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Changes in corticospinal excitability during consolidation predict acute exercise-induced off-line gains in procedural memory

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ABSTRACT

A single bout of cardiovascular exercise performed immediately after practicing a motor task improves the long-term retention of the skill through an optimization of memory consolidation. However, the specific brain mechanisms underlying the effects of acute cardiovascular exercise on procedural memory are poorly understood. We sought to determine if a single bout of exercise modifies corticospinal excitability (CSE) during the early stages of memory consolidation. In addition, we investigated if changes in CSE are associated with exercise-induced off-line gains in procedural memory. Participants practiced a serial reaction time task followed by either a short bout of acute exercise or a similar rest period. To monitor changes in CSE we used transcranial magnetic stimulation applied to the primary motor cortex (M1) at baseline, 15, 35, 65 and 125 min after exercise or rest. Participants in the exercise condition showed larger (~24%) improvements in procedural memory through consolidation although differences between groups did not reach statistical significance. Exercise promoted an increase in CSE, which remained elevated 2 h after exercise. More importantly, global increases in CSE following exercise correlated with the magnitude of off-line gains in skill level assessed in a retention test performed 8 h after motor practice. A single bout of exercise modulates short-term neuroplasticity mechanisms subserving consolidation processes that predict off-line gains in procedural memory.

1. Introduction

The positive effects that different modalities of cardiovascular exercise have on different types of memory and learning in humans are well established (Roig, Nordbrandt, Geertsen, & Nielsen, 2013). We have shown recently that, when performed immediately after practicing a tracking visuo-motor task, a single bout of cardiovascular exercise facilitates the long-term retention of the motor skill (Roig, Skriver, Lundbye-Jensen, Kiens, & Nielsen, 2012). Retention tests performed 1 and 7 days after motor practice revealed a significantly better performance of the motor skill in the group of subjects that performed 15 min of high-intensity intervallic exercise compared to a non-exercise control group. The effects of acute cardiovascular exercise on procedural memory are possibly time-dependent (Thomas et al., 2016) and based, to a large extent, on the temporal coupling between the exercise stimulus and each specific phase of the memory formation process (Roig et al., 2016). When performed immediately after motor practice, acute exercise improves the retention of the motor skill through an optimization of the memory consolidation process (Roig et al., 2012). However, the specific neural mechanisms underlying the positive effects that a single bout of cardiovascular exercise has shown to have on the consolidation of procedural memory are poorly understood (Taubert, Villringer, & Lehmann, 2015). Gaining insight into these mechanisms would improve our capacity to design more effective exercise protocols aimed at improving motor skill learning, which has important implications for rehabilitation and sports practice.

The primary motor cortex (M1) is an area of the brain engaged in multiple forms of motor skill learning (Hardwick, Rottschy, Miall, & Eickhoff, 2013) which is actively involved in the early consolidation of procedural memory (Muellbacher et al., 2002). Rapid synaptic reorganization occurs in M1 as a result of motor skill

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learning (see for review Sanes & Donoghue, 2000). A recent study (Tunovic, Press, & Robertson, 2014) showed that the level of corticospinal excitability (CSE) assessed through the stimulation of M1 during the early stages of consolidation predicts off-line gains in procedural memory, which occurred over wakefulness and without additional motor skill practice (Robertson, Pascual-Leone, & Miall, 2004). The authors used transcranial magnetic stimulation (TMS) applied to M1 in order to monitor changes in CSE at different time points after practicing an implicit version of a serial reaction time task (SRTT) that shows off-line gains in skill level and another explicit version that does not (Robertson, Pascual-Leone, & Press, 2004). The level of CSE remained high immediately after (~6 min) practicing the SRTT leading to off-line gains but decreased after the version of the SRTT showing no skill improvements. More importantly, CSE levels assessed immediately after motor practice were positively correlated with the magnitude of off-line gains in skill performance assessed 10 h after motor practice. In light of these findings, the authors proposed that CSE might act as a physiological mechanism signaling the consolidation of procedural memory (Tunovic et al., 2014).

Investigations using TMS have demonstrated that a single bout of cardiovascular exercise can modify different parameters of CSE assessed from M1 (Roig et al., 2016; Singh & Staines, 2015). Twenty min of moderate-intensity cycling increase intra-cortical facilitation and reduce short-interval intra-cortical inhibition assessed from the representational area of a non-exercised upper limb muscle on M1 (Singh, Duncan, Neva, & Staines, 2014). Furthermore, a bout of exhaustive cycling increases CSE on the M1 map of the tibialis anterior muscle (Coco, Perciavalle, Cavallari, & Perciavalle, 2016). Singh et al. demonstrated recently that the combination of acute exercise and motor skill practice increased CSE within the M1 map of the muscles involved in motor learning to a greater extent than when practice was performed alone (Singh, Neva, & Staines, 2016). However, the time course and functional relevance of these CSE changes in relation to the consolidation of procedural memory and motor skill learning were not determined.

The main aim of the present study was to determine if a single bout of cardiovascular exercise performed immediately after motor practice modifies CSE during the early stages of the memory consolidation process (Dudai, 2012). Furthermore, we investigated if potential exercise-induced changes in CSE are associated with off-line gains in procedural memory. To this end, we asked participants to practice a SRTT followed by either a short (15 min) bout of high-intensity cardiovascular exercise or a similar period of rest. Then, we used TMS applied to M1 to monitor changes in CSE prior to the practice of the motor skill and 15, 35, 65 and 125 min after the exercise or rest period. Improvements in procedural memory were inferred from a retention test of the motor skill. Based on previous studies (Mang, Snow, Campbell, Ross, & Boyd, 2014; Roig et al., 2012; Skriver et al., 2014; Thomas et al., 2016), we anticipated that acute exercise would improve the retention of the acquired motor skill. Furthermore, we hypothesized that this exercise intervention would promote increases in CSE assessed from M1 during consolidation that would be associated with off-line gains in procedural memory obtained through exercise.

2. Materials and methods

2.1. General procedures

Participation in the study required two laboratory visits. On the first visit, participants undertook an incremental graded exercise test (GXT) on a cycle ergometer to determine their maximal oxygen consumption (VO_{2peak}) and heart rate (HR) at different exercise intensity levels (Roig et al., 2012). To minimize potential long-term effects of exercise on memory (Berchtold, Castello, & Cotman, 2010; Hopkins, Davis, Vantieghem, Whalen, & Bucci, 2012), the second laboratory visit took place at least 48 h after the GXT. On the second visit (Fig. 1), participants reported to the laboratory at 9 am. First, baseline CSE was assessed with TMS applied to M1 (see Section 2.7) followed by electrical stimulation (ES) of the ulnar nerve to obtain the maximal M-wave (M_{max}) (see Section 2.6). Then, participants practiced the SRTT (see Section 2.4). Immediately after motor skill practice, participants were randomly divided into two groups (EXE and CON). Participants in EXE performed a warm-up followed by a bout of 15 min of high-intensity exercise (see Section 2.5) on the cycle ergometer while participants in CON seated on the ergometer, without pedalling, also for 15 min. To investigate the potential effects of exercise on muscle contractility the M_{max} was reassessed 10 min after exercise (EXE) or rest (CON). To monitor changes in excitability during consolidation, CSE was measured 15, 35, 65 and 125 min after exercise (EXE) or rest (CON). To assess potential off-line gains in procedural memory during consolidation both groups underwent a retention test of the SRTT performed 8 h after motor skill practice. During these 8 h, participants were not allowed to sleep, exercise or engage in any activity that could increase physiological arousal (i.e. drink coffee).

2.2. Participants

Forty-eight participants (CON = 23 and EXE = 25) were included in the study but only 34 (CON = 16 and EXE = 18) underwent electrophysiological assessments (CSE and M_{max}). This was due to the fact that after testing all the subjects who went through the electrophysiological assessment, we kept recruiting subjects to increase the sample size for the behavioural analysis (i.e. SRTT). Both groups were similar in terms of age, gender, body mass index (BMI), aerobic fitness (VO_{2peak}) as well as working and episodic memory level (Table 1). We included only young healthy participants that were right-handed, as defined by the Edinburgh handedness questionnaire (Oldfield, 1971), and naïve to the motor task (SRTT) used in the experiment. Exclusion criteria for participation were: age below 18 or above 36, BMI above 30, self-reported history of neurological, psychiatric or medical diseases as well as current intake of medications and/or recreational drugs affecting the central nervous system and/or the ability to learn (Roig et al., 2012). In addition, participants were excluded from participation if they obtained a score that deviated 2 SDs below the age-corrected normative score in the working (WMS) and episodic short-term memory (SMW) tests of the NIH Toolbox Cognition Battery (http://www.nihtoolbox.org) or had any contraindication regarding the exercise protocol and/or TMS testing. Potential participants that reported to play any musical instrument involving the performance of repetitive sequential finger movements (e.g. piano) were not allowed to be part of the study given the similarity of their instrumental practice with the SRTT and the effects of extensive musical training on the motor cortex (Hund-Georgiadis & von Cramon, 1999).

2.3. Graded exercise test (GXT)

A similar GXT protocol is described in detail elsewhere (Roig et al., 2012). The protocol, which was performed on a bike ergometer (Corival, Lode), started with a 2 min warm-up at a workload of 50 W. After the warm-up, the workload was gradually increased 30 W every minute until exhaustion. Subjects maintained a pedalling rate between 70 and 80 rpm throughout the entire protocol (Roig et al., 2012). Exhaustion was defined as the point where the subject could not continue pedalling at the minimum requested rate (70 rpm) for more than 5 s. An on-line gas analyzing system (Vmax Encore 29C, Carefusion) registered pulmonary ven-