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Corticospinal excitability during walking in humans with absent and partial body weight support

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HIGHLIGHTS

- MEPs are modulated in a phase-dependent pattern under conditions of reduced body loading.
- The phase-dependent modulation pattern of the MEPs recorded from ankle muscles is reproducible over time.
- Reduced body loading utilized for gait rehabilitation will not change the strength of corticospinal drive.

ABSTRACT

Objective: To establish changes in corticospinal excitability with absent and partial body weight support (BWS), and determine test–retest reliability of motor evoked potentials (MEPs) recordings during stepping in healthy humans.

Methods: The tibialis anterior (TA) and soleus MEPs during stepping at 0 and at 25 BWS were recorded in two experimental sessions in the same subjects. Transcranial magnetic stimulation was delivered randomly across the step cycle at 1.2 × TA MEP resting threshold. The non-stimulated associated electromyogram (EMG) was subtracted from the TA and soleus MEPs at identical time windows and bins of the step cycle, and the resultant values were normalized to the maximal homologous EMG activity during stepping. The relationship between MEPs and background EMG activity was determined for each BWS level and session tested.

Results: The TA MEPs were facilitated at heel contact, progressively decreased during the stance phase, and facilitated throughout the swing phase of the step cycle. In contrast, the soleus MEPs were progressively increased at early-stance, depressed at the stance-to-swing transition, and remained depressed throughout the swing phase. The TA and soleus MEPs were modulated in a similar pattern across sessions at 0 and at 25 BWS, and were linearly related to the associated background EMG activity.

Conclusions: These results provide evidence that reduced body weight loading does not alter the strength of corticospinal excitability, and that MEPs can be reliably recorded at different sessions during stepping in healthy humans.

Significance: A rehabilitation strategy to restore gait in neurological disorders utilizes BWS during stepping on a motorized treadmill. Based on our findings, the strength of corticospinal drive will not be affected negatively during stepping under conditions of partial body loading.

1. Introduction

Spinal neuronal networks integrating sensory afferent feedback interact continuously with supraspinal centers to produce efferent activity appropriate to the task and to the phase of the step during walking (task- and phase-dependent neuronal activity) (Nielsen, 2003; Knikou, 2010, 2012). However, most of evidence on the role of motor cortex in the neural control of locomotion comes from experiments conducted in the cats (Armstrong and Drew, 1984; Drew et al., 2002). Consequently, studying how corticospinal drive

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adapts under different conditions of sensory feedback can provide valuable information on the suprasegmental control of human locomotion.

The modulation patterns of the ankle stretch reflex, quadriceps tendon reflex, and electrically induced soleus or quadriceps H-reflexes during walking are well established in humans. These reflexes increase progressively during the stance phase, are depressed at the stance-to-swing transition phase, while at late-swing and at heel contact the reflex amplitude is increased compared to the other phases of the step cycle (Capaday and Stein, 1986; Crenna and Frigo, 1987; Dietz et al., 1990a,b; Edamura et al., 1991; Yang and Whelan, 1993; Sinkjær et al., 1996; Andersen and Sinkjær, 1999; Larsen et al., 2006; Knikou et al., 2009a). The amplitude of the transcranial magnetic stimulation (TMS) induced motor evoked potentials (MEPs), recorded from the tibialis anterior (TA) and gastrocnemius medialis muscles, is modulated in a phase-dependent pattern during human walking (Schubert et al., 1997). The TA MEP amplitude increases before swing phase initiation and at late-swing, while the gastrocnemius medialis MEP amplitude increases at mid and late-stance phases (Schubert et al., 1997). Although the phase-dependent amplitude modulation of MEPs did not follow linearly the gait-mediated modulation of electromyographic (EMG) activity (Schubert et al., 1997), they are generally facilitated when the muscle from which they are recorded is active and small when the antagonist muscle is active (Schubert et al., 1997; Capaday et al., 1999). These findings suggest that the TA and soleus MEPs are modulated in a reciprocal pattern, similar to that known for the spinal reflexes.

Proprioceptors that transmit information on the amount of body loading contribute to the spinal reflex-mediated regulation of locomotion (Dietz, 2002; Knikou, 2010). Thus, one would expect that under conditions of reduced body loading, the function of the spinal reflex circuits that are prone to descending control would be altered. We have recently shown that the soleus H-reflex, reciprocal Ia inhibition, and presynaptic inhibition phase-dependent modulation pattern remains unaltered when body weight support (BWS) is provided during stepping or when stepping in a specific limb trajectory imposed by a robotic exoskeleton (Knikou et al., 2009a, 2011; Mummidisetty et al., 2013). Collectively, in this study we established the modulation pattern of the MEPs across multiple phases of the step cycle in healthy humans during stepping with absent and partial BWS. We also recorded MEPs in the same subjects under identical experimental procedures 2–7 days after the first experiment, in order to establish test–retest reliability of MEPs recordings during stepping.

2. Methods

2.1. Subjects

People with tooth implants, assistive hearing devices, pacemaker, history of seizures, and medications known to alter central nervous system excitability were excluded from participation. Seven healthy volunteers with an age range of 23–44 years (27.7 ± 7.4, mean ± SD) participated in the study. All subjects signed an informed consent form for neurophysiological tests before study participation, which was approved by the Northwestern University (IL, USA) institutional review board. The study was conducted in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki.

2.2. Experimental procedures

The purpose of this study was to establish the modulation pattern of the MEPs recorded from the TA and soleus muscles, and demonstrate test–retest reliability of MEPs recordings with absent and partial BWS during treadmill walking. With the subjects seated, bipolar differential surface electrodes of fixed inter-electrode distance (Motion Lab Systems Inc., Baton Rouge, LA, USA) were placed on the right (contralateral to the magnetic coil) TA and soleus muscles following standard procedures for EMG recordings. Single 1-ms TMS pulses over the left primary motor cortex were delivered with a Magstim 200 stimulator (Magstim, UK) via a 110 mm double-cone coil and the induced current to flow in a posterior-to-anterior direction. The point where the lines between the inion and glabellum, and the left and right ear tragus met was marked on an EEG cap. The double-cone coil was placed parallel and approximately 1 cm posterior and 1 cm lateral to the left from this intersection point. With the double-cone coil held at this position, the stimulation intensity was gradually increased and the MEPs recorded from the right TA and soleus muscles were observed on a digital oscilloscope (TDS 2014, Tektronix, Beaverton, OR, USA). When in three out of five TMS pulses, MEPs could not be evoked at low stimulation intensities with the subject at rest in the TA muscle only, the magnetic coil was moved by few mm and the procedure was repeated. When the optimal position was found, the TA MEP resting threshold was established and corresponded to the stimulation intensity that induced repeatable MEPs in size that were approximately 100 μV of peak-to-peak amplitude (Rossini et al., 1994; Rothwell et al., 1999). Ten MEPs, each evoked once every 10 s, were recorded at 1.0 and at 1.2 times the MEP resting threshold. Then, the MEP input–output curve was constructed, and the optimal position of stimulation was marked again on an EEG cap for each subject.

Then, the subject stood on the treadmill, and wore an upper body harness that was connected through an overhead pulley to the frame of the TheraStride® system (Innoventor, St. Louis, MO, USA) (Fig. 1A), and a mouth guard and ear plugs to minimize discomfort due to TMS. The magnetic coil was positioned on the head, and the optimal stimulation position was verified again with the subject standing, based on the procedures utilized during seated. The position of the magnetic coil was maintained through a customized chin strap and was supported by a Velcro connected to the frame of the TheraStride system (Fig. 1A). With the subject standing, the right leg was held by an experimenter in a flexed and/or in an extended position without being loaded, and the TA MEP resting threshold was re-established. Ten MEPs, each evoked once every 10 s, were recorded at 1.0 and at 1.2 times the MEP resting threshold with the leg extended or flexed. In the first experimental session, the mean TA MEP resting threshold with the right leg flexed and extended during standing on the left leg was 38.4 ± 6.1 (mean ± SD)% and 45 ± 6.6% of the stimulator output, respectively. In the second experimental session, the mean TA MEP resting threshold with the right leg flexed and extended during standing on the left leg was 38.4 ± 6.1% and 45.3 ± 6.6% of the stimulator output, respectively.

With the subject standing, the right common peroneal nerve was stimulated with a single shock of 1-ms duration, that was triggered from a computer (controlled by customized Labview software) and delivered by a constant current stimulator (DS7A, Digitimer, UK). The stimulus to the common peroneal nerve was delivered by a bipolar stainless-steel electrode placed distal to the head of the fibula. The stimulation intensity corresponding to the TA maximal M-wave was established, and 10 TA maximal M-waves, each evoked once every 5 s, were recorded.

The treadmill speed for all subjects was set at 0.98 m/s, which corresponds to a comfortable medium gait speed (Bohannon, 1997). The TMS output was adjusted at 1.2 times the TA MEP resting threshold while subjects stepped at 0 and at 25 BWS. TMS delivered at 1.2 MEP threshold corresponded largely to the linear portion of the TA MEP input–output curve constructed with the