Exercising control over memory consolidation

Edwin M. Robertson[1] & Adam Takacs[1,2]

[1]Institute of Neuroscience and Psychology, University of Glasgow, Glasgow, UK

[2]Institute of Psychology, Eötvös Loránd University, Budapest, Hungary

Forum

Keywords (2-6): consolidation, cortical excitability, exercise, motor skill, offline processing

Please address all correspondence to
Edwin Robertson
Institute of Neuroscience and Psychology
58 Hillhead Street
University of Glasgow
Glasgow, G12 8QB, U.K.
Email: edwin.robertson@glasgow.ac.uk

Exercise can improve human cognition. A mechanistic connection between exercise and cognition has been revealed in several recent studies. Exercise increases cortical excitability, and this in turn leads to enhanced memory consolidation. Together these studies dovetail with our growing understanding of memory consolidation, and how it is regulated through changes in motor cortical excitability.

Many have hailed exercise as a new wonder "drug" [1]. There is mounting evidence that exercise can even enhance human cognition. For example, exercise can improve our ability to remember facts and skills [2]. Yet, what has remained poorly understood is how exercise affects human cognition. Several recent studies have provided important mechanistic insight into the connection between exercise and cognition [2–4], and reveal that memory processing may be an important conduit through which exercise benefits human cognition [3,4].

Traditionally, memory consolidation refers to the increasing resistance of a memory to interference after its formation [5]. It can also refer to the "offline" improvement in performance between the initial formation of a memory, and its subsequent retrieval. These improvements develop over wakefulness, requiring several hours to develop, and are dependent upon brain circuits that include the primary motor cortex [6–8]. How these offline improvements are affected by exercise has been revealed in recent studies [3,4].

Offline improvements of a motor skill task are enhanced by exercise [3,4,9]. Learning a motor skill, and then immediately exercising, as opposed to an equivalent amount of resting time enhanced the development of offline improvements. Young adults learnt a skill, were tested on that skill, were randomly allocated to either an exercising or resting group, and subsequently 5-8hr later were retested (please, see Figure 1B, and [3,4]). The difference between skill at initial testing and subsequent retesting provided a measure of the offline improvement. In one study the motor learning task was tracking a visual target [3], while in the other, it was a motor sequence learning task [4]. Both tasks showed offline improvements demonstrating that the improvements, and the effect of exercise upon them is not restricted to a specific task, but may be a general feature of motor skill memories. The type of exercise, however, shows less diversity across studies [3,4,10]. The commonly investigated form of exercise is high intensity interval cardiovascular training (i.e., cycling), in which parameters of the exercise (i.e., intensity, length) can be manipulated, and the level of exercise can be tailored to each participant's individual level of fitness [4]. Understanding how the circuits critical to the development of offline improvements are affected by exercise has provided fresh insight into the connection between exercise and human memory.

Offline improvements are critically dependent upon a circuit that includes the primary motor cortex (M1, [8]). One way to measure the functional state of this circuit is to apply a Transcranial Magnetic Stimulation (TMS) pulse over M1, and observe the magnitude of the evoked muscle response in the hand contralateral to the site of stimulation (Figure 1A). When the elicited response, the so-called motor-evoked potential (MEP) is high, the cortical excitability is said to be high; conversely, a low magnitude MEP is consistent with a low cortical excitability. Changes in cortical excitability have been causatively linked to offline improvements [11]. These changes are reliable and individually stable measurements which make TMS protocols particularly suitable for studying experimental interventions, such as exercise [4,10].

Exercise increased cortical excitability [3,4,10]. This change was indicated by either direct enhancement of MEP [4], or indirectly, by change in disinhibiton in the hand representation of M1 [3]. For example, in one study MEP magnitude increased by approximately 50% between baseline and post-exercise [4]. The changes in cortical excitability were associated with enhanced offline improvements. Specifically, the increase in excitability due to exercise was positively correlated with enhanced performance at subsequent retesting [4].

Similarly, the change in disinhibition was positively correlated with offline gains in visuomotor tracking [3]. Offline improvements took different forms in the two tasks [3,4]. Exercise induced offline improvements to develop that would not normally occur over wakefulness following learning in the visual tracking task; while, exercise enhanced offline improvements that normally do develop over a period of wakefulness following learning in the sequence learning task.

Across the studies, a single bout of exercise increases cortical excitability, and this leads to, and is correlated with, either induced or enhanced offline improvements. Together, these findings provide converging evidence that cortical excitability plays a critical role in motor memory consolidation [11], and it is through this mechanism that exercise enhances human performance [3,4,10,12].

Cortical excitability and memory processing have also been linked by earlier work. Cortical excitability immediately after learning predicts the subsequent fate of a motor memory. There is a correlation between excitability after learning and the development of offline improvements over the subsequent 10-hrs [11]. Modifying cortical excitability with repetitive bursts of TMS modifies the fate of the memory. Specifically, increasing cortical excitability is able to induce the development of offline improvements that would not normally occur over wakefulness. Rewarding participants for their performance at retesting similarly increased cortical excitability after learning, and led to the subsequent enhancement of offline improvements [13]. Together, these studies manipulating the amount of exercise, stimulation, or reward have provided a consistent picture of the critical importance of cortical excitability to memory consolidation.

Exactly how these changes induced by cortical excitation arise at the cellular and molecular level is less clear, though altered synaptic plasticity appears to be one emerging candidate [3,10]. Exercise, especially high intensity cardiovascular training, can promote the synthesis of brain-derived neurotrophic factor, which may enhance plasticity leading to an increase in excitability, and improved consolidation ([3]; for a detailed review on this topic [14]). Equally, learning itself may alter plasticity leading to a change in excitability [11]. A homeostatic response to these changes perhaps through mechanisms, such as GABA increase, following learning may drive the network back to a homeostatic set point, and simultaneously regulate early consolidation of motor memory [3,8,10].

Another potential way to link excitability changes with memory consolidation is through memory reactivation. In rodents, patterns of activity present during the formation of a motor memory are replayed offline, and correlated with subsequent offline improvements [5]. Potentially, increased replay leads to an increase in excitability, whilst also driving enhanced consolidation. One intriguing possibility coming from this idea is that exercise may increase memory reactivation.

These frameworks largely concern local mechanisms, yet it is also possible that broader network level changes also occur. Local changes in M1 excitability may be due to other brain areas such as the prefrontal cortex, controlling processing within the M1 network. For example, applying TMS to the prefrontal cortex modifies M1 excitability, which demonstrates a functional connection between these brain areas [11]. Finally, an interaction between procedural and declarative memory systems prevents memory consolidation, and this is associated with low cortical excitability [5]. Changes in excitability through exercise or the application of TMS may be lead to, or be due to, broad changes in the organization between memory systems. Within this scenario, exercise may enhance consolidation while the benefits of an interaction between memory systems may be lost [15].

While numerous intriguing questions remain, a consistent picture is now emerging that suggests that exercise increases cortical excitability, and this increase leads to enhanced memory consolidation. These findings provide a tentative mechanistic framework explaining how exercise benefits the human brain and its cognitive operations, centered on the process of memory consolidation. Moreover, these insights open new avenues to understand the physiological mechanisms underlying memory systems interaction, and consolidation.

Figure Legend

Figure 1, Schematic Experimental Design and Results A) Cortical excitability can be measured using Transcranial Magnetic Stimulation (TMS). A single pulse of TMS is applied over the primary motor cortex (M1), inducing a current within the motor cortex, which in turn leads to a contraction of the muscles in the contralateral hand. This contraction is measured with EMG as a motor evoked potential (MEP), which provides a measure of cortical excitability. B) Cortical excitability was measured (baseline) then participants learnt a sequence learning task, and subsequently either rested or exercised before having their excitability measured. Participants were retested on the sequence learning task 8-hrs later. The difference in skill in the sequence learning task (ΔSkill) between testing and subsequent retesting provided a measure of offline learning. Skill in the sequence learning task was quantified as the difference in response time between the sequential and subsequent random trials. C) Cortical excitability increased above baseline following exercise indicated by an increase in mean MEP amplitude; whereas, cortical excitability changed little following a period of rest. D) Offline motor skill improvements (ΔSkill) were enhanced following exercise E) and the magnitude of these improvements in both the exercise and rest conditions were correlated with changes in cortical excitability (i.e., exercise and rest). These schematic results are based on a study with a sequence learning task [4]. A similar relationship between offline improvements and excitability was discovered in another recent study using a visual tracking task, and a complementary measure of cortical excitability [3].

References

1 Carroll, A. 20-Jun-(2016) , Closest Thing to a Wonder Drug? Try Exercise. , *The New York Times*

2 Roig, M. *et al.* (2013) The effects of cardiovascular exercise on human memory: A review with meta-analysis. *Neurosci. Biobehav. Rev.* 37, 1645–1666

3 Stavrinos, E.L. and Coxon, J.P. (2016) High-intensity Interval Exercise Promotes Motor Cortex Disinhibition and Early Motor Skill Consolidation. *J. Cogn. Neurosci.* DOI: 10.1162/jocn_a_01078

4 Ostadan, F. *et al.* (2016) Changes in corticospinal excitability during consolidation predict acute exercise-induced off-line gains in procedural memory. *Neurobiol. Learn. Mem.* 136, 196–203

5 Cohen, D. a and Robertson, E.M. (2011) Preventing interference between different memory tasks. *Nat. Neurosci.* 14, 953–955

6 Press, D.Z. *et al.* (2005) The time course of off-line motor sequence learning. *Cogn. Brain Res.* 25, 375–378

7 Robertson, E.M. *et al.* (2004) Awareness Modifies the Skill-Learning Benefits of Sleep. *Curr. Biol.* 14, 208–212

8 Robertson, E.M. (2005) Off-Line Learning and the Primary Motor Cortex. *J. Neurosci.* 25, 6372–6378

9 Roig, M. *et al.* (2012) A Single Bout of Exercise Improves Motor Memory. *PLoS One* 7, 28–32

10 Singh, A.M. *et al.* (2016) Aerobic exercise enhances neural correlates of motor skill learning. *Behav. Brain Res.* 301, 19–26

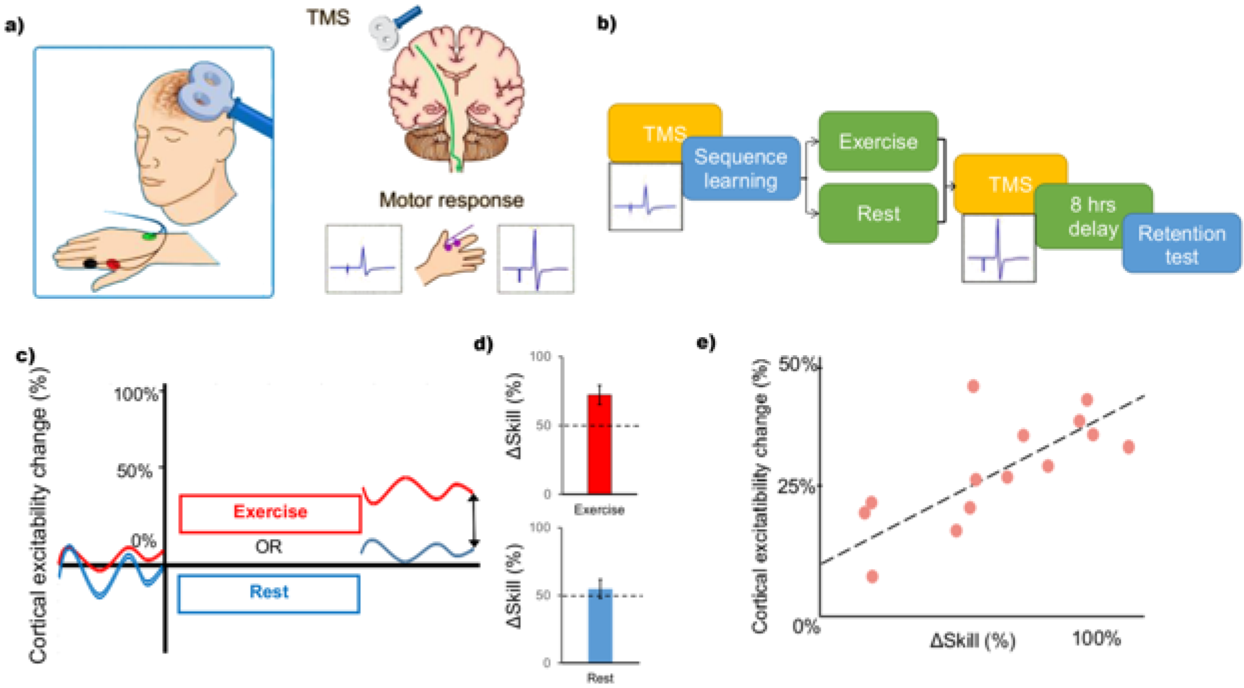
11 Tunovic, S. *et al.* (2014) A Physiological Signal That Prevents Motor Skill Improvements during Consolidation. *J. Neurosci.* 34, 5302–5310

12 Mooney, R.A. *et al.* (2016) Acute aerobic exercise modulates primary motor cortex inhibition. *Exp. Brain Res.* DOI: 10.1007/s00221-016-4767-5

13 Abe, M. *et al.* (2011) Reward improves long-term retention of a motor memory through induction of offline memory gains. *Curr. Biol.* 21, 557–562

14 Roig, M. *et al.* (2016) Time-Dependent Effects of Cardiovascular Exercise on Memory. *Exerc. Sport Sci. Rev.* 44, 81–88

15 Mosha, N. and Robertson, E.M. (2016) Unstable Memories Create a High-Level Representation that Enables Learning Transfer. *Curr. Biol.* 26, 100–105


a)
TMS
Motor response
b)
TMS
Sequence learning
Exercise
Rest
TMS
8 hrs delay
Retention test
c)
Cortical excitability change (%)
100%
50%
0%
Exercise
OR
Rest
d)
ΔSkill (%)
100
50
0
Exercise
ΔSkill (%)
100
50
0
Rest
e)
Cortical excitability change (%)
50%
25%
0%
ΔSkill (%)
100%