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Voluntary breathing increases corticospinal excitability of lower limb muscle during isometric contraction

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ABSTRACT

The aim of the present study was to determine the effects of voluntary breathing on corticospinal excitability of a leg muscle during isometric contraction. Seven subjects performed 5-s isometric knee extension at the intensity of 10% of maximal voluntary contraction (10% MVC). During the 10% MVC, the subjects were instructed to breath normally (NORM) or to inhale (IN) or exhale (OUT) once as fast as possible. Motor-evoked potentials (MEPs) induced by transcranialmagnetic stimulation in the right vastus lateralis (VL) during the 10% MVC were recorded and compared during the three breathing tasks. MEPs in IN and OUT were significantly higher than that in NORM. Effort sense of breathing was significantly higher in IN and OUT than in NORM. There was a significant positive correlation between MEP and effort sense of breathing. These results suggest that activation of the breathing-associated cortical areas with voluntary breathing is involved in the increase in corticospinal excitability of the VL during isometric contraction.

1. Introduction

Respiratory control during exercise is a vital function for maintaining the internal environment of the body. However, this homeostatic function is not the only role of the respiratory system during exercise. For instance, activation of respiratory afferents by resistive loaded breathing or a respiratory stimulant has been reported to alter the tonic vibratory reflex in the extensor digitorum and vastus lateralis (Balzamo et al., 1997) and the H reflex in the soleus (Gandevia et al., 1998). At the same time, Gandevia et al. (1998) demonstrated that only when, in addition to the stimulation of respiratory afferents, respiratory discomfort occurred, corticospinal excitability of the biceps brachii muscle increased. This indicates that change in the excitability of the limb muscle motoneuron pool induced by activation of respiratory afferents may be modulated by increased descending excitation occurring with respiratory sensations or arousal (Gandevia et al., 1998). Furthermore, it has been proposed that in a voluntary exercise with respiratory muscle fatigue, central motor output to exercising limbs is inhibited through the activation of respiratory muscle metaboreceptors (Dempsey et al., 2006). Thus, it appears that the respiratory control system is involved in the formation process of voluntary and reflex limb movements through an interaction between activation of respiratory afferents and excitability of the limb muscle motor cortex and/or spinal motoneurons.

In order to maintain pulmonary ventilation against respiratory resistive load or respiratory muscle fatigue, it would be necessary to increase the motor command to respiratory muscles. The respiratory motor command is output from not only the brainstem respiratory center but also the breathing-associated cortical motor area (Butler, 2007; Gandevia and Plassman, 1988; Gandevia and Rothwell, 1987). In fact, activation of the breathing-associated cortical motor area has been identified during resistive loaded breathing (Ramsay et al., 1993) as well as during voluntary breathing (Colebatch et al., 1991; Macefield and Gandevia, 1991; Petersen et al., 2011). Using a transcranial magnetic stimulation (TMS) technique, Li and Rymer (2011) found that voluntary breathing increased the corticospinal excitability (motor-evoked potentials, MEPs) of finger muscles during 10% maximal voluntary contraction. Since the electrical stimulation-induced force response of finger muscles during the same breathing maneuver provided a

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sufficient time for supraspinal mechanisms to become involved to affect the response, they suggested the possibility that activation of the breathing-associated cortical motor areas could enhance the motor functions of nonrespiratory muscles (Li and Rymer, 2011). In practice, they demonstrated that electrical stimulation to finger extensors delivered during voluntary inspiration was efficacious in enhancing finger extension strength and reducing finger flexor spasticity in post-stroke patients. Thus, it is conceivable that the respiratory system has a role in the control of limb movements through not only the activation of respiratory afferents but also a supraspinal mechanism such as activation of the breathing-associated cortical motor areas. However, it is not known whether the increase in MEPs by voluntary breathing occurs in contracting muscles other than finger muscles (Li and Rymer, 2011). It has been reported that cortical stimulation results in larger excitatory postsynaptic potentials (EPSPs) in spinal motoneurons for finger muscles than for proximal arm or lower limb muscles (Palmer and Ashby, 1992; Phillips and Porter, 1964). Since this suggests that the strength of corticospinal projections to finger muscles is greater than that to other limb muscles (Chen et al., 1998), there is a possibility that an increase in MEP induced by voluntary breathing (Li and Rymer, 2011) is a reaction specific to finger muscles. Therefore, in the present study, we examined the effects of voluntary breathing on the corticospinal excitability of a leg muscle by using the TMS technique. If an increase in MEP by voluntary breathing occurs in other limb muscles, clinical applications reported by Li and Rymer (2011) might be able to be extended to muscles other than finger muscles.

2. Methods

2.1. Subjects

Seven healthy males participated in this study (means ± SD: age, 22 ± 1 yr; height, 172.1 ± 4.9 cm; body mass, 66.8 ± 4.6 kg). Each subject gave written informed consent following an explanation regarding the experimental procedures and potential risks involved. This study was compliant with the Declaration of Helsinki and was approved by our institutional review board. Intense exercise and alcohol intake were prohibited for a period of 24 h prior to a test.

2.2. Experimental design

Throughout the entire experiment, subjects maintained a seated position on an adjustable chair with a backrest board. It was possible to prevent movement of the upper body during knee extension tasks by using this chair, which was equipped with a stopper to fix the position of the shoulders and head. After the knee angle had been set at 90 degrees, maximal voluntary contraction (MVC) during 5-s isometric knee extension of the right leg was measured. Three trials were performed for each measurement, and the highest value was used as MVC.

After that, each subject performed 5-s isometric knee extension of the right leg at the intensity of 10% MVC. This knee extension trial (="10% MVC") was carried out under three different breathing conditions: (1) normal breathing (NORM), with no specific instructions on breathing; (2) forced inspiration (IN), which involved inhaling once as fast as possible from the resting expiratory level at about 2 s after the start of 10% MVC; and (3) forced expiration (OUT), which involved exhaling once as fast as possible from the resting inspiratory level at about 2 s after the start of 10% MVC. Each breathing condition was repeated 7 times in random order. Thus, each subject performed 10% MVC 21 times in total with 1-min rest periods between trials. Transcranial magnetic stimulation (TMS) was applied to the cortical representation of the right vastus lateralis (VL) during 10% MVC performed under the designated breathing condition. The subjects were instructed not to move their head during the knee extension and breathing.

2.3. Measurement and recordings

During the 10% MVC test, subjects breathed through a mouthpiece connected to a hot-wire flow meter (AE-280s, Minato Medical Science) to measure respiratory flow. Knee extension force was measured using a load cell (LC1205-K500, A&D) that was connected to a wire and belt fixed over the ankle joint. Both signals of the knee extension force and respiratory flow were converted into digital signals at a sampling rate of 1 kHz using an analog-digital converter (MacLab/8s, ADInstruments). The signal of the knee extension force was processed with a low-pass filter of 40 Hz and displayed on a PC monitor so that subjects could produce the required knee extension force (10% of MVC). A red target line corresponding to 10% of MVC was created and displayed on the PC monitor.

By using the modified Borg scale for the assessment of rating of perceived exertion (RPE) (Borg, 1982), we asked each subject to assess effort senses of breathing (Breath-RPE) and legs (Leg-RPE) during the breathing task immediately after each 10% MVC.

A surface electromyogram (EMG) was recorded from the right VL with a bipolar EMG sensor that had an interelectrode distance of 20 mm (SX230, Biometrics Ltd.). Before attachment of the EMG sensor, the skin was shaved, abraded, and cleaned with alcohol in order to reduce skin impedance. The sensor was placed longitudinally over the muscle belly. The ground electrode was placed over the styloid process of the right wrist. The raw EMG signals were amplified using an amplifier imbedded in the EMG sensor (bandwidth = 20–450 Hz; common mode rejection ratio, CMRR > 96 dB; input impedance > 10^{13} Ω; gain = 1000) and converted into digital signals at a sampling rate of 2 kHz.

2.4. Transcranial magnetic stimulation (TMS)

A transcranial magnetic stimulator (Magstim 200^2, Magstim) with a double-cone coil (110 mm in diameter) was used to elicit MEPs in the right VL. The optimal coil position and stimulation intensity were determined prior to the experiment as follows. The intersection of the TMS coil was aligned tangentially with the sagittal plane, with the center of the coil being <2 cm to the left on the vertex (Cz). The coil was oriented so that the induced current flow within the cortex was in a posterior-to-anterior direction. During this procedure, the magnetic stimulator was set at about 45% of maximal output and the coil was moved over the vertex until the position evoking the largest MEP in the right VL was found while the subjects were performing isometric knee extension at 10% of MVC. The optimal location for the stimulation was determined as the position where the largest MEP was observed. The position was marked on a tight-fitting swimming cap that was placed on the subject's head to ensure constant positioning of the coil throughout the experiment. Subsequently, active motor threshold (AMT) intensity (mean intensity: 38.7 ± 4.6% of maximum stimulator output) was determined. AMT was defined as the lowest intensity of the stimulator that elicited an MEP clearly distinguishable from the background EMG in five out of ten pulses during isometric knee extension at 10% of MVC. Then, throughout the experiment (10% MVC trial), the intensity of the stimulation was set at 120% of the AMT (MEP amplitude in NORM: 547.7 ± 152.1 μV).

2.5. Data processing

Raw EMG signals were full-wave-rectified and then background integrated EMG (iEMG) was calculated over a 100-ms window prior