Differential Regulation of Cutaneous and H-Reflexes During Leg Cycling in Humans

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Zehr, E. Paul, Kathryn L. Hesketh, and Romeo Chua. Differential regulation of cutaneous and H-reflexes during leg cycling in humans. J Neurophysiol 85: 1178–1184, 2001. Reflexes undergo modulation according to task and timing during standing, walking, running, and leg cycling in humans. Both cutaneous and Hoffman (H-) reflexes are modulated by movement and task. However, recent evidence suggests that the modulation pattern for cutaneous and H-reflexes may be different. We sought to clarify this issue by reducing the effect of movement phase and altering the level of background muscle activation (low and high) in static and dynamic (leg cycling) conditions. Electromyography was recorded from the ankle extensors soleus and medial gastrocnemius (MG) and the knee extensor vastus lateralis (VL). Reflexes were evoked during the downstroke of stationary leg cycling. Cutaneous reflexes were evoked with trains of 5 × 1.0 ms pulses at 300 Hz delivered to the distal tibial nerve, whereas H-reflexes were evoked in soleus by stimulation with single 1.0-ms pulses. There were two main observations in this study: 1) middle latency cutaneous reflexes were facilitatory during static contraction but were dramatically attenuated or reversed to suppressive responses during cycling (task-dependent modulation); 2) soleus H-reflexes were larger in the high muscle activation condition but were unaffected by task (no task-dependent modulation). Thus opposite results were obtained in the two reflex pathways. It is concluded that cutaneous and H-reflexes are modulated by different mechanisms during active locomotor-like movements.

INTRODUCTION

Cutaneous and muscle afferent (particularly the Hoffman or H-reflex) reflex pathways have been studied during rhythmic leg movement (Brooke et al. 1997). The extent to which these two pathways are similarly controlled during movement has received recent study. Brooke et al. (1999) showed that during passive movement, cutaneous reflexes have quite different behavior than H-reflexes. There was little passive movement-related modulation of cutaneous reflexes, perhaps in keeping with the suggestion that a central pattern generator (CPG) controls this pathway during rhythmic movement (DuySENS and Van de Crommert 1998). In contrast, H-reflexes seem to show features of both central (Schneider et al. 2000) and peripheral (Brooke et al. 1997) control. Cutaneous and H-reflexes in soleus show some similarities in that they are phase and task modulated. For example, under certain circumstances, both types of reflexes can be of greatest magnitude while the muscle is contracting. It is not yet known how they behave under varying conditions of voluntary muscle activity during rhythmic movement. An emerging concept is that while these reflexes may share similar features, the nature of the modulation they undergo may be quite different. Thus both types of reflexes were elicited under the same conditions to remove this as a factor affecting the two reflex pathways. If the reflexes behave similarly, it might point to some common mechanism for controlling reflexes during rhythmic locomotor movements of the lower limb.

In recent years, there have been many studies examining the modulation of reflexes during leg cycling. Researchers have mainly focused on the study of the soleus H-reflex (Brooke et al. 1997). These studies have suggested that discharge from velocity-sensitive stretch receptors in heteronymous and contralateral muscles is a possible influence (Brooke et al. 1992a, 1997; Cheng et al. 1995b, 1998; McIlroy et al. 1992; Misiaszek et al. 1995). Other experimental results indicate that a more central influence is responsible for reflex behavior during rhythmic movements such as treadmill locomotion (Capaday and Stein 1986, 1987; DuySENS 1998; DuySENS and Van de Crommert 1998; DuySENS et al. 1990, 1992; Lavoie et al. 1997; Yang and Stein 1990). However, there has only been limited investigation into the effects of muscle activity on reflex modulation during cyclic movement (Boorman et al. 1992). Evidence from static comparisons of background electromyographic (EMG) levels indicates that the H-reflex should scale with background muscle activity (Crenna and Frigo 1987; Verrier 1985).

METHODS

All methods and procedures were approved by the Health Research Ethics Committee at the University of Alberta. Twelve adults who were healthy and free of any known neuromuscular disease participated with informed, written consent.

EMG

EMG was collected from the medial gastrocnemius (MG), soleus (SOL), tibialis anterior (TA), vastus lateralis (VL), and biceps femoris
(BF) of the ipsilateral (relative to site of nerve stimulation) leg. Sites over the selected muscles were cleansed with rubbing alcohol tow-
ettes, then Ag-AgCl surface electrodes (Kendall-LTP, Chicopee, MA) were applied in bipolar configuration. Individual ground elec-
trodes were placed over bony landmarks near each muscle. To min-
imize movement at the ankle, an ankle-foot orthosis was worn on the
right foot.

Protocol

A Monark cycle ergometer was modified so that potentiometer data of the
movement could be collected concurrently with the EMG data. Particip-
ants pedaled at a cadence of 60 RPM while at two workloads that corresponded approximately to loads requiring low (0.25–0.75
kp) and heavy (2.5–3.25 kp) effort.

Data were collected when the ipsilateral leg was at 90°, and the
the crank arm was thus parallel to the floor. This position corresponded to
the 3 o’clock position, where 12 o’clock is top dead center. Stimula-
tion was applied at this point while pedaling and during static con-
traction held at either low or high muscle activity (SOL). During static
contraction trials, the pedal was placed on wooden blocks to hold it in
the 3 o’clock position. Participants were given visual feedback by
means of an oscilloscope monitoring SOL and TA activity. Maximum
voluntary contractions (MVC) were collected for static plantar flexion
and knee extension, so that it was possible to normalize muscle activa-
tion levels across subjects to compare values.

The 3 o’clock position was chosen for three reasons. At this parti-
cular position the leg extensors are the most active, making it the
easiest position to observe changes in muscle activity with changing
workload. Second, at this point in the movement cycle, the least
amount of reflex depression is observed, thus avoiding possible
“floor” effects. Third, it was possible to elicit an M-H curve at that
position.

Nerve stimulation

Nerve stimulation was applied with a Grass S88 Stimulator coupled
to a SIU5 stimulus isolation unit and a CCU1 constant current isolation
unit (Grass Instruments, Astco-Med, Inc.).

Cutaneous reflexes

Stimulation was delivered to the distal tibial nerve at the ankle (near
the medial malleolus) as a train of 5 × 1.0 ms pulses at 300 Hz.
Stimulation intensity was set at two times radiating threshold (2 ×
RT), where RT is defined as the lowest intensity of stimulation at
which participants felt the stimulus radiating into the heel and sole of
the foot toward the toes (e.g., cutaneous distribution of the distal tibial
nerve). Further details can be obtained from other recent papers (Zehr
et al. 1997, 1998a,b). Thirty sweeps were collected for movement
with and without stimulation (control) and for static trials with fo-
cused plantar flexion and knee extension.

H-reflex

The stimulating electrodes were placed in bipolar arrangement over
the tibial nerve, on the back of the right leg just above the crease in
the knee. In some cases, it was necessary to arrange the electrodes
such that one was placed over the tibial nerve and the other was
located over the patella. A neoprene knee brace was used to wrap the
stimulating electrodes to hold them in place. One hundred sweeps
were collected in each condition, with the stimulus intensity (1.0-ms
pulse) varied such that a full M-H response curve could be plotted.
Thus in each condition, both M and Hmax were collected. To ensure
that Mmax was reached, stimulus intensity was increased until the
H-reflex was abolished and the M wave failed to get any larger when
monitored on an oscilloscope. Each sweep was initiated 40 ms pre-
stimulus and lasted 100 ms, at a sampling frequency of 2,000 Hz.
Participants were instructed to maintain the same head, neck, and
torso orientation during data collection. During movement conditions,
participants pedaled for bouts of approximately 5 min while data were
collected, with brief rest periods in between trials. During static trials,
participants held contractions for 1 min at a time (15–20 sweeps) then
were allowed to rest for a few minutes to avoid fatigue effects. Stimuli
were delivered pseudorandomly during static trials, approximately
every 3–4 s.

Data reduction

EMG signals from each muscle were amplified (∗×500–5,000) using Grass P-511 amplifiers and band-pass filtered at 30–300 Hz.
Data from each EMG channel and the potentiometer were digitized
using an A/D interface, sampled at a rate of 1,000 Hz (cutaneous
reflexes) or 2,000 Hz (H-reflex) using Labview (National Instruments)
data acquisition software, then stored on an IBM compatible micro-
computer. A custom-designed computer program (MATLAB, Math-
Works, Nantick, MI) was used to process the raw data. Each EMG
channel was rectified and stimulus artifacts removed. The latency and
peak-to-peak amplitude for M-wave and H-reflex of the unrectified
EMG for soleus, as well as the mean and standard deviation of the
prestimulus level of activity of each channel were determined. These
values were used for further calculations.

Analysis

BACKGROUND EMG. Background muscle activity was quantified by
averaging the mean EMG level over a 150-ms poststimulus period for
each sweep of control trials. The sweeps were then each normalized
to MVC and averaged.

CUTANEOUS REFLEXES. Raw data were examined using an interac-
tive computer program. The stimulus artifact was removed, and the
EMG was filtered using a 21-point moving average filter. The control
EMG traces were subtracted from the stimulated EMG. The resultant
subtracted traces were used for subsequent analysis of the latency and
magnitude of all significant facilitations and suppressions of the EMG
signal. To be considered significant, reflexes had to exceed a 2 SD
band centered about the mean prestimulus EMG. The responses were
divided into early (40–65 ms), middle (70–120 ms), and late (130 ms
and longer) latencies. These distinctions are similar to those used in
other papers (Duyssens et al. 1990; Yang and Stein 1990). Addition-
ally, as with previous studies, we focused on the middle latency
response that typically shows the most interesting patterns of modu-
lation (Duyssens and Tax 1994). Reflexes were normalized to back-
ground EMG levels for each trial.

H-reflexes

M-H curves were generated in each condition. Analyses were
performed on three sizes of H-reflex: 1) 30% of Mmax, 2) Hmax, and
3) H that occurred at the midpoint of the descending limb of the M-H
curve. These three points were compared to see whether there were
any differences in the behavior of the H-reflex with changing back-
ground levels at different points on the M-H curve. These points of the
M-H curve were chosen as there had been some differences in the
H-reflex sizes used previously (Brooke et al. 1992b; Capaday and
Stein 1987; Cheng et al. 1995a; Taylor et al. 1990). Mmax was
calculated by averaging the five highest peak-to-peak M-waves.

To have consistent M-wave size within a type of analysis for
individual subjects, M-H pairs were chosen by using the specific
criteria for each type (e.g., M-wave size where the H-reflex was 30% of
Mmax) from the low muscle activation cycling condition. Next, this
M-wave size was used to choose M-H pairs in the other conditions
(e.g., low muscle activation during static contraction). This is an
extension of a method we have used previously to examine H-reflex
modulation in different conditions (Zehr and Stein 1999). Eight to 10 M-H pairs were taken from each participant in each condition to find an average for each subject. Since no difference in behavior of the reflex across the M-sizes was found (see RESULTS), 20–30 sweeps of consistent M-wave size (on the ascending limb of the M-H curve) from each subject were averaged for further analyses.

To make direct comparisons between cutaneous and H-reflexes, SOL middle latency responses were normalized to $M_{\text{max}}$ and compared with H-reflexes in the same conditions. Obviously, this was only possible to do with SOL, since M and H data were only available for this muscle.

Statistics

Background muscle activity and peak-to-peak M-wave and H-reflex amplitude comparisons as well as H-reflex behavior at different points on the M-H curve were made using repeated measures ANOVA (RM ANOVA). When analyzing cutaneous reflex data, it was not possible to use a RM ANOVA, since not all of the participants exhibited a significant reflex response at each latency, particularly in VL. A one-way ANOVA was performed on the significant responses for early, middle, and late latencies comparing the magnitudes of all significant responses in each condition. A separate ANOVA was calculated for each muscle and latency. Values are given as means ± SD, and statistical significance was set at $P < 0.05$.

RESULTS

Background EMG

Background EMG levels were larger during the high versus low load condition in MG ($P < 0.05$), SOL ($P < 0.01$), and VL ($P < 0.01$). However, the EMG levels were not different between static and movement trials. That is, background EMG was matched in the static low versus movement low and static high versus movement high conditions. As we attempted to manipulate background EMG by changing workload, this result allows for comparisons of reflex amplitudes at different levels of muscle activation and between movement or static conditions.

Cutaneous reflexes

In MG, the middle latency response (70–120 ms poststimulus) reversed from excitatory under static conditions to suppressive during movement ($P < 0.01$). Sample reflex data from one subject are plotted in Fig. 1, and mean subject data averaged across all subjects are shown in Fig. 2 (top). There were no significant effects at the other latencies, an observation in keeping with previous studies in which the middle latency response is most sensitive to modulation (Duysens and Tax 1994). SOL demonstrated the same general pattern as in MG: there was also a task-dependent modulation of the middle latency cutaneous reflex ($P < 0.01$) with very small or inhibitory responses during movement and larger excitatory responses predominating during static contraction (Fig. 2, middle). As with MG, there was no significant difference in SOL response between conditions at either the early or late latency.
Reflexes in VL were similar to MG and SOL except that both early \((P < 0.05)\) and middle \((P < 0.05)\) latency responses were either very small or inhibitory during movement and larger excitatory responses during matched static contractions (Fig. 2, bottom). There was no effect of background EMG (as influenced by workload) on cutaneous reflex amplitude.

**H-reflexes**

The SOL H-reflex was significantly smaller at low levels of muscle activation \((P < 0.05)\), but there was no difference in H-reflex size between movement and static conditions (Fig. 3, top). Hence there was no task-dependent modulation of the H-reflex. M-wave amplitude \((14.5 \pm 7\% M_{\text{max}}, \text{ mean } \pm \text{ SD})\) did not differ significantly across conditions (see Fig. 3, bottom), and thus the intensity of stimulation was consistent across all conditions. When analyzing the data from different points on the M-H curve, it was determined that neither the M-wave nor H-reflex showed any significant differences across movement conditions or contraction level when comparing these different points on the M-H curve. Thus the size of the "test" H-reflex is not a confounding factor in these types of experiments.

**DISCUSSION**

In these experiments a novel approach was taken to examine the issue of reflex control in different pathways. The main observation from this experiment was that cutaneous and H-reflexes behaved differently in the same controlled, experimental situation. We observed task-dependent reflex modulation only in middle latency cutaneous reflexes and background-
dependent reflex scaling only in the SOL H-reflex pathway. Second, it is of interest to note that the H-reflex scaled with EMG amplitude regardless of task.

**Task modulation of cutaneous reflexes**

The significant differences in cutaneous reflex amplitude between dynamic and static contraction adds further to the suggestion that cutaneous reflexes are task dependent. Previously, Burke and colleagues (Burke et al. 1991) observed differential reflex behavior when the lower limb muscles were active or silent. Further, Duyssen and colleagues (Duyssen et al. 1993) showed that cutaneous reflexes to sural nerve stimulation were much larger during treadmill running than during standing. Using a similar approach, we observed task-dependent behavior of lower leg cutaneous reflexes between walking and standing (while matching postural orientation to walking) (Komiyama et al. 2000). If afferent feedback related to muscle stretch and limb loading was the same in both the static and dynamic tasks here, the task-dependent behavior possibly has central origin and does not depend on interactions between afferents. The potential source of the central input cannot be determined from this experiment, but could be of either spinal or cortical origin.

The task-dependent reversal of the middle latency response in the leg extensors adds credence to the notion that cutaneous reflexes are controlled by a CPG for rhythmic movement (Duyssen and Van de Crommert 1998). It is of interest to note the recent observations of Bastiaanse et al. (2000). These researchers tested an integration of cutaneous reflexes and load receptor input during treadmill walking. Interestingly, cutaneous reflexes in MG muscle were largest when the body load was smallest, but there was a complicated interaction at work. In concert with the present results, a possibility is a gating mechanism, with differential control of reflexes arising from a switch in the type of movement. Parallel pathways of inhibitory and excitatory control could be switched on and off by a mechanism either in the spinal cord or the brain. Duyssen and colleagues (Duyssen et al. 1992) suggested that such a mechanism would rely on a CPG to open and close excitatory pathways at the appropriate times during gait. A similar suggestion was made earlier by Yang and Stein (1990) with respect to observed phase dependence of cutaneous reflex responses (see also De Serres et al. 1995).

Interestingly, the results we documented previously when comparing standing (suppressing responses) and walking (facilitation) (Komiyama et al. 2000) were opposite to those here. In those experiments, suppressive responses predominated while subjects held standing postures that mimicked walking positions. Also, there was a strong negative correlation between reflex amplitude and background EMG. However, during walking, reflexes were typically excitatory and uncorrelated with EMG level. With the considerable similarity between the two experimental methods, a possible explanation for the opposite results is that there may be differences in the neural control of reflexes during walking versus cycling.

**Background modulation of the soleus H-reflex**

Pedaling cadence and joint position at which stimuli were delivered were kept constant so that the velocity of muscle shortening would be consistent across all conditions. The underlying assumption was that both the central pattern for generating the cycling movements and the dynamic input from the Ia afferents were similar in all conditions due to the control of movement velocity and joint angle. In previous animal experiments Ia input from VL has been reported to be the major afferent source affecting H-reflex modulation associated with cyclical movement of the limb in dogs (Misiaszek et al. 1995). However, we observed modulation of the reflex with a presumed tonic level of Ia input. We also observed that the H-reflex is graded simply by the background level of excitation of the motoneuronal pool, and this is maintained during controlled movement as well as static contraction. This was an unexpected observation. However, one must be cautious in oversimplifying this relationship since measurements here were made only at one point in the movement cycle. Further, Yang and Whelan (1993) observed that SOL H-reflex amplitudes were different at comparable EMG levels during swing and stance. Thus the H-reflex amplitude scales with other factors including EMG level during movement.

During static contraction, as the level of excitability increases, the amplitude of the H-reflex increases (Pierrot-Desilligny 1997). However, Capaday and Stein (1986, 1987) showed that there were significant differences in H-reflex size at similar EMG levels when comparing the static task of standing to the dynamic task of walking. They observed that the H-reflex amplitude was larger at a given level of EMG during standing than during walking (and also larger while walking than running) and concluded that reflex amplitude was independent of EMG drive. They attribute this difference to central mechanisms acting at a pretomoneuronal locus and causing an increase in presynaptic inhibition of the SOL Ia afferents. In contrast, the recent study of Simonsen and Dyhre-Poulsen (1999) suggests a task independence of H-reflex amplitude between walking and running. The discrepancy between their observations and those of Capaday and Stein (1986, 1987) could be due to the fact that the method of Simonsen and Dyhre-Poulsen (1999) accounts for variations in $M_{\text{max}}$ throughout the movement cycle. It is of interest to compare these observations during walking to our task independence here during leg cycling, where variations in $M_{\text{max}}$ were also taken into account by sampling $M_{\text{max}}$ in each condition. Further, Misiaszek and Pearson (1997) observed that, during locomotion in decerebrate cats, large H-reflexes (i.e., with M-waves present) did not modulate when background EMG was also high. They suggest that the effect of presynaptic inhibition can be overcome with high levels of muscle activation. Although it is uncertain how large an effect this might have had in this study, it is possible that there was some saturation in the H-reflex pathways of our subjects, which could have masked any task-dependent modulation.

Another possibility is that input from force-sensitive receptors (i.e., Golgi tendon organs) from extensor muscles (VL, SOL, or MG) make excitatory synaptic connections via interneuronal pathways, as demonstrated in the cat (Pearson and Collins 1993) and suggested in the human (Stephens and Yang 1996). An increase in muscle activation would lead to increased Golgi tendon organ firing, which would in turn cause increased Ib discharge onto a network. Whether Ib input causes increased excitation or decreased inhibition, the result would be a larger reflex amplitude.
Differences between H- and cutaneous reflex modulation

Our results indicate that central drive and peripheral feedback (from changing background muscle activation) had an effect on the resultant amplitude of the H-reflex. Therefore the control of the H-reflex seems to be a complicated interaction between peripheral and central factors. On the other hand, cutaneous reflexes seem to be influenced more centrally. The absence of load-dependent modulation, in addition to the observation of task dependence in our results suggests that cutaneous reflexes are likely governed by central influences, either from the brain or spinal cord. There is ample evidence from previous work to support this idea (Brown and Kukulka 1993; De Serres et al. 1995; Duyens et al. 1992; Komiyama et al. 2000; Van Wezel et al. 1997; Yang and Stein 1990). Brown and Kukulka (1993) observed phase-dependent modulation of cutaneous reflexes during cycling movements, but not during matched static positioning and activity of the lower leg muscles. In concert with the evidence that cutaneous reflexes are unaffected by passive leg cycling movement (Brooke et al. 1999), our data would seem to corroborate the assertion that cutaneous reflexes are modulated during movement only in the presence of a rhythm-generating network. However, a limitation of this experiment was that we were not able to control all types of afference. It is not known how differences in acceleration between the two types of activity (moving and static contraction) might have affected the results, or if they even play a role in controlling cutaneous reflex activity.

Therefore while cutaneous and H-reflexes show some similarities in behavior under certain conditions (e.g., phase modulation), they do not appear to be controlled by the same mechanisms. When a direct comparison of cutaneous and H-reflexes was made (Fig. 4), H-reflexes scale to background muscle activity, while cutaneous reflex behavior was dependent on task. During cycling, the H-reflex has been shown previously to be highly sensitive to the velocity of movement (Cheng et al. 1995a; McIlroy et al. 1992), and our results also indicate a sensitivity to muscle activity levels. Cutaneous reflexes have not been shown to change with either of these variables but do change as the mode of locomotion changes as we have observed in these experiments, as well as in previous research (Komiyama et al. 2000). Thus the changes in reflex response will be different as the context of movement changes for each type of reflex.

In summary, the main observation in this study was a reflex reversal of a middle latency cutaneous when comparing static contraction to movement. Overall, cutaneous responses were larger and excitatory during static contraction but much smaller and/or inhibitory during movement. H-reflexes were not task modulated in these experiments, which adds to the accumulating evidence that cutaneous and H-reflexes may be modulated by completely separate mechanisms.

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