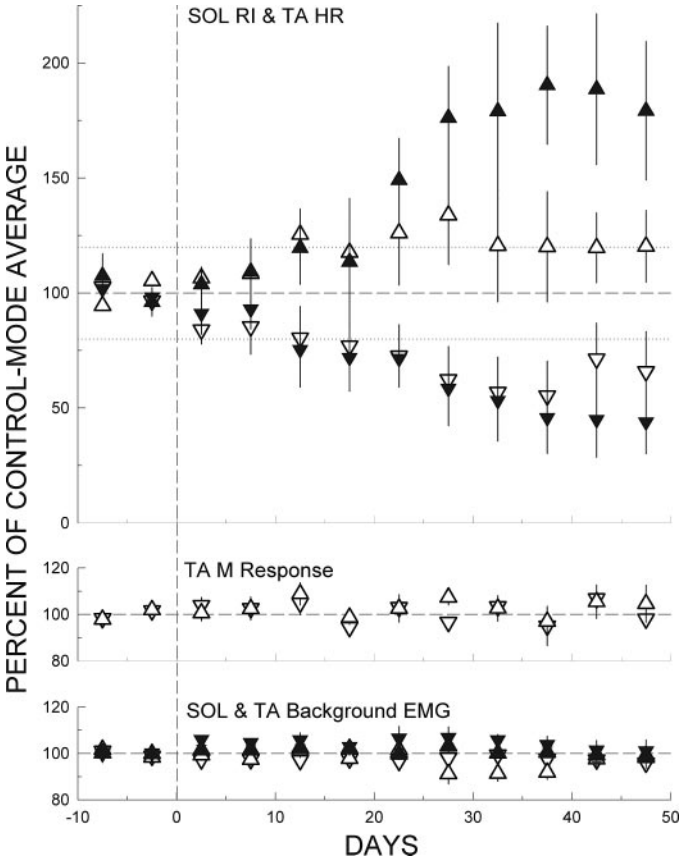

FIG. 3. Average (±SE) SOL RI and background EMG (▲, ▼) and average TA H-reflexes, M responses, and background EMG (△, ▽) for all RIup animals (▲, △) and RIdown animals (▽, ▼) for each 5-day period during the last 10 days of the control mode and the subsequent 50 days of exposure to the RIup or RIdown mode (in percent of control-mode value). SOL RI gradually rises (RIup animals) or falls (RIdown animals) over several weeks. The TA H-reflex increases slightly with RIup conditioning and decreases substantially with RI down-conditioning. SOL and TA background EMG and TA M response remain stable throughout data collection.

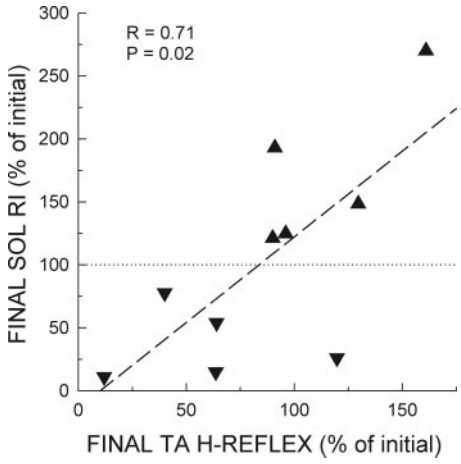

FIG. 4. Final SOL RI (in percent of initial) vs. final TA H-reflex size (in percent of initial) for all RIup rats (▲) and RIdown rats (▼) at the end of RIup or RIdown conditioning. There is a significant but weak positive correlation between final SOL RI size and TA H-reflex size ($R = 0.71$, $P = 0.02$).

factors (Wolpaw et al. 1993). Initial reflex size is clearly important (Wolpaw et al. 1993).

In both primates and rats, H-reflex conditioning produces persistent anatomical and physiological changes at multiple sites in the spinal cord, including the motoneuron, several different synaptic populations on the motoneuron, and probably interneurons as well (Carp and Wolpaw 1994, 1995; Feng-Chen and Wolpaw 1996; Pillai et al. 2004; Wang et al. 2004, 2006; Wolpaw and Lee 1989). Recent studies of the effects of specific spinal cord pathway transections on H-reflex conditioning, and related clinical data (Segal 1997), indicate that the main CST is essential for conditioning and that other major spinal cord tracts (i.e., the rubrospinal, vestibulospinal, and reticulospinal tracts, and the dorsal column ascending tract) are not (Chen and Wolpaw 1997, 2002; Chen et al. 2002, 2003). Cerebellar output to sensorimotor cortex, the principal origin of the CST, also appears to be important (Chen and Wolpaw 2005; Wolpaw and Chen 2006).

In this context, the tendency for conditioning of SOL RI to be accompanied by comparable change in the TA H-reflex is important. That there is a significant positive correlation is clearly evident in Fig. 4. At the same time, the correlation is not very strong. Thus in only 6 of the 10 rats was the mode-appropriate change in RI accompanied by change in the same direction in TA H-reflex size. Indeed, in the remaining four rats, the TA H-reflex changed slightly in the opposite direction. Furthermore, the correlation did not get stronger as RI change continued to progress; and within the RIup and RIdown rat groups H-reflex change was not significantly greater in those rats in which RI changed more [though it should be noted that these groups were small ($n = 5$ for each)]. Thus it is unlikely that RI and H-reflex conditioning are simply two aspects of the same basic phenonenon: if they were, agonist H-reflex conditioning and antagonist RI conditioning would always occur together and would tend to correlate in magnitude and time course of change.

This rough linkage between RI conditioning and H-reflex change could be in part mechanistic. For example, the same change in oligosynaptic inhibition that may contribute to H-reflex up-conditioning by affecting synaptic input to the motoneuron (Feng-Chen and Wolpaw 1996; Pillai et al. 2004; Wang et al. 2004, 2006) might contribute to RI up-conditioning by affecting synaptic input to the Ia inhibitory interneuron. Furthermore, although the change in motoneuron firing threshold that largely accounts for H-reflex down-conditioning (Carp and Wolpaw 1994) would not directly affect RI, the mechanism responsible for the motoneuron threshold change might conceivably produce a comparable change in threshold in the Ia inhibitory interneuron and thereby affect RI. On the other hand, it is possible that the mechanisms of the H-reflex changes that accompany RI conditioning are entirely different from those responsible for H-reflex conditioning. For example, the H-reflex increase with RIup conditioning could be due to decreased presynaptic inhibition at the Ia-motoneuron synapse, even though decreased presynaptic inhibition does not appear to contribute to H-reflex up-conditioning (Carp and Wolpaw 1995; Wolpaw 2001).

It seems likely that the H-reflex changes that accompany RI conditioning could reflect aspects of the complex pattern of spinal and supraspinal plasticity associated with even the simplest conditioning (Carp and Wolpaw 1994, 1995; Carp et al. 2001; Chen and Wolpaw 2005; Feng-Chen and Wolpaw 1996; Pillai et al. 2004; Wang et al. 2004, 2006; Wolpaw and Chen 2006; Wolpaw and Lee 1989; reviewed in Wolpaw and Tennissen 2001). As discussed in detail elsewhere, this complexity appears to be both necessary, to preserve the organism's entire roster of behaviors, and inevitable, due to the ubiquity of activity-dependent plasticity in the CNS (Wolpaw and Tennissen 2001). For example, SOL H-reflex conditioning affects SOL participation in locomotion and is therefore likely to lead to additional wider plasticity that preserves normal locomotion in spite of the change in the contribution of SOL (Chen et al. 2005a,b). The parallel change in the TA H-reflex that usually accompanies SOL RI conditioning could also represent compensatory plasticity.

RI conditioning, like H-reflex conditioning, might be used to modify aspects of the locomotor and other functional abnormalities associated with spinal cord injuries or other chronic disorders of motor control and might thereby help to produce more effective function (e.g., Chen et al. 2005a,b). For example, spinal cord injury in humans is associated with increased stretch reflexes and flexor reflex afferent reflexes (Barbeau and Norman 2003; Dietz 2000; Roby-Brami and Bussel 1987; Schmit et al. 2002), and with decreases in RI, recurrent inhibition, and presynaptic inhibition. These reflex abnormalities are thought to contribute to spasticity (Boorman et al. 1996; Dietz 2000; Faist et al. 1994; Hiersemenzel et al. 2000; Mazzocchio and Rossi 1997; Morita et al. 2001). Just as H-reflex down-conditioning might be used to decrease hyper-

TABLE 1. *Correlation between SOL RI and TA H-reflex for each 10-day period of the 50-day conditioning period for the 10 RIup or RIdown rats*

Days Post Conditioning	Correlation Coefficient (R)	P Value
1–10	0.44	0.24
11–20	0.75	0.02
21–30	0.67	0.05
31–40	0.78	0.02
41–50	0.71	0.02

Sol, soleus; RI, reciprocal inhibition; and TA, tibialis anterior.

active stretch reflexes, RI up-conditioning might be used to produce a more normal level of RI. Furthermore, spasticity tends to be most pronounced in those with incomplete injuries (Little et al. 1989; Young 1994), in whom reflex operant conditioning is often still possible (Chen and Wolpaw 1997, 2002; X. Y. Chen et al. 2002; Chen et al. 2005a; Segal and Wolf 1994). On the other hand, the H-reflex increase that often accompanies RI up-conditioning might reduce its functional benefits. Factors such as this variable correlation between RI change and H-reflex change (Table 1) must certainly be taken into account in designing and implementing therapeutic efforts. More complex conditioning protocols may be required, and therapeutic efficacy may differ markedly across individuals.

In sum, the present study demonstrates that a spinal cord reflex pathway other than the SSR/H-reflex pathway, specifically the RI pathway, can be operantly conditioned. It also indicates that conditioning of one spinal reflex pathway can affect another reflex pathway as well. In conjunction with other work (Chen et al. 2005a,b), the present study suggests that conditioning of the RI pathway and other spinal reflex pathways could be a valuable new method for helping to achieve more effective spinal cord function in people with partial spinal cord injuries or other chronic neurological disorders.

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