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Research article

Modulation of quadriceps corticospinal excitability by femoral nerve stimulation

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HIGHLIGHTS

- The time course of MEP modulation induced by electrical stimulation is showed.
- Electrical stimulation of the femoral nerve induced a short latency inhibition.
- Long latency facilitation was evoked in the rectus femoris by TMS.

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ABSTRACT

Introduction: We explored the conditioning effect of a percutaneous electrical pulse of the femoral nerve on cortical motor evoked responses in the rectus femoris muscle.
Methods: Corticospinal excitability of rectus femoris muscle was measured in sixteen healthy subjects, when a single transcranial magnetic pulse was preceded by an electrical femoral nerve stimulus, using twelve inter-stimulus intervals (from 10 to 275 ms). We also evaluated the effects of the intensities of the transcranial magnetic and of the electrical pulses.
Results: Quadriceps motor evoked potentials were inhibited and facilitated when a single femoral nerve electrical stimulus was delivered at inter-stimulus intervals of 25 ms and 150 ms, respectively. The facilitation was reduced when low electrical intensity was used, while the inhibition decreased with high intensity transcranial magnetic pulse.
Conclusion: Afferent inputs of a femoral stimulation modulate the responses elicited by transcranial magnetic pulses of the contralateral quadriceps motor cortex. This modulation indicates a sensorimotor integration of proximal lower limb muscles that may be mediated via different types of afferents. This could be of relevance for studies that explore the role of lower limb muscles in postural control and balance.

1. Introduction

Complex motor activities require appropriate inputs from muscular and cutaneous afferents. The integration of the sensory input with the motor output is of importance foran appropriatecontrol of movement. The functionality of this sensorimotor integration varies according to the muscle involved in the motor action. For instance, blockage of sensory inputs from finger muscles lead to a loss of finger coordination and appropriate grip force [1], while anaesthesia of the plantar sole of a foot can affect the recovery from a forward fall [2].

The circuitry underlying sensorimotor integration can be tested using paired pulse paradigms, where an electrical stimulus given to a peripheral nerve is followed by a transcranial magnetic stimulation (TMS) pulse on the motor cortex [3,4]. This paradigm has been mostly used in upper limb muscles, to explore the time course of the modulation that the somatosensory inputs exert on the motor output [5,6]. Typically, a conditioning electrical stimulus applied to a mixed nerve (most often the median or digital nerve of the wrist) can induce an inhibitory or facilitatory effect on motor cortex excitability. The inhibitory effects, more evident at inter-stimulus

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intervals of around 20 ms and 200 ms, have been described as short and long latency afferent inhibition, respectively [6].

Several studies have shown that peripheral nerve stimulation can also modulate the cortical excitability of lower limb muscles, with a main focus on the tibial and soleus muscles [3,4,7,8]. Only a couple of studies explored the effects of peripheral nerve stimulation on MEPs in quadriceps muscle [4,7]. These studies showed that a peripheral electrical stimulus induced an increase in the amplitude of the motor response evoked by a TMS pulse at several inter-stimulus intervals. However, the stimulated nerves were the common peroneal, gastrocnemius medialis and tibial nerves. Therefore, it remains unknown whether an electrical pulse of the femoral nerve, which supplies innervation to the quadriceps, is able to modulate the cortical response of this muscle. This is of relevance since the quadriceps muscle is one of the most important lower limb muscles for a wide range of physical functions [9], and the sensory inputs from this muscle may play an important role in its spinal and cortical control. For instance, poor peripheral nerve function has been associated with low and fast declining quadriceps strength in older adults [10], which may lead to impairments in balance [11], gait [12] and an increased risk of falls [13].

In summary, the study of the sensorimotor integration of the quadriceps muscle can provide new insight in to the role of the sensory inputs in the control of this muscle. In the current study we conducted a series of experiments in order to explore the conditioning effect of a percutaneous electrical pulse of the femoral nerve on cortical motor evoked responses in the rectus femoris muscle. In addition, we examined the time course of this modulation.

2. Methods

2.1. Subjects and general procedure

A total of sixteen neurological healthy subjects (9 males, 7 females, 19–21 years of age) participated in the study. Some subjects took part in more than one experiment. Written informed consent was obtained from all subjects. Experimental procedures conformed to the declaration of Helsinki and were approved by the Local Ethics Committee of the University of A Coruña. Subjects were screened for contraindications to TMS [14]. None of the subjects reported any neurological (including a past medical history of head injury or seizures), psychiatric or other significant medical problems. Prior to the experimental sessions, subjects were familiarized with the general procedure of the transcranial magnetic and percutaneous electrical stimulation.

During the experiments the subjects were comfortably seated in a reclining armchair; with the hips flexed at 90°, the right knee flexed at 90° and the ankles were at 110° of a plantar flexion, with the feet resting on a foot support. Subjects kept their eyes open and were asked not to engage in conversation during the experiment.

2.2. Surface electromyography (EMG) recording

Electromyographic (EMG) signals were recorded using bipolar self-adhesive Ag/AgCl electrodes of 10-mm diameter in a bipolar configuration of the rectus femoris (RF), vastus lateralis, vastus medialis and biceps femoris, following the SENIAM recommendations [15], with an inter-electrode distance of 25 mm and with the reference electrode located on the patella. The position of the electrodes was marked on the skin so that these were used in the subsequent session. The recording sites were shaved, abraded and cleaned with isopropyl alcohol to obtain low impedance (Z,5 kΩ). EMG signals were amplified and filtered with a bandwidth frequency ranging from 10 Hz to 1 kHz (gain = 1,000). The EMG signals were simultaneously digitized using an acquisition card at a sampling rate of 5 kHz per channel (Digitimer D360, Welwyn Garden City, UK) and stored for later analysis on a computer with a custom built Signal Software script [Cambridge Electronics Design (CED), Cambridge, UK].

2.3. Femoral nerve stimulation (FNS)

Electrical stimulation was used to activate the femoral nerve of the right leg. A cathode, a circular self-adhesive electrode of 1 cm diameter (Cefar-Compex Scandinavia AB, Sweden), was positioned on the femoral triangle, 3–5 cm below the inguinal ligament. The anode, a 130 × 80 mm self-adhesive electrode, was applied to the gluteal fold. Square-wave pulses with a width of 1 ms, at a maximal voltage of 400 V from a constant current stimulator (Digitimer DS7A, Welwyn Garden City, UK), were delivered to the resting muscle.

2.4. Transcranial magnetic stimulation (TMS)

Single TMS pulses (MagstimBiStim 2002, The Magstim Company, Dyfed, UK) were delivered via a concave double-cone coil (diameter: 110 mm; maximum output: 1.4 T). The handle of the TMS coil was positioned over the vertex of the head and held tangential to the skull in an anterior–posterior orientation. The coil was positioned over the left motor cortex and the orientation of the coil was determined by localizing the largest motor evoked potential (MEP) in the right RF muscle, with the lowest motor response in the biceps femoris muscle. The optimal stimulation site was marked with an indelible red marker to ensure reproducibility of the stimulus conditions for each subject throughout the sessions. The resting motor threshold (RMT) was determined as the minimum stimulus intensity required to elicit an MEP in the RF, of at least 50 μV, in 5 of 10 consecutive trials.

2.5. Main experiment. Effects of FNS on corticospinal excitability

Fourteen subjects participated in the main experiment. To explore the effects of peripheral sensory stimulation on corticospinal excitability, a single TMS pulse (test stimulus, TS) was preceded by an electrical femoral nerve stimulus (conditioning stimulus, CTS) at twelve inter-stimulus intervals: 10 (CTS_{10}), 25 (CTS_{25}), 50 (CTS_{50}), 75 (CTS_{75}), 100 (CTS_{100}), 125 (CTS_{125}), 150 (CTS_{150}), 175 (CTS_{175}), 200 (CTS_{200}), 225 (CTS_{225}), 250 (CTS_{250}) and 275 (CTS_{275})ms. TMS intensity was adjusted to 120% of the RMT. However, in some cases the intensity was increased in order to obtain a more stable MEP. The electrical femoral nerve stimulation was adjusted to the individual motor threshold, and was defined as the minimum intensity able to evoke a visible twitch in the RF.

Since MEP amplitudes (induced by magnetic cortical stimulation) have a large variability, partly due to the liability of the attention level [16], we distributed TS and CTS trials in 4 blocks as follows: (TS, CTS_{10}, CTS_{100}, CTS_{200}); (TS, CTS_{25}, CTS_{125}, CTS_{225}); (TS, CTS_{50}, CTS_{150}, CTS_{250}) and (TS, CTS_{75}, CTS_{175}, CTS_{275}). The order of the blocks was randomized across subjects. Each block included 12 TS trials and 12 CTS trials at three different intervals making a total of 48 trials. The order of the trials was randomized in each block and the time between the trials was set at 7 s with a 10% variation. Between blocks subjects rested for 5 min, remaining seated in the same position.

2.6. Complementary experiment 1: effects of different FNS intensities on corticospinal excitability

To explore whether the intensity of the FNS affects the modulation of the TMS pulse, we tested eleven subjects using two different FNS intensities,while the TMS pulse intensity remained constant.