Transcranial Magnetic Stimulation in the Assessment of Acupuncture Effect on Exercise-Induced Fatigue

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Abstract
This study aims to evaluate the acupuncture effect on exercise-induced fatigue utilizing transcranial magnetic stimulation (TMS). A total of 20 sports enthusiasts were recruited in this study, all participants would be assigned to receive acupuncture and sham acupuncture intervention on exercise-induced fatigue randomly. TMS and heart rate monitor would be used to measure the amplitude and latency of motor evoked potential (MEP) and heart rate every 5 minutes over a 30-minute period. Lactate Scout+ was used to measure the blood lactic acid (BLA) in baseline, 0 minutes and 30 minutes after fatigue. Two-way repeated measures ANOVA was used to compare the difference between acupuncture method and time effects. Bonferroni post hoc tests were conducted to compare specific differences. Significance was set at P < 0.05. Interaction effect was found between acupuncture method and time effect in amplitude (F (1, 38) = 5.40, P < 0.001, η² = 0.12) and latency (F (1, 38) = 3.78, P = 0.008, η² = 0.09) of MEP. Acupuncture intervention can promote the recovery of heart rate especially at 30 minutes (P < 0.05), but which seem insufficient to generate significant difference in BLA (F (1, 38) = 0.067, P = 0.797, η² = 0.002). Preliminary findings provide new perspectives for sports enthusiasts to relieve fatigue and reduce the inhibition of motor cortex excitability utilizing acupuncture.

INTRODUCTION
Exercise-induced fatigue is a self-protective response of the body after a high training load, which may be caused by numerous physiological factors, like body’s energy consumption, accumulation of lactic acid and dysfunction of the neuroendocrine system (Heil et al., 2020; Liu et al., 2022). Fatigue can be divided into central and peripheral fatigue (Meeusen et al., 2021), which may cause negative impact on sports performance and even contribute to the occurrence of sports injuries (Chennaoui et al., 2021). Acupuncture as a traditional Chinese therapy, has been widely studied in the late recovery phase of exercise-induced fatigue (Yang et al., 2017). However, the mechanism of acupuncture to relieve exercise-induced fatigue is not entirely clear, especially for the central mechanism of fatigue.

Transcranial magnetic stimulation (TMS) is a non-invasive brain stimulation technique that acts on the central nervous system (Vernillo et al., 2021) and widely used in the diagnosis and treatment of various diseases in neuroscience and neurology (Al-Sultan et al., 2019). Because of the advantage of its high safety, low side effects and better elucidation of the principle, TMS often utilized as the main assessment index for cerebral cortex detection. Given to the fact that motor evoked potential (MEP) can be easily obtained by peripheral muscle electromyography, more and more studies explore the actual effect of acupuncture on the motor cortex excitability (Lo and Cui, 2003; Maioli et al., 2006).

Zusanli (ST 36) is one of the most commonly acupoint for acupuncture. Studies believed that Acupuncture at ST 36 can effectively reduce subjective fatigue levels, blood lactic acid (BLA), lactate dehydrogenase, heart rate and other indicators of fatigue during exercise (Jiang et al., 2019), and has anti-inflammatory
effects (Oh and Kim, 2021). Sun et al (Sun et al., 2019) have found that acupuncture at ST 36 can increase the excitability of the motor cortex at rest state, decrease the inhibition of the motor cortex and produce lasting effects. In relation to these issues, the present study aims to applied TMS technique to investigate the effect of needling ST 36 on the motor cortex in the state of exercise-induced fatigue. Meanwhile, heart rate, BLA and other indicators were observed to provide a theoretical basis for acupuncture to alleviate exercise fatigue.

MATERIALS AND METHODS

Participants
A total of 20 sports enthusiasts were recruited for this experiment (20.7 ± 1.6 y, 178.5 ± 10.8 cm and 70.4 ± 12.6 kg). All subjects were right-handed and exercised more than 3 times per week. There was no metal implant in the body, no history of epilepsy, no caffeine, alcohol or drugs in the 24 hours before the start of the experiment (Yu et al., 2020). All subjects signed an informed consent, and the experiment was approved by the Ethics Committee of Shanghai University of Sport (NO.102772021RT105).

Experimental design
First, the participants’ height and body mass were measured, thereafter each subject received acupuncture or sham acupuncture intervention immediately after exercise-induced fatigue randomly with a one-week washout interval. All interventions were performed by the same acupuncturist, who was not involved in the subsequent data collection and analysis. The needle was inserted immediately after fatigue and removed 15 minutes later. MEP and heart rate were collected baseline and after exercise 0 min, 5 min, 10 min, 15 min, 20 min, 25 min and 30 min, respectively. BLA was measured in baseline, after exercise and after acupuncture intervention (Figure 1).

Figure 1. Experimental design
(MEP: motor evoked potential, HR: heart rate, BLA: blood lactic acid)

Exercise-induced fatigue modeling
Bicycle ergometer incremental-load exhaustive exercise was used as dynamic training to construct muscle fatigue models. A heart rate monitor (Polar H10, Polar Electro Oy, Kempele, Finland) was also used to record participant’s heart rate during the experiment. After the seat was corrected according to the height of the participant, the subject warmed up at 0 W for 2 min, then took 60W as the initial power and gradually increased the power by 30 W/2 min. Every participant need kept the bicycle ergometer speed no lower than 60 rpm throughout the experiment until they cannot maintain 60 rpm more than 5 seconds (Angius et al., 2019). Meanwhile, rating of perceived exertion (RPE) and BLA (Lactate Scout+, EKF, Germany) were combined to assess the fatigue condition of subjects immediately.

Acupuncture intervention
After the subject was confirmed to be fatigued, ST 36 acupoint was sterilized utilizing 75% alcohol cotton balls, then the acupuncturist inserted the disposable needle vertically (Hwato, [?]0.30*25mm, Suzhou Medical Appliance Factory, China), pulled and twisted, and stopped the needle when feeling the needle sunken and tight. For the sham acupuncture intervention, transparent plastic tube filling with coupling agent was applied based on the principle of park sham needles (To and Alexander, 2015), which was attached on a double-sided adhesive tape on one side, and covered with stainless-steel stickers glued to ST 36 on the other side. The needle tip touched the bottom but didn’t pierce the sticker, giving the subject the sensation of needle.
TMS technique

The Ag-AgCl electrodes were placed at the First Dorsal Interosseous (FDI) muscle at the right hand, metacarpal and phalangeal joints of the index finger and near the ulna stem process to record surface EMG before the study began. For the TMS (Magstim, Whitland, Dyfed, UK) assessment, the figure-of-eight coil was maintained between the coil and the sagittal line at 45°. In order to find the maximum amplitude of MEP that can stimulate first dorsal interosseous muscle, a single TMS stimulation was performed on the left primary motor cortex (M1) to find the most appropriate stimulus spot, which was marked with a red marker. The experiment could start when the difference between the mean amplitude of the twice MEP was less than 20%. MEP amplitude is defined as the peak-to-peak amplitude, MEP latency is the time between the onset of the stimulus and its maximum peak, all taken as the average of 10 consecutive TMS trials with an interstimulus interval of 5 seconds.

Statistical analysis

All dependent variables were presented as mean and standard deviation (SD). Shapiro-Wilk test was performed to confirm the normal distribution. Two-way repeated measures ANOVA was used to compare the difference between acupuncture method and time effects. Bonferroni post hoc tests were conducted to compare specific differences. Significance was set at $P < 0.05$. All statistics were performed using SPSS 26 software (IBM, Armonk, NY, USA).

RESULTS

Changes in amplitude and latency of MEP

The results showed that MEP amplitude had an interaction effect on acupuncture method and acupuncture time ($F_{(1, 38)} = 5.40, P < 0.001, \eta^2 = 0.12$). Post hoc analysis showed that the MEP amplitude of acupuncture intervention was significantly higher than that of sham acupuncture intervention after 5 min intervention ($P < 0.01$) (Figure 2). For the acupuncture intervention, the amplitude of MEPs at 15 min ($P = 0.007, MD = 0.43, 95\% CI = 0.07-0.78$) and 30 min ($P = 0.002, MD = 0.47, 95\% CI = 0.11-0.83$) were significantly higher than baseline. MEP amplitude at 30 min of sham acupuncture intervention was lower than baseline ($P = 0.047, MD = -0.36, 95\% CI = -0.71-0.00$) (Figure 2). With regard to latency of MEP, we also found significant interaction effect ($F_{(1, 38)} = 3.78, P = 0.008, \eta^2 = 0.09$), Post hoc analysis revealed significant difference in acupuncture time ($F_{(1, 38)} = 16.16, P < 0.001, \eta^2 = 0.30$) (Figure 3).

Figure 2. Comparison of the amplitude of MEP between two acupuncture methods
Figure 3. Comparison of the latency of MEP between two acupuncture methods

( * : time effect; # : acupuncture effect. */# P < 0.05, **/# P < 0.01)

Change in heart rate

The results of heart rate showed that there was an interaction effect between the acupuncture method and acupuncture time ($F_{(1, 38)} = 2.85, P = 0.029, \eta^2 = 0.07$). The heart rate reached the highest immediately after exercise and then decreased, with the largest decreasing range 5 min after exercise. At 30 min after the intervention, the heart rate of acupuncture intervention was lower than that of sham acupuncture intervention ($P < 0.05$) (Figure 4).

Figure 4. Comparison of the heart rate between two acupuncture methods

( * : time effect; # : acupuncture effect. */# P < 0.05, ** P < 0.01)

Changes in BLA

The results showed that there was no interaction effect between acupuncture method and acupuncture time but had a significant difference in acupuncture time ($F_{(1, 38)} = 529.11, P < 0.001, \eta^2 = 0.93$) in BLA. Post hoc
analyses revealed differences between baseline and 0 min ($P < 0.001, MD = 9.50, 95\% CI = 8.74-10.26$) and 30 min ($P < 0.001, MD = -6.88, 95\% CI = -7.63–6.12$) (Figure 5).

**Figure 5.** Comparison of the BLA between two acupuncture methods

**DISCUSSION**

Our study aimed to explore the acupuncture effect on exercise-induced fatigue utilizing TMS. The results demonstrated that acupuncture can produce positive effects on the recovery of motor cortex excitability and the heart rate especially at 30 minutes.

Given to the fact that the change in excitability in the M1 region was correlated with exercise intensity, The fatigue model constructed in this experiment utilizing high-intensity exercise to explore MEP amplitude after exercise intervention (Balbi et al., 2002). This study showed that the MEP amplitude was significantly higher than sham acupuncture, the latency of MEP after acupuncture was also significantly shortened compared with baseline after acupuncture intervention. These findings are similar to results previously reported by Li et al (Li et al., 2022), where demonstrated that electroacupuncture at back-Shu points could improve the excitability of the motor cortex and improve the chronic fatigue state of the subjects. Also, this study support those of other recent analyses reporting that acupuncture is an appropriate treatment for relieving fatigue and acupuncture can improve the subjective rating of fatigue (Akimoto et al., 2003). The positive results after acupuncture intervention maybe explained from metabolomics perspectives, compared with the relaxation after exercise, acupuncture can better regulate disturbances in the body, promote energy metabolism and choline metabolism, and improve reactive oxygen stress (Ma et al., 2015).

For the heart rate after 30min intervention, this study found heart rate was significantly lower in the acupuncture intervention than in the sham acupuncture intervention, the current data combined with previous data confirmed that acupuncture can improve heart rate in the fatigue state and promote the recovery of body functions (Li et al., 2005; Jiang, et al., 2019). Also, Shu et al (Shu et al., 2016) showed that both acupuncture and moxibustion could improve fatigue, especially for the chronic fatigue.

BLA is generally reaches its highest concentration 3-5 min after exercise, so which seem often act as a common parameter to evaluate fatigue (Lucertini et al., 2017). However, we did not monitor the dynamic process of change in BLA immediately and 30 min after exercise. A possible explanation for these results would be that blood sampling at the fingertip exerts an invasive stimulus on the subjects’ skin. Which may produce pain sensation in the brain and affects the MEP during the experiment. Our findings seem contradict the
data presented by Poton et al (Poton and Polito, 2016), where demonstrated that high-intensity exercise can promote the increase of BLA after short time training, this study maybe indicating that short training sessions are better at increasing BLA levels than long training sessions (Kondoh et al., 1992). Further, Lin et al observed BLA was lower in the acupuncture group than in the sham group and the control group during 30 min and 60 min after acupuncture at ST 36 and PC 6 points (Lin et al., 2009; Lin et al., 2011). Xia et al (Xia and Wang, 2016) demonstrated acupuncture could promote the significant reduction of BLA and creatine kinase in adolescent weightlifters with symptoms of lumbago. Possible explanations for these discrepancies may lie on the single intervention point and lower retention time of acupuncture, which may contribute to insignificant effect of acupuncture on the regulation of BLA.

There are several limitations to the present study that should be mentioned. Firstly, due to insufficient time interval, it’s hard to recorded cortical long-interval cortical inhibition; Secondly, only a single intervention was conducted using ST 36 acupoints on exercise fatigue, which may contribute to the intervention intensity of acupuncture is not enough. Furthermore, this study only explored the influence of acupuncture on the M1, future studies could explore the mechanism of acupuncture on the brain utilizing functional near-infrared spectroscopy and functional magnetic resonance imaging.

**Conclusion**

The results indicate that acupuncture intervention can improve the fatigue-induced decrease in motor cortex excitability, promote the increase of MEP amplitude, shorten MEP latency and restore heart rate. Therefore, acupuncture was suggested as an important invention method for sports enthusiasts to relieve fatigue and enhance sports performance.

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**CONFLICT OF INTEREST STATEMENT**

No conflicts of interest, financial or otherwise, are declared by the authors.

**REFERENCES**


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