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Research report

Changes in cortico-spinal excitability following uphill versus downhill treadmill exercise

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HIGHLIGHTS

- Locomotor exercise enhance corticospinal excitability in a non-exercised muscle.
- No effect of the mode of muscle contraction in corticospinal excitability changes.
- After PAS_{25}, exercise induced changes in corticospinal excitability were different.

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ABSTRACT

An acute bout of aerobic exercise induces neuroplasticity in the motor cortex. Moreover, paired associative stimulation (PAS) is known to induce neuroplasticity in M1. However, the possible influence of the type of exercise on the neuroplastic changes remains unknown. The present study investigated the effects of two different modes of muscle contraction produced during locomotor exercise on changes in corticospinal (CS) excitability. Subjects performed two 30-min treadmill exercises at an intensity corresponding to 60% of their maximal heart rate with either a +10% (uphill) or −10% (downhill) slope. These exercises were followed or not by paired associative stimulation method (PAS_{25}) which consisted of 200 paired stimuli (0.25 Hz, 15 min) of median nerve electrical stimulation followed by transcranial magnetic stimulation of the hand M1 area (ISI 25 ms). Motor evoked potentials (MEP), assessed through abductor pollicis brevis (APB) activity were obtained before exercise, at 5 min, 15 min and 30 min after exercise. A significant ($P < 0.05$) increase of the MEP amplitude was observed 30 min after both exercises but was not different between the two modes of locomotion. On the contrary, MEP amplitude with PAS_{25} increased only 30 min after downhill exercise. We conclude that sub-maximal treadmill exercise increases CS excitability within a period of 30 min. However, the predominant mode of muscle contraction during uphill versus downhill locomotion does not influence CS excitability when assessed using a non-exercised muscle. However, results from PAS_{25} suggest that specific neuroplastic changes occur likely due to homeostatic mechanisms induced by exercise plus a PAS protocol.

1. Introduction

It has been shown that physical activity, in particular endurance type training, enhances plasticity of the corticospinal (CS) pathway [1] and improves neurocognitive function [2]. Specifically, individuals who undertake regular physical activity are more responsive to experimentally-induced CS plasticity compared to a sedentary population [3]. The effects of physical activity on CS excitability has previously been studied using transcranial magnetic stimulation (TMS), which elicits a motor evoked potential (MEP) recorded in a relaxed muscle that is not directly implicated in the exercise

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(e.g. abductor polis brevis or first dorsal interosseous). An enhancement of MEP amplitude in non-exercised muscles shows clearly that exercise has an effect upon the neural control of the whole body and not just the specific muscles involved in the activity [4].

Exercise-induced changes in CS excitability in the primary motor cortex (M1) have been demonstrated following an acute bout of aerobic exercise. Additionally, changes in CS excitability were induced using non-invasive brain stimulation techniques such as paired associative stimulation (PAS) [5]. Previous studies have suggested that these changes were mostly mediated at a cortical level [6] and also via indirect *trans*-cerebellar sensory pathways [7]. Using this technique, a greater enhancement of CS excitability was recorded when a facilitating PAS protocol (PAS_{25}) was preceded by an acute bout of aerobic exercise than when applied alone [4,8–10]. Interestingly, enhanced sequence specific learning when motor practice was performed after a 20-min submaximal intermittent cycling exercise was demonstrated by Mang et al. (2014). Additionally, this exercise enhanced the long-term potentiation-like (LTP) plasticity induced by a PAS_{25} protocol after the exercise [11]. In the same manner, an inhibitory PAS applied in stroke patients targeting the non-paretic limb during aerobic cycling exercise has been shown to induce a down-regulation of CS excitability [12]. However, Müller et al. [13] demonstrated interestingly that the LTP like-plasticity induced by a PAS_{25} protocol was completely suppressed if neuronal activity was already potentiated. These authors shed light on the homeostatic regulatory mechanism that drives changes in CS excitability in the human M1 as suggested by the Bienenstock-Cooper-Munroe (BCM) theory [14]. The aforementioned studies suggest that there is a potential interest in aerobic exercise and paired associative stimulation as therapeutic tools to drive CS excitability modulation and thus optimize neural repair strategies.

Physical exercise can be characterized by its duration, its intensity and the mode of contraction of the muscles involved. The concentric mode can be defined as muscle shortening during contractions due to the higher muscular torque compared to the external load (e.g., lifting a load, uphill walking/running). In contrast, an eccentric mode occurs when the external load is higher than muscular torque or during action against gravity (e.g. down stairs, jump landing, downhill walking/running) leading to muscle lengthening during the contraction [15]. Eccentric contractions differs from concentric ones in terms of the production of higher torque for both upper and lower limbs [16,17], adding to a lower energy cost for several locomotor exercises, such as walking, running or cycling, performed at the same mechanical workload [18,19]. The exercises involving eccentric contractions may be of interest for patients with disabilities. For example, it has been shown that the higher muscular work achieved during eccentric exercises resulted in more-efficient performance in people with multiple sclerosis [20] and Parkinson's disease [21]. Locomotor exercises with an eccentric component such as downhill walking/running are used for strengthening or rehabilitation programs.

Interestingly, compared to concentric contractions, eccentric contractions are known to induce specific neural adaptations [22]. Specifically, EMG activity is decreased during eccentric muscle contraction compared to concentric contraction for the same submaximal torque achieved [23,24]. This results in a lower number or a weaker discharging rate of motor units [25,26] explained by inhibitory spinal mechanisms that occur during eccentric contraction [27]. These mechanisms are suggested to prevent muscle damage by reducing the motoneuronal excitability [25,28] which leads to a reduced activation level [29]. However, a greater cortical excitability is associated with eccentric contractions [30], explained by a larger amount of sensory information to the brain from muscle lengthening, and the improved planning of eccentric actions [31]. Furthermore, this greater excitability was also suggested to counteract the inhibitory spinal mechanisms, during eccentric contraction [24,28]. Thereafter, when assessed using TMS, CS excitability was shown to be reduced during eccentric contractions [32,33].

Within this context, the aim of the present study was to (i) determine whether the mode of locomotor exercise influences CS excitability and (ii) if it could differentially modulate changes in CS excitability changes induced using a PAS protocol. We hypothesized that locomotor exercise with dominant eccentric contractions (i.e. downhill treadmill exercise) would lead to greater CS changes compared to exercise with dominant concentric contractions (i.e. uphill treadmill exercise) due to specific neural adaptations that occur during the former, compared to the latter. In addition, it has been suggested that brain activation during movement preparation and execution increases more for eccentric than concentric exercise, a finding that may have implications for CS excitability following specific physical training in either contraction modes [24,31,34]. Thus, the application of a PAS_{25} protocol after exercise should lead to a different modulation of CS excitability in a non-exercised muscle with an up-regulation of CS excitability after uphill treadmill exercise, and a down-regulation after downhill treadmill exercise according to the BCM theory [13,14]. To test our hypothesis, we asked individuals who undertook regular physical activity to execute uphill and downhill treadmill exercises at the same intensity with and without the application of a PAS_{25} protocol immediately after exercise. We then examined changes in the MEP evoked in a muscle of the dominant hand that was not involved in the exercise, using TMS. Thus, we were able to assess changes in CS excitability occurring in the whole system and not specifically-induced changes in the exercised muscles.

2. Materials and methods

2.1. Participants

Twelve (age: 25 ± 4 years) healthy active volunteers (7.5 ± 3.3 h of physical activity per week) were recruited for this study, which included two paradigms. All were right handed and gave their written consent prior to experimentation. The study conformed to the standards set by the World Medical Association Declaration of Helsinki "Ethical Principles for Medical Research Involving Human Subjects" (2008) and was approved by the Institutional Research Ethics Board.

2.2. Experimental protocol

This study was divided into two paradigms; 1) exercise alone (EX) and 2) exercise following by PAS_{25} (EX + PAS_{25}). First, subjects were familiarized with TMS and PAS_{25} protocols in order to determine whether they were responsive to PAS_{25} or not. Subjects were included in the study if the MEP amplitude assessed after the PAS_{25} protocol alone was enhanced to at least 120% of pre-stimulation values. For all included subjects, we then determined the maximal aerobic running velocity and the maximal heart rate (HR_{max}) during an incremental treadmill running test.

Both paradigms included 2 sessions each consisting of a 30-min treadmill uphill (UP) or downhill (DOWN) exercise at a submaximal intensity with assessment of CS excitability before and following the intervention (EX and EX + PAS_{25}) (see Fig. 1). The four sessions were completed over a period of 4 weeks with a minimum of 48 h recovery between visits. All participants were given instructions not to undertake vigorous physical activity the day before each session. Participants were also instructed not to consume caffeine and nicotine at least 3 h before testing, and were asked to declare if they had taken any medication or had any acute illness, injury or