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Maintenance of cutaneomuscular neuronal excitability after leg-cycling predicts lower limb muscle strength after incomplete spinal cord injury

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HIGHLIGHTS

- Rhythmic leg exercise changes spinal neuronal activity after spinal cord injury (SCI).
- Leg-cycling may improve cutaneous sensorimotor function after incomplete SCI.
- Cutaneous sensorimotor function after leg-cycling predicts leg strength after iSCI.

ABSTRACT

Objective: Controlled leg-cycling modulates H-reflex activity after spinal cord injury (SCI). Preserved cutaneomuscular reflex activity is also essential for recovery of residual motor function after SCI. Here the effect of a single leg-cycling session was assessed on cutaneomuscular-conditioned H-reflex excitability in relation to residual lower limb muscle function after incomplete SCI (iSCI).
Methods: Modulation of Soleus H-reflex activity was evaluated following ipsilateral plantar electrical stimulation applied at 25–100 ms inter-stimulus intervals (ISI's), before and after leg-cycling in ten healthy individuals and nine subjects with iSCI.
Results: Leg-cycling in healthy subjects increased cutaneomuscular-conditioned H-reflex excitability between 25 and 75 ms ISI ($p < 0.001$), compared to a small loss of excitability at 75 ms ISI after iSCI ($p < 0.05$). In addition, change in cutaneomuscular-conditioned H-reflex excitability at 50 ms and 75 ms ISI in subjects with iSCI after leg-cycling predicted lower ankle joint hypertonia and higher Triceps Surae muscle strength, respectively.
Conclusion: Leg-cycling modulates cutaneomuscular-conditioned spinal neuronal excitability in healthy subjects and individuals with iSCI, and is related to residual lower limb muscle function.
Significance: Cutaneomuscular-conditioned H reflex modulation could be used as a surrogate biomarker of both central neuroplasticity and lower limb muscle function, and could benchmark lower-limb rehabilitation programs in subjects with iSCI.

1. Introduction

Cutaneous sensory processing is essential for the performance of voluntary motor tasks such as locomotion and balance (Van Wezel et al., 1997; Zehr and Stein, 1999; Rossignol et al., 2006) and the execution of phasic lower limb movements associated with leg cycling (Zehr et al., 2001). After spinal cord injury (SCI) experimental studies have also demonstrated that cutaneous afferent information contributes to the recovery of residual gait function

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(Rossignol et al., 2008; Panek et al., 2014), and may represent a central mechanism of neuroplasticity (Frigon et al., 2009). However, the relationship between activity-based rehabilitation performed by subjects with incomplete SCI (iSCI) and an improvement in cutaneomuscular spinal processing has not been assessed.

Previously several neurophysiological studies have demonstrated that cutaneous stimuli facilitate motor function (Schouenborg, 2003; Rossignol et al., 2006; Wolpaw, 2007; Panek et al., 2014). At the cortical level in man, stimulation of the superficial peroneal, sural (Nielsen et al., 1997) or tibial nerve (Poon et al., 2008) has been shown to facilitate long-latency motor-evoked potentials following transcranial magnetic stimulation. Furthermore the effect of this conditioning protocol depends on the integrity of the spinal cord, because facilitation of Tibialis Anterior motor evoked potentials following common peroneal nerve stimulation has only been detected in subjects with a less severe iSCI (Roy et al., 2010). Finally clinical neurophysiological evidence also suggests that cutaneous input to the subcortical level is also responsible for the facilitation of vestibulospinal-evoked motor activity in healthy individuals during rest (Lowrey and Bent, 2009). Studies are now required to assess the effect of controlled motor activity, associated with rehabilitation tasks such as leg-cycling, on spinal cutaneomuscular neuronal activity both in healthy subjects and individuals with iSCI.

Cutaneomuscular-conditioned Soleus H-reflex modulation has been assessed in healthy non-injured subjects and persons with SCI to assess the state of spinal neuronal activity and motor control mechanisms (Knikou, 2007; Sayenko et al., 2009). The demonstration that the Soleus H-reflex can be inhibited following a preceding cutaneous conditioning stimulus has been used to assess the role of presynaptic (Morita et al., 1998) or postsynaptic modulatory mechanisms (Knikou, 2007) with inhibitory effects observed between 3 and 90 ms inter-stimulus interval in healthy subjects (Knikou, 2007). Furthermore application of metatarsal non-noxious cutaneous conditioning stimuli applied at 25 ms (Sayenko et al., 2009) or 45 ms at rest in healthy subjects (Fung and Barbeau, 1994) has been used to show a loss of Soleus H-reflex excitability in individuals with iSCI, indicating sensorimotor dysfunction. Interestingly, loss of Soleus H reflex excitability to cutaneous afferent input following SCI can be partially reversed following conditioning of the superficial peroneal nerve at ISI's of between 30 and 190 ms (Levin and Chapman, 1987), which suggests that cutaneomuscular spinal neuronal activity may also be modulated by activity-based rehabilitation tasks.

Modulation of spinal reflex function has been observed following cycling tasks in healthy subjects (Mazzocchio et al., 2006; Meunier et al., 2007), where the ability of a healthy subject to follow a target recumbent cycling speed was associated with a reduction in H-reflex activity, possibly mediated by an increase in homosynaptic depression. Phadke et al. (2009) also showed that the H-reflex was further inhibited in individuals with SCI following a single 20-min leg cycling session, similar to that observed in a subject diagnosed with the SCI spasticity syndrome during a 12-week passive leg cycling training program (Kiser et al., 2005). Furthermore dynamic, rather than static, exercise has been shown to induce greater H-reflex modulation in healthy subjects, since isometric muscle contraction has been shown to be ineffective compared to other dynamic motor tasks (Jessop et al., 2013). The effect of a single session of leg-cycling on changes in H-reflex modulation induced by cutaneous conditioning stimuli remains to be characterized.

The hypothesis of this study is that leg-cycling may improve cutaneous spinal neuronal activity after iSCI which would reflect individual residual motor function and specific signs of the spasticity syndrome. Therefore, the objective of this study was to determine whether a short single-session of controlled leg-cycling c.f. (Phadke et al., 2009), would change Soleus H-reflex excitability in response to plantar cutaneomuscular conditioning stimuli. We show here that leg-cycling in healthy subjects leads to an increase in cutaneomuscular-conditioned H-reflex excitability, compared to a small loss of excitability in the iSCI group. Furthermore maintenance of cutaneomuscular-conditioned H-reflex excitability after leg-cycling in subjects with iSCI predicts good-moderate Triceps Surae muscle strength and lower ankle joint hypertonia.

2. Materials and methods

2.1. Subjects

All applicable institutional and governmental regulations concerning the ethical use of human volunteers were followed during this research. The protocol was approved by the Toledo Hospital clinical ethical committee (CEIC 07/05/2013, CEIC 15/07/2013 and CEIC 17/1/2012). All recruited subjects signed the informed consent form before the study commenced. Ten healthy volunteers were recruited from the hospital staff and nine subjects with iSCI (AIS C-D, neurological level of lesion between C5 and T10), capable of cycling autonomously were recruited as inpatients during their rehabilitation at the National Paraplegic Hospital. The exclusion criteria for these subjects included epilepsy, pregnancy, lower limb musculoskeletal injury or peripheral nervous system disorders. All subjects were only recruited for this study and received the standard rehabilitation treatment program administered at the hospital, according to their treating physician.

2.2. Clinical outcome measures

Clinical evaluation of the patients with iSCI was performed with the following set of scales: ASIA Impairment Scale (AIS, Maynard et al., 1997) to diagnose the level and grade of iSCI; WISCIII gait function index (Dittuno and Ditunno, 2001); manual muscle score (0–5) of the Quadriceps, Hamstring, Tibialis Anterior and Triceps Surae muscles (Medical Research Council of the UK, 1976); the modified Ashworth scale to measure lower limb muscle hypertonia with knee and ankle joint flexion–extension (Bohannon and Smith, 1987); Penn spasm scale (Penn et al., 1989); and the Spinal Cord Assessment Tool for Spastic Reflexes Scale (SCATS) (Benz et al., 2005) to measure the severity of evoked spasms.

2.3. Controlled leg cycling task

During the experimental protocol, participants were seated in a static leg ergometer, with the feet firmly tied to the pedals with velcro straps (Fig. 1A). Two ankle–foot orthoses were placed on each leg to prevent excessive ankle movement during leg-cycling, which is known to influence Soleus H-reflex excitability (Hwang, 2002). Soleus H-reflex activity was tested before and after a 10 min 42 rpm leg-cycling session performed at an intensity that the subject felt moderate and comfortable (Fig. 1D). Soleus H-reflex testing was performed at rest before and after leg-cycling at the 300° crank position shown in Fig. 1(A).

2.4. Soleus H-reflex measurement

Soleus H-reflex activity was evoked with a 1 ms electrical stimulus pulse delivered to the right tibial nerve with a superficial bipolar electrode applied to the popliteal fossa (Fig. 1(C), IntFES, Tecnalia, San Sebastián, Spain) (Malesevic et al., 2012). The stimulation intensity was set to generate a control Soleus H-reflex