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Original Article

Benefits of using transcranial magnetic stimulation as a tool to facilitate the chronic knee injury rehabilitation

Jae-Moo Lee[1)], Ji-Hang Lee[1)*]

[1)] College of Sport Science, Sungkyunkwan University: 300 Chunchun-dong, Jangan-gu, Suwon, Kyungki-do 440-746, Republic of Korea

Abstract. [Purpose] While primary motor cortex activation has been implicated as a key factor in the arthrogenic muscle inhibition after knee joint injury, no viable rehabilitation protocol has been developed to accommodate this factor. In this study, transcranial magnetic stimulation was applied as a means of dissipating arthrogenic muscle inhibition by introducing temporary motor cortex excitation prior to the rehabilitation. [Subjects and Methods] Twenty-four subjects who have underwent the surgery due to knee injury were recruited, and randomly assigned to the control or the simulation groups. The levels of electromyography signals during the maximum voluntary contraction of the quadriceps muscle before, during, and after training designed for the quadriceps strength rehabilitation were measured. [Results] When compared to controls, subjects who received the transcranial magnetic stimulations showed significantly increased levels of voluntary muscle contraction after the training. Moreover, the beneficial effect of the stimulation increased as the rehabilitation progressed. [Conclusion] Transcranial magnetic stimulation itself does not directly improve the symptoms related to knee injuries. However, the use of this technique can provide a time window for effective intervention by dissipating the unwanted effect of the arthrogenic muscle inhibition during rehabilitation.

Key words: Knee joint injury, Transcranial magnetic stimulation, Rehabilitation

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INTRODUCTION

The knee joint is commonly injured during sports[1)]. Although injuries such as anterior cruciate ligament tears can be effectively treated with modern medical intervention techniques, patients are often unable to regain the level of pre-injury performance. This performance deficit is commonly seen in patients who are recovering from traumatic knee injuries, but have ongoing deficits even after the injured knee joint has fully recovered. Researchers often attribute quadriceps activation failure to arthrogenic muscle inhibition (AMI)[2)]. This unconscious neural inhibition mechanism protects an injured area from being damaged again. However, if it persists, successful rehabilitation can be hindered, and, further, muscle atrophy and degenerative joint diseases can eventually develop[3)]. In this study, we investigated means of circumventing the influence of AMI during an intervention.

Although the problem of AMI originates in the joint reflexes, the neural consequence of AMI is the decreased level of motor neuron activation, resulting in limited muscle contraction ability[4)]. To overcome the AMI effect, previous research attempted to modulate the motor neuron activity at the neuromuscular junction or at a lower level of the central nervous system[5, 6)], but no viable intervention protocol has been suggested. Therefore, researchers now suggest the possibility of disinhibiting the neural signal at the cortical level[7)]. Based on neuroanatomy of the corticospinal circuit, the primary motor cortex, as the final output region of the cortical motor areas, is the prime candidate for disinhibition of the effects of AMI[4)].

*Corresponding author. Ji-Hang Lee (E-mail: jihanglee@skku.edu)

Transcranial magnetic stimulation (TMS) is a technique that can artificially modulate the excitability of a given brain area by delivering a brief magnetic pulse over the scalp in a noninvasive manner[8]. When applied onto the quadriceps area of the primary motor cortex region, the motor neuron becomes activated, and cause a given muscle to contract. This artificial motor neuron activation has been reported to persist following application[9]. Pietrosimone et al.[10] showed a decrease in AMI for 60 minutes following a single pulse of TMS, when applied to the primary motor cortex.

The purpose of this study was to examine the feasibility of using TMS as a therapeutic tool to disinhibit the AMI effect during the rehabilitation process. Thus, it is important to acknowledge that TMS itself is not a technique that can directly influence the rehabilitation. Rather, patients who experience knee injury could expect to experience the maximal benefit from rehabilitation because of the AMI-free (rehabilitation) time window introduced by the TMS.

SUBJECTS AND METHODS

Twenty-four young males with a history of knee injury and surgery (more than 12 months prior) were recruited as subjects (19–30 years old, 17 male, 7 female, mean age 28). All subjects underwent either partial/whole meniscectomy for meniscus tear or restoration of anterior/posterior cruciate ligament tear. Participation was restricted if there was pain in any other body parts or any other pathological symptoms. All 24 subjects were confirmed to display the AMI characteristic. The maximum knee extension force generated by an injured leg should be no more than 85% of the force generated by the non-injured leg (tested prior to the participation). All participants were informed of possible risks (acoustic artifacts, seizure, local pain, headache, discomfort, acute psychiatric changes) from the experimental procedures. The experience of TMS was thoroughly explained, and the participants were aware that they could withdraw from the experiment at any point. Subjects were confirmed to be appropriate for the experiments using the TMS technique[9].

After completing the consent form, the subjects were randomly assigned to either a sham (control) or TMS (experimental) group (12 subjects each). Electromyography (EMG) sensors (MyoSystem 1400A, Noraxon Inc., Scottsdale, AZ, USA) were attached to the belly of the vastus lateralis while subjects were sitting on a chair with 70° hip flexion and 60° knee flexion. Then, voluntary maximum quadriceps contraction (MVC) was measured 3 times (pre-test). Immediately after the pre-test, each subject's quadriceps muscle representation on the motor cortex was identified by the Rapid 2 TMS system (Magstim, UK). The magnitude of the EMG signal elicited by the TMS was monitored, and the stimulation site with the greatest EMG signal was chosen as described by Huh et al[10].

Once the stimulation location was confirmed, a single pulse of TMS at maximal output (about 2 T) was delivered 3 times to the TMS group. Fake (sham) stimulation was delivered to the control group by tilting the stimulation coil 90° so the effect of the stimulation pulse would not reach the scalp; subjects were unaware of this difference.

After the TMS treatment, all subjects participated in an identical rehabilitation program; there was no need for an individualized program as all the surgeries were performed more than a year prior to the study. The rehabilitation protocol[11] consisted of quadriceps (knee) extension, mini-squatting using a physioball, and four directional straight knee raises (10 minutes each). After the 10 minutes of each rehabilitation training session, the MVC measurement and TMS application were repeated. Once this training protocol ended, a 30 minute break followed, to allow recovery from fatigue. A licensed physical therapist (Korean Physical Therapy Association) and a certified athletic trainer (National Athletic Trainers' Association) were present and gave instructions/advices throughout the training protocol. Both individuals have years of experience working with the sport related knee injury patients, and they physically assisted and gave verbal instruction/feedback for every participants throughout the training.

Immediately after the break, another MVC measurement (without TMS) was performed as a retention test. The 3 EMG measurements of MVC (peak iEMG amplitude) during each data collection were averaged as a dependent variable (micro-volt). Raw EMG signals were sampled at 1,000 Hz displayed by MyoResearch XP program (gain=2,000, bandwidth 10–500 Hz, CMRR >100 db, input impedance >100 M ohm) accompanying the EMG system.

With 2 groups (TMS and sham) and 5 different data collections (pre-test, after training−1, −2, and −3, and a post-test), repeated two-way analysis of variance (ANOVA) was performed. If there was a significant effect, post-hoc comparisons were performed (corrected for multiple comparisons using the Bonferroni adjustment). The statistical significance level was set to 0.05. The subjects' recruitment process and the experimental protocols followed the Declaration of Helsinki, and were approved by the local Internal Review Board (IRB SKKU 2014-05-004-002).

RESULTS

Table 1 displays the means and standard deviations of EMG data collected from each group throughout the experiment. In the pre-test conditions, the EMG values measured during the MVC were similar between the groups. However, as TMS was applied prior to training, the EMG values tended to increase, while those of the sham group remained at the pre-test level.

The results from the statistical analyses confirmed this observation. There was no significant test main effect ($F(4, 88)=1.53$, $p=0.20$), but the group main effect showed significance ($F(1, 22)=8.146$, $p=0.01$). This group main effect reflected the strong influence of TMS, as this significance was achieved in spite of the almost identical between-group pre-test results. Importantly, there was a significant interaction between test and group ($F(4, 88)=2.648$, $p=0.04$).

Table 1. Average EMG level during maximum voluntary contraction measured during 5 test periods (μV)

Test	Group			
	Sham (n=12)		TMS (n=12)	
	M	SD	M	SD
Pre-test	175.37	24.94	172.75	30.25
Training 1 test	171.75	18.49	191.58	34.32
Training 2 test	169.17	24.68	199.25	33.04
Training 3 test	171.42	25.14	199.92	40.76
Post-test	170.50	22.79	213.75	43.40

DISCUSSION

Patients recovering from knee injuries often experience frustration during rehabilitation because of unintended obstacles such as the AMI[12]. Although there have been numerous attempts to solve this problem by administering interventions at peripheral nervous system or at musculoskeletal levels[13], few studies reported success. The purpose of this study was not to evaluate TMS as a rehabilitation technique. Rather, we used TMS to enhance access to the planned benefit of rehabilitation training. It was hypothesized that during a limited time period, the application of TMS may temporarily dis-inhibit the negative effect of AMI. Thus, subjects were expected to benefit from the previously proven effects of rehabilitation training.

The results of this study provided strong evidences for our hypothesis. Only the actual TMS group showed the effect of rehabilitation, while the sham group had no benefit from the training. The peak EMG amplitude of the sham group while performing the MVC was relatively unchanged throughout the training. In fact, there was a tendency of decrease from 175.37 to 170.50 (although not significantly different). This tendency may reflect the muscular fatigue induced by the training. In spite of this possible effect of fatigue, the amplitudes of peak EMG signals showed increasing patterns. This was the main finding of the study strongly supporting our hypothesis. Also, this TMS plus rehabilitation procedure seemed to have prolonged effect. The peak EMG amplitude during the post-test showed noticeable improvement over the training 3 test result. It is possible that the fatigue inducing training might have diluted the training effect, but, after 30 minute break, patients in the TMS group could show the real effects of rehabilitation without the AMI effect. The neurological interpretation of this result would be that TMS of the primary motor cortex at high intensity might have temporarily excited the motor neuron pool to a maximal level. Therefore, the effect of AMI might have been dissipated while training was administered. Although this interpretation is still speculative, the increased muscle strength was substantial, and provides a significant reason for applying the results in practice.

While the results of this study indicate a promising role of TMS in a clinical setting, further investigation is needed. In this study, 3 pulses of strong TMS were sufficient to introduce the changes in training effects for 10 minutes, while previous studies showed the sustained TMS effects for more than 30 minutes after the stimulation[11]. Therefore, optimal TMS parameters for the ideal rehabilitation such as stimulation intensity and frequency should be defined. The use of EMG signal as a dependent variable might not been the best experimental option. The EMG MVC data are known to have session-to-session and subject-to-subject variability. Although previous studies have similarly used MVC to investigate AMI changes[13] and we've tried our best to obtain reliable EMG data, however, the changes in AMI can be more precisely evaluated with peak-to-peak or the burst superimposition techniques by using joint torque measurement. The availability of the experimental techniques in our lab limited the use of any joint torque measurement technique. On the other hand, because this study was intended to provide information applicable to the practitioners, this limited use of data collection technique can be, conversely, beneficial for real world application. In summary, while the neural nature of our results indicates the need for future studies, the beneficial and promising role of TMS for knee joint rehabilitation protocols is evident in this study.

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