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Short-term effects of electrical nerve stimulation on spinal reciprocal inhibition depend on gait phase during passive stepping

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ABSTRACT

A combination of electrical nerve stimulation (ENS) and passive or active cyclic movements (i.e., pedaling and stepping) has been suggested to induce stronger short-term effects in spinal circuits as compared to either intervention alone. The purpose of the present study is to determine whether the effects of ENS during passive stepping are dependent on the timing of the stimulation during the stepping cycle. A total of 10 able-bodied participants were recruited for the study. Two interventions were assessed during passive ground stepping: (1) ENS of the common peroneal nerve (CPN) during the swing phase (ENS_{swing}) and (2) stance phase (ENS_{stance}). ENS was applied at the motor threshold intensity on the tibialis anterior muscle for a total of 30 min. Spinal reciprocal inhibition (RI) was assessed by conditioning the H-reflex in the soleus muscle with electrical stimulation to the CPN before (baseline), as well as 5, 15, and 30 min after each intervention. Compared to the baseline, the amount of RI was increased 5 and 15 min after the ENS_{swing} intervention, whereas it was decreased after the ENS_{stance} intervention. This suggests that ENS has a phase-dependent effect on RI during passive stepping. Overall, the results imply that phase-dependent timing of ENS is essential for guiding plasticity in the spinal circuits.

1. Introduction

Induction and guidance of activity-dependent plasticity are imperative for functional recovery of walking after spinal cord injury, stroke, and other neuromuscular disorders. Sensory input pathways that provided afferent information to the central nervous system can be used to induce plasticity in the spinal and supraspinal circuits (Field-Fote, 2004; Wolpaw, 2007).

There are two main methods for inducing activity-dependent spinal plasticity through the sensory input pathways. The first one involves assistive interventions, such as manual or robotic-assisted guidance of the lower limbs during body-weight-supported walking (Wolpaw, 2007; Dunlop, 2008). Such interventions aim to induce activity of spinal locomotor circuits through movement-induced sensory input (Harkema, 2001). They have been shown to enhance recovery of the ability to walk in patients with incomplete spinal cord injuries (Dietz et al., 1995; Wernig et al., 1995; Dobkin et al., 2006). The other method for providing sensory input to the spinal circuits involves the artificial activation of afferent fibers using electrical nerve stimulation (ENS) (Perez et al., 2003; Kitago et al., 2004). Perez et al. (2003) reported the lasting enhancement of spinal reciprocal inhibition (RI) of the soleus (Sol) H-reflex (up to 10 min) when sensory ENS was applied to the common peroneal nerve (CPN) while subjects were at rest. Moreover, Kitago et al. (2004) showed the short-term effects (up to 16 min) of tetanic ENS of the tibial nerve on the Sol H-reflex amplitude.

Recently, our group has demonstrated that 30 min of passive ground stepping (PGS) on a treadmill combined with ENS of the CPN reduced the amount of spinal RI to the Sol H-reflex (Obata et al., 2015). These effects lasted for 15 min after the intervention. However, no changes were found when either intervention was applied independently. Similarly, it was previously shown that spinal RI is affected more when active pedaling was combined with ENS of the CPN, as compared to when ENS was delivered at rest (Yamaguchi et al., 2013). These results suggest that a combination of CPN stimulation and cyclic movements (i.e., pedaling and stepping) is more effective than either intervention alone.

In our previous study, ENS of the CPN was applied during the swing phase of the stepping cycle (Obata et al., 2015). It is well known that RI

Abbreviations: CPN, common peroneal nerve; EMG, electromyography; ENS, electrical nerve stimulation; PGS, passive ground stepping; RI, reciprocal inhibition; Sol, soleus muscle; TA, tibialis anterior muscle

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of the Sol H-reflex is modulated in a phase-dependent manner during unsupported human walking. Specifically, RI was reported to be larger during the swing phase as compared to the stance phase, when it was absent (Lavoie et al., 1997; Petersen et al., 1999). Our previous study provided evidence in support of the notion that concomitant sensor inputs caused by ENS of the CPN during the swing phase activate the Ia-inhibitory interneurons to inhibit Sol motoneurons. However, it is still unknown how ENS of the CPN during the stance phase of the stepping cycle affects the induction of spinal RI plasticity.

Therefore, the purpose of the present study is to determine whether the effects of CPN stimulation and passive ground stepping are dependent on the phase of the stepping cycle. We hypothesized that ENS of the CPN during the swing phase would activate the Ia-inhibitory interneurons more effectively than CPN stimulation during the stance phase. Specifically, we applied ENS during the swing and stance phases of passive ground stepping and compared their short-term effects on the spinal RI.

2. Methods

2.1. Subjects

Ten able-bodied male subjects (age: 23–37 years) participated in the study. All participants gave written informed consent to participate in the experiments. The experiments were performed in accordance with the Declaration of Helsinki (1964), and they were approved by the Human Ethics Committee at the University of Tokyo and the Ethics Committee at the National Rehabilitation Center for Persons with Disabilities.

2.2. Electromyography (EMG) recording

EMG activity was recorded from the right Sol and right tibialis anterior (TA) muscles using surface self-adhesive Ag/AgCl electrodes (5 mm diameter). Recording electrodes were placed longitudinally along the muscle fibers with an inter-electrode distance of 20 mm (center to center) on the: (i) TA muscle one third of the distance between the tibial tuberosity and the center of the ankle joint and 1 cm lateral edge of the tibia; (ii) Sol muscle 2 cm medial from the Achilles tendon and 1 cm below the lower edge of medial gastrocnemius belly (Fujio et al., 2016). A reference belt-shaped electrode was placed around the lower leg 5 cm below the right fibular head (Fig. 1). EMG signals were pre-amplified (500–1000 ×) and bandpass filtered between 15 and 3,000 Hz (Obata et al., 2015) with a conventional bioamplifier (AB-621B, Nihon Kohden Co., Japan, input impedance > 10 MΩ, CMRR > 60 dB). All data were sampled at 10 kHz using a 16-bit A/D converter (PowerLab, ADinstruments, USA) and stored on the computer.

2.3. Passive ground stepping (PGS)

PGS on the treadmill was performed using a robotic driven-gait orthosis (Lokomat®, Hocoma AG, Switzerland) for a duration of 30 min. A detailed description of the device was reported by Colombo et al. (2000). The settings were consistent with our previous study (Obata et al., 2015). The treadmill speed was set at 2.0 km/h. The body weigh was not unloaded by a harness system, which means that the subjects were not suspended. To ensure fully passive stepping, subjects were instructed to relax as much as possible so as not to prevent lower limb movements imposed by the driven-gait orthosis.

2.4. Electrical nerve stimulation (ENS)

ENS was delivered to the right CPN using a battery-driven stimulator (GD-611, OG Giken Co. Ltd., Japan) with a bipolar rectangular stimulus waveform at 25 Hz with a 0.05-ms pulse width. Stimulation was delivered in a train of 3 pulses using a surface electrode (Ag/AgCl, Vitrode F-150S, Nihon Kohden, Japan). The electrodes for ENS were placed near the fibula head and carefully positioned to avoid activation of the peroneus muscles, thus ensuring more selective stimulation of the deep branch of the peroneal nerve. The intensity of CPN stimulation was set to just above the motor threshold intensity for the TA muscle for each subject. The motor threshold of the TA was defined as the lowest intensity required to elicit five responses with and amplitude greater than 100-μV in ten consecutive attempts (Rossini et al., 1994).

2.5. Experimental paradigm

The following interventions were randomly tested on separate days: (1) PGS with ENS during the swing phase of the stepping cycle (ENS_{swing}); and (2) PGS with ENS during the stance phase of the stepping cycle (ENS_{stance}). Each intervention was administered for a period of 30 min. Assessments were performed before (i.e., baseline) as well as 5, 15, and 30 min after each intervention (Fig. 1) by recording the Sol H-reflex, Sol M_{max}, TA M_{max}, and RI. All assessments were performed in the sitting posture while subjects were asked to relax their Sol and TA muscles.

2.6. Reciprocal inhibition (RI) test

RI was assessed by evaluating changes in the amplitude of the test Sol H-reflex following conditioning stimulation to the CPN (i.e., the Sol H-reflex conditioning-test paradigm). Ten tests and 10 conditioned Sol H-reflex trials were recorded with 5-s intervals between tests. The test Sol H-reflex was elicited in the right leg by stimulating the posterior tibial nerve using an electrical stimulator (SEN-7203, Nihon Kohden, Japan). The cathode was placed on the popliteal fossa, and the anode was placed over the patella. The test Sol H-reflex amplitude was maintained at 15–25% of the M_{max} (Crone et al., 1990). Conditioning

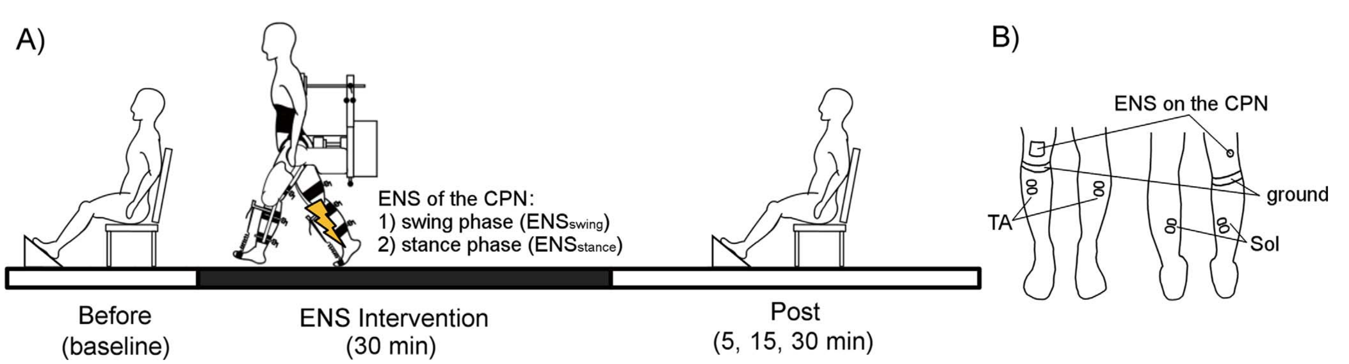

Fig. 1. Experimental setup showing: (A) assessment times before (baseline) as well as post (5, 15, 30 min) after the ENS_{swirng} and ENS_{stance} interventions; and (B) EMG electrode placement for the TA and Sol muscles as well as the ground electrode and ENS stimulation location on the CPN.