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Modification of reflex responses to lumbar posterior root stimulation by motor tasks in healthy subjects

Ursula S. Hofstoetter[1], Karen Minassian[1], Christian Hofer[2], Ilse Persy[3], Helmut Kern[2], Frank Rattay[3], Milan R. Dimitrijevic[4]

[1] Center of Biomedical Engineering and Physics, Medical University of Vienna, Vienna, Austria

[2] Ludwig Boltzmann Institute of Electrical Stimulation and Physical Rehabilitation, Vienna, Austria

[3] TU-BioMed Association for Biomedical Engineering, Vienna University of Technology, Vienna, Austria

[4] Department of Physical Medicine and Rehabilitation, Baylor College of Medicine, Houston, TX, USA

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Abstract

Dynamic task-dependent regulation of reflexes controlled by the central nervous system plays an integral part in neurocontrol of locomotion. Such modifications of sensory-motor transmission can be studied by conditioning a test reflex with specific motor tasks. To elicit short-latency test reflexes we applied a novel transcutaneous spinal cord stimulation technique that depolarizes large-diameter posterior root afferents. These responses, termed posterior root-muscle reflexes (PRM reflexes), are equivalent to the monosynaptic H reflex but can be evoked in several muscles simultaneously. We elicited PRM reflexes in quadriceps, hamstrings, tibialis anterior, and triceps surae in subjects with intact nervous system. During three different conditioning-test paradigms in a standing position, i.e. volitional unilateral single- and multi-joint lower limb movements and leaning backward/forward, we recorded characteristic movement-induced modulations of PRM reflexes in the thigh and leg muscle groups. We could thus demonstrate that monosynaptic PRM reflexes in functional extensor and flexor muscles of thigh and leg can be elicited in upright standing subjects and can be modulated during the execution of postural maneuvers. The significance is that transcutaneous posterior root stimulation allows extending H reflex studies of a single muscle to the assessment of synaptic transmission of two-neuron reflex arcs at multiple segmental levels simultaneously.

Introduction

The central nervous system control of sensory-motor transmission is an essential element of neural control of locomotion, since successful limb movement depends on an effective interaction of specific sensory flow with motor plans. To assess synaptic transmission between afferents and motoneurons and how its gain is modulated by central and peripheral neural mechanisms in humans, conditioning-test paradigms utilizing the monosynaptic Hoffmann-reflex (H reflex) have commonly been used (1). Due to the superficial location of the tibial nerve in the popliteal fossa, the possibility to stimulate large-diameter afferents selectively to some degree, and the state of central excitability of the corresponding two-neuron reflex arc, the H reflex of the soleus muscle is the one most commonly studied in the human lower limb. Equivalents of the H reflex can be also evoked in other lower limb muscles by peripheral nerve stimulation, however, some require special conditions such as reflex reinforcement (2). In any case, elicitation of H reflexes from periphery is difficult to be obtained under constant stimulation conditions from a methodological point of view, especially during movement at the stimulation site.

While in the lower limbs, peripheral nerves are separated in numerous branches to supply all muscles, tendons, joints, and cutaneous and subcutaneous tissues, the respective axons leave or enter the lumbosacral cord via the anterior and posterior roots within a small longitudinal extent of approximately 5 cm in humans. Thus, it appears plausible that stimulation at that site might allow eliciting reflex responses at multiple segmental levels to study how the central nervous system controls the reflex gain of several lower limb muscles simultaneously.

We have previously demonstrated that spinal cord stimulation via implanted electrodes can elicit muscle twitch responses in multiple bilateral lower limb muscles in spinal cord injured subjects (3). These responses were shown to be initiated in large-diameter afferents of posterior roots and were thus of reflex nature. According to their initiation and recording sites they were named posterior root-muscle reflexes (PRM reflexes) (4). PRM reflexes elicited by stimulation at low frequencies (e.g. 2 Hz) are independent, segmental monosynaptic reflexes initiated within group Ia muscle spindle afferents (3,4,5).

Recently we described a novel method of transcutaneous spinal cord stimulation (tSCS) that is effective to elicit PRM reflexes through surface electrodes (6). The advantage of this technique is its non-invasive nature, allowing for a convenient application in neurophysiological studies in humans. Evidence was provided that monosynaptic PRM reflexes were equivalent to the H reflex. It was shown that the PRM reflex and the H reflex of TS were both elicited in the same afferents, but at different sites of the afferent reflex arc, either in the posterior roots or the mixed peripheral nerve (6).

Within the present paper we will demonstrate that PRM reflexes can be (i) elicited in upright standing, healthy subjects and (ii) used to assess the central gain control of short-latency reflexes at multiple segmental levels simultaneously. In particular, we will focus on the modification of PRM reflexes by volitional motor tasks during standing.

Material and Methods

Subjects

Three subjects (aged 30-34, male) with intact nervous system were recruited. The stimulation and recording protocols used in this study were approved by the local ethics committee.

Stimulation and recording set-up

Transcutaneous spinal cord stimulation was applied through self-adhesive surface electrodes (Schwa-medico GmbH, Ehringshausen, Germany). A pair of stimulating electrodes (Ø 5 cm) was placed over the T11-T12 vertebral processes, 1 cm laterally to each side of the spine, with a pair of indifferent rectangular electrodes (8 cm x 13 cm) placed over the abdomen. The two electrodes of each pair were connected to function as a single electrode. A constant-voltage stimulator was used to generate symmetric, biphasic rectangular impulses with total widths of 2 ms. For details see (6).

Electromyographic (EMG) activity was recorded with pairs of surface electrodes placed bilaterally over the bellies of quadriceps (Q), hamstrings (H), tibialis anterior (TA), and triceps surae (TS). The EMG signals were amplified using Phoenix amplifiers (EMS-Handels GmbH, Korneuburg, Austria) with a gain of 502 over a bandwidth of 10-1000 Hz and digitized at 2048 samples per second and channel.

Study protocol

Elicitation of test reflexes. Electrode placement was adjusted to stimulate posterior roots of L2-S1 segments for simultaneous, symmetric elicitation of reflex responses in all recorded muscles with subjects in a standing position. Stimulus intensity was increased stepwise until amplitudes of all responses were > 100 µV (Fig. 1A). At such intensity, TA responses had generally lowest amplitudes, while responses in all other muscles were of distinctly larger magnitudes.

Verification of reflex nature. With the designated stimulation site and intensity we applied pairs of stimuli with interstimulus intervals of 50 ms. Attenuation of the second response gives information on a prolonged refractory period and thus confirms the reflex nature of the responses (Fig. 1B).

Conditioning-test paradigms. The stimulation mode was changed to application of single stimuli, repetitively delivered at 0.2 Hz. All recordings started with elicitation of 5 unconditioned PRM reflexes, followed by 5 responses elicited under constant stimulation conditions but modified by one of three different conditioning-test paradigms (Fig. 1C).

In particular, the conditioning-test paradigms were executed as follows: (i) Subjects were asked to perform volitional unilateral dorsi- and plantar flexion, while standing on the contralateral lower limb on the edge of a small podium. To support posture, subjects rested gently on a bar with one hand. The cycle duration was approximately 6 s. Excessive EMG activity during voluntary innervation was avoided. Five conditioned responses were elicited during arbitrary segments of each of the two phases of the movement. (ii) Volitional unilateral hip and knee flexion-extension movement was performed, with the joint angles being approximately 90° at the end of the flexion phase. Again, subjects used a bar to stabilize equilibrium. Five stimuli were applied during the actual extension as well as flexion movements when the lower limb was unloaded. (iii) Subjects were asked in separate trials to lean backward and forward from neutral standing, and 5 test responses were elicited in the respective phases. Subjects were asked to alter only the ankle joint angle without alteration of knee and hip joint angles.

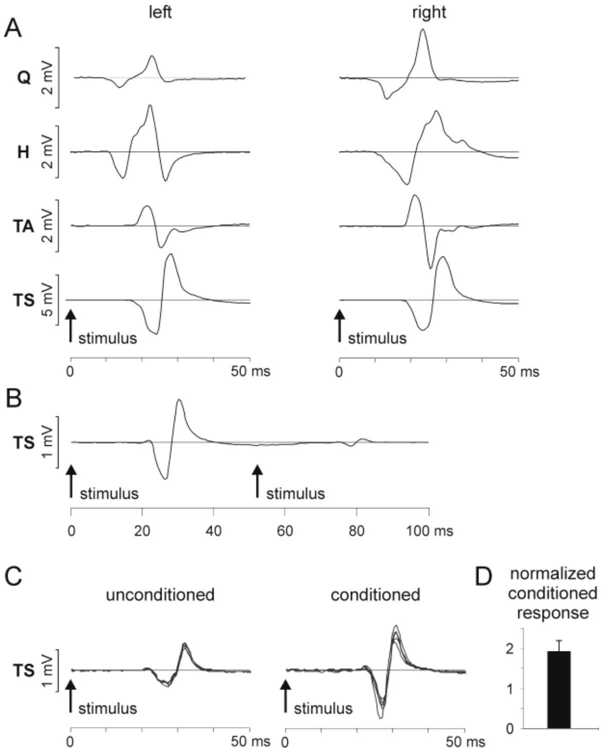

Figure 1. Electromyographic recordings and analysis of conditioning test-paradigms. (A) Elicitation of PRM reflexes in bilateral Q, H, TA, and TS with amplitudes > 100 µV marking appropriate site and intensity of transcutaneous spinal cord stimulation. (B) Responses to pairs of stimuli with 50 ms-interstimulus interval; depression of the second response indicates the reflex nature; example shown in TS. (C) Unconditioned and conditioned PRM reflexes of TS elicited under constant stimulation conditions; 5 stimulus-triggered responses displayed superimposed; (D) Group results displayed as bar chart, based on the normalization of conditioned values with respect to the unconditioned ones for each subject, muscle group, and conditioning-test paradigm.

Data analysis

For each subject, muscle group, and conditioning test-paradigm, the amplitudes of the 5 unconditioned and the 5 conditioned PRM reflexes were calculated and averaged. The mean conditioned responses were normalized with respect to the corresponding unconditioned values. Group results were obtained as follows: Since unilateral conditioning–test paradigms were conducted on both sides in separate trials in 3 subjects, arranging left and right muscle groups into ipsilateral and contralateral groups (with respect to the conditioned side) resulted in 6 values for each studied muscle. These 6 values were averaged for each conditioning-test paradigm and displayed as bar diagrams (Fig. 1D). Modification of the conditioned PRM reflexes was assumed to be "significant", if at least 5 out of the 6 responses showed the same sign of modification, i.e. either suppression or facilitation with respect to the unconditioned response.

In case of the postural motor task of leaning backward and forward that affected both lower limbs simultaneously, muscle groups were not arranged in ipsilateral and contralateral groups.

In TA, the compound muscle action potential (the electromyographic representation of a PRM reflex) could be obscured by EMG activity associated with the motor task-related activation of the muscle. If potential peaks could not be identified unequivocally after averaging, they were rejected from further analysis. Since such rejections resulted in less than 6 values for evaluation, respective results were never reported to be significant.

Data were analyzed off-line using Matlab 6.1 (The MathWorks, Inc., Natick, MA, USA).

Results

Test reflexes for conditioning-test paradigms

PRM reflexes could be elicited in all studied muscles while subjects were standing upright. The common threshold intensity required to elicit responses with a single pulse in bilateral Q, H, TA, and TS with amplitudes larger than 100 μV was on average 34.3 ± 3.4 V in the 3 subjects. Characteristic EMG recordings of the test reflexes are shown in Fig. 1A.

Volitional unilateral dorsi- and plantar flexion

Ankle dorsiflexion led to a significant suppression of the ipsilateral H and TS responses and facilitation of the ipsilateral Q response, respectively (Fig. 2A, black bars). Normalized mean peak-to-peak amplitudes derived from the 3 subjects amounted to Q, 1.5 ± 0.8; H, 0.7 ± 0.5; TA, 1.2 ± 0.4; and TS, 0.3 ± 0.2. PRM reflexes showed modifications during ankle plantar flexion, but without an overall tendency towards either facilitation or suppression (Fig. 2A, white bars). Group results were Q, 1.3 ± 0.4; H, 1.0 ± 1.0; TA, 0.8 ± 0.3; and TS, 1.1 ± 0.7. In spite of the lack of any distinct pattern of modulation there was a consistent finding in that magnitudes of PRM reflexes in H and TS were always smaller during dorsiflexion than plantar flexion; mean normalized response amplitudes of H and TS were 1.29 and 6.36 times larger during plantar flexion than dorsiflexion, respectively.

Volitional unilateral multi-joint movement

Hamstrings and TS responses of the moving lower limb were significantly suppressed during both flexion and extension phases in all subjects (Fig. 2B, black and white bars, respectively). Mean normalized response magnitudes were Q, 1.1 ± 0.6; H, 0.2 ± 0.3; TA, 1.0 ± 0.0; and TS, 0.1 ± 0.1 (flexion phase); and Q, 1.0 ± 0.2; H, 0.4 ± 0.3; TA, 0.8 ± 0.1; and TS, 0.3 ± 0.1 (extension phase). Another significant finding was that attenuation of PRM reflexes in H and TS was more profound during flexion than extension phases.

Postural motor tasks

Leaning backward (Fig. 2C, black bars) resulted in significantly reduced H and TS response magnitudes and at the same time in significant facilitation of Q responses. The group results for conditioning PRM reflexes with leaning backward were Q, 2.1 ± 1.0; H, 0.5 ± 0.4; TA, 2.0 ± 0.4; and TS, 0.5 ± 0.3. Leaning forward (Fig. 2C, white bars) led to significant facilitation of H, TA, and TS in all subjects with normalized amplitudes being Q, 1.3 ± 0.4; H, 1.4 ± 0.6; TA, 1.3 ± 0.2; and TS, 2.1 ± 0.8.

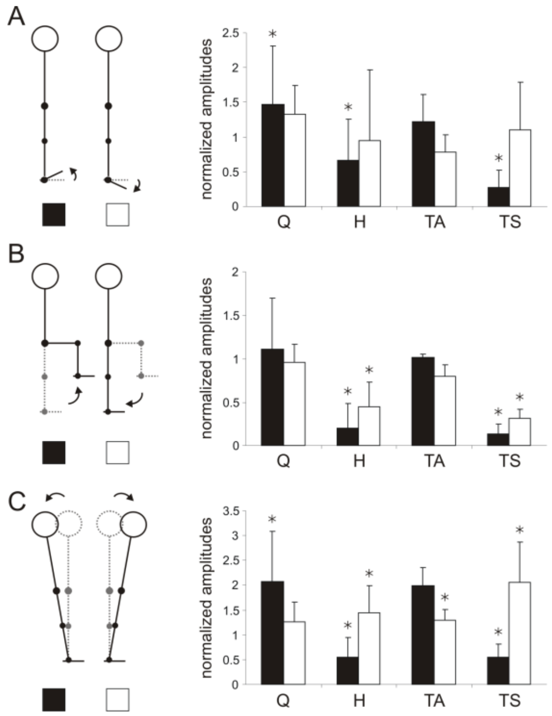

Figure 2. Group results of conditioning-test paradigms with conditioned responses normalized with respect to corresponding unconditioned ones. Quadriceps (Q), hamstrings (H), tibialis anterior (TA), and triceps surae (TS) PRM reflexes elicited during: (A) volitional unilateral single-joint dorsi- (black bars) and plantar flexion (white bars); (B) volitional unilateral multi-joint flexion (black bars) and extension movement (white bars); and (C) postural motor tasks of leaning backward (black bars) and forward (white bars). All recordings conducted in upright standing subjects; significant results marked with an asterisk.

Discussion

We have applied a novel technique based on surface electrode stimulation of lumbar posterior roots for studying the motor control of reflex activity in lower limb muscles. The test responses were PRM reflexes, monosynaptic muscle reflexes initiated within the posterior roots (6). Within the present study we have shown that these test reflexes could be elicited bilaterally in 4 thigh and leg flexor and extensor muscles in subjects with intact nervous system while standing upright. In such position, stimulus intensities to elicit PRM reflexes in all studied muscles simultaneously were somewhat higher than shown in a previous study in supine position (34.3 ± 3.4 V vs. 28.6 ± 6.3, the latter see (6)). These differences can be most probably ascribed to changes of the volume conductor properties associated with the stimulated anatomical structures. Changes of the curvature of the spine and correspondingly decreasing distances of adjacent vertebral processes can, for instance, result in increased screening of the spinal cord from stimulation.

The main finding of the present work is the demonstration that the gain of PRM reflexes is characteristically modified by volitional motor acts during the postural task of upright standing. Voluntary dorsiflexion of the foot suppressed PRM reflexes in TS. This attenuation could be expected since it is well-known that volitional dorsiflexion inhibits the monosynaptic H reflex of the calf muscles evoked by tibial nerve stimulation (7). The value of our novel method is, however, the extension of information obtained by classical H reflex studies confined to leg extensors also to other muscles of the lower limbs. As we could demonstrate, dorsiflexion not only suppressed the ankle extensor but also the hip extensor responses with a concomitant facilitation of Q and TA. The functional role of H and TS as extensors within the motor tasks of dorsi- and plantar flexion was confirmed by their relatively larger response amplitudes during “extension”.

Volitional unilateral multi-joint movements at the hip and knee joints led to reduction of the PRM reflex magnitudes of H and TS during both flexion and extension movements while the limb was unloaded. Although stimuli were applied at moments when the hip angle was approximately 135° during both flexion and extension, different degrees of attenuation were observed when this angle was passed in opposite directions. These results suggest that the mechanisms underlying the reflex modulation do not solely hinge on muscle stretch and joint position but also on the motor task setting the role of a particular muscle as either flexor or extensor.

Leaning backward from an upright standing position requires automatic contraction of the anterior compartments of thigh and leg, i.e. Q and TA, to counteract perturbation of equilibrium. Our tests revealed facilitation of the central excitability of Q and TA reflexes while leaning backward. PRM reflexes of H and TS, two muscles that are quiescent during this particular motor task, were suppressed at the same time. This finding is of particular interest since it not only hints on a absence of activation but also on a presence of inhibition.

Leaning forward, on the other hand, is normally accompanied by activation of H and TS to avoid falling. Accordingly, during this postural task, we detected increased motornuclei excitability of the posterior compartments of the lower limbs, recorded as increased magnitudes of PRM reflexes of H and TS. However, we also found facilitation of TA responses, probably due to the necessity to increase the effective stiffness of the ankle joint for stabilization.

To summarize, with the present study we demonstrated modifications of PRM reflexes by selective (single-joint movement) and more generalized (multi-joint movement) volitional motor tasks as well as postural tasks. Such modifications were simultaneously detected in flexor and extensor muscle groups of the lower limbs. Generally, reflexes were modified in a way to functionally meet the requirements of a particular motor task. By utilizing conditioning-test paradigms, information on motornuclei excitability could be obtained even of muscles that were quiescent during a particular motor task.

The presented approach opens a new avenue to analyze how motor control is triggered and maintained in individuals with intact or altered nervous system functions. Apart from the basic sciences value of studying mechanisms underlying human motor control, the assessment of "automatic" postural capacities and volitional skilful movements will be crucial to design and adjust rehabilitation strategies for restoration of locomotor functions in people with different neurological disorders.

Acknowledgements

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References

1. Schieppati M. The Hoffmann reflex: a means of assessing spinal reflex excitability and its descending control in man. Prog Neurobiol 1987; 28: 345-376.
2. Burke D, Adams RW, Skuse NF. The effects of voluntary contraction on the H reflex of human limb muscles. Brain 1989; 112: 417-433.
3. Murg M, Binder H, Dimitrijevic MR. Epidural electric stimulation of posterior structures of the human lumbar spinal cord: 1. muscle twitches - a functional method to define the site of stimulation. Spinal Cord 2000; 38: 394-402.
4. Minassian K, Jilge B, Rattay F, Pinter MM, Binder H, Gerstenbrand F, Dimitrijevic MR. Stepping-like movements in humans with complete spinal cord injury induced by epidural stimulation of the lumbar cord: electromyographic study of compound muscle action potentials. Spinal Cord 2004; 42: 401-416.

5. Minassian K, Persy I, Rattay F, Pinter MM, Kern H, Dimitrijevic MR. Human lumbar cord circuitries can be activated by extrinsic tonic input to generate locomotor-like activity. Hum Mov Sci 2007; 26: 275-295.
6. Minassian K, Persy I, Rattay F, Dimitrijevic MR, Hofer C, Kern H. Posterior root-muscle reflexes elicited by transcutaneous stimulation of the human lumbosacral cord. Muscle Nerve 2007; 35: 327-336.
7. Crone C, Nielsen J. Spinal mechanisms in man contributing to reciprocal inhibition during voluntary dorsiflexion of the foot. J Physiol (Lond) 1989; 416: 255-272.