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Original Article

Effect of high-frequency repetitive transcranial magnetic stimulation on motor cortical excitability and sensory nerve conduction velocity in subacute-stage incomplete spinal cord injury patients

Hyun Gyu Cha, PT, PhD[1)], Sang-Goo Ji, PT, PhD[2)], Myoung-Kwon Kim, PT, PhD[3)*]

[1)] *Department of Physical Therapy, Kyungbuk College, Republic of Korea*
[2)] *Department of Physical Therapy, Eulji University Hospital, Republic of Korea*
[3)] *Department of Physical Therapy, College of Rehabilitation Sciences, Daegu University: Jillyang, Gyeongsan, Gyeongbuk 712-714, Republic of Korea*

Abstract. [Purpose] The aim of the present study was to determine whether repetitive transcranial magnetic stimulation can improve sensory recovery of the lower extremities in subacute-stage spinal cord injury patients. [Subjects and Methods] This study was conducted on 20 subjects with diagnosed paraplegia due to spinal cord injury. These 20 subjects were allocated to an experimental group of 10 subjects that underwent active repetitive transcranial magnetic stimulation or to a control group of 10 subjects that underwent sham repetitive transcranial magnetic stimulation. The SCI patients in the experimental group underwent active repetitive transcranial magnetic stimulation and conventional rehabilitation therapy, whereas the spinal cord injury patients in the control group underwent sham repetitive transcranial magnetic stimulation and conventional rehabilitation therapy. Participants in both groups received therapy five days per week for six-weeks. Latency, amplitude, and sensory nerve conduction velocity were assessed before and after the six week therapy period. [Results] A significant intergroup difference was observed for posttreatment velocity gains, but no significant intergroup difference was observed for amplitude or latency. [Conclusion] repetitive transcranial magnetic stimulation may be improve sensory recovery of the lower extremities in subacute-stage spinal cord injury patients.

Key words: Repetitive transcranial magnetic stimulation, Spinal cord injury, Sensory

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INTRODUCTION

When patients with spinal cord injuries have pain as an accessory symptom, training in the activities of daily living (ADL) is affected and sometimes does not progress smoothly[1)]. Transcranial magnetic stimulation (TMS) pulses have been used as a noninvasive and painless means of stimulating the brains of intact conscious human subjects through the scalp[2)]. TMS pulses were first used in patients with spinal cord injury (SCI) in the early 1990[3)] and are now used most extensively in the corticospinal system because the output of the primary motor cortex can be easily assessed in the form of motor-evoked potentials (MEPs) using surface electromyographic recording electrodes. rTMS can be applied as continuous trains of low frequency (1 Hz) or as bursts of higher frequency (≥5 Hz). Generally, low-frequency rTMS (stimulus rates ≤1 Hz) inhibits motor cortical excitability, leading to a reversible ‘virtual lesion’, whereas high-frequency rTMS (5–20 Hz) usually promotes an increase in cortical excitability[4)]. Belci et al.[5)] first tested the efficacy of rTMS in modulating corticospinal inhibition and

*Corresponding author. Myoung-Kwon Kim (E-mail: skybird-98@hanmail.net)

improving functional recovery in four patients with chronic incomplete (American Spinal Injury Association Impairment Scale D) cervical (C5 level) SCI. Perceptual thresholds for electrical stimulation of the skin, ASIA clinical measures of motor and sensory functions, and times to complete a pegboard were found to improve during the entire 3-week follow-up period. The activation of motor nerves due to repetitive movements induces plastic changes in the primary somatosensory cortex[6) which indicates that sensory and motor nerves are directly related with each other. Although it is relatively well known that sensory nerves directly affect motor nerves, it has not been established whether motor nerves affect sensory nerves. In this study, we hypothesized that high-frequency rTMS can improve sensory recovery of the lower extremities in SCI patients.

SUBJECTS AND METHODS

Patients were recruited from the neurological physical therapy outpatient clinic of the Faculty of Physical Therapy, Eulji University, after they agreed to participate in the study. The Research Ethics Committee of Eulji University Hospital approved the study, and all participants provided informed, written consent prior to enrollment. All patients had been diagnosed with SCI, which was confirmed by computed tomography or magnetic resonance imaging. Patients that met the following criteria were enrolled: (1) incomplete SCI (AIS C or D) by trauma (traffic accident or fall), (2) cervical or thoracic SCI, and (3) time elapsed since SCI of <6 months. Twenty SCI patients met the study criteria. After completing initial assessments, the subjects were randomly assigned to an experimental group (*n*=10) or a control group (*n*=10). For randomization, sealed envelopes were prepared in advance and marked inside with A or B, indicating the experimental or control group, respectively. Subjects in the experimental group received rTMS and conventional rehabilitation therapy for a total of 50 min (rTMS, 20 min; conventional rehabilitation therapy, 30 min) per day, with a 10 min rest period halfway through the session. A Magstim Rapid2 (Magstim Co., Ltd., Wales, UK) and a figure-of-eight coil with a diameter of 80 mm were used to administer rTMS. In each patient, 1 Hz rTMS was applied to the hemispheric hotspot in 10 second trains, with 50 second intervals between trains. Subjects in the experimental group received training five days per week for 6 weeks. Conventional rehabilitation therapy consisted of neurodevelopmental facilitation techniques and was administered by therapists unaware of the study protocol or group assignments. The objectives of SCI rehabilitation were to improve functional abilities, such as, transfer, ambulation, and balance, so as to help patients achieve earlier and/or greater independence. Subjects in the control group received sham rTMS therapy and conventional rehabilitation therapy for a total of 50 min (sham rTMS, 20 min, conventional rehabilitation therapy, 30 min) per day 5days/week for 6 weeks; the subjects in both groups received therapy on the sameday.

An electromyography/evoked potential system (Medelec, Oxford Instruments, Abingdon, Oxfordshire, UK) was used for the sensory nerve conduction study (SNCS); stimuli were applied at a position 10 cm above the lateral malleolus, and SNCS was conducted at the sural nerve in the lateral malleolus region. Stimuli were administered at 2 Hz to 10 kHz and an intensity of 10 to 20 mA, and the time was 0.5 sec[7)]. Intragroup comparisons of variables before and after training were made using the paired t test, whereas intergroup comparisons were performed using the independent t-test. IBM SPSS Statistics ver. 20.0 (IBM, Armonk, NY, USA) was used for statistical analysis, and p values of <0.05 were considered significant.

RESULTS

A summary of the clinical and demographic features of the sample (n=20) is provided in Table 1. A significant difference was observed between group post-test velocity results (p<0.05), and significant differences were found between pre- and post-test results for all variables (p<0.05). The effect sizes of gains in the experimental and control groups were very high for the sensory nerve conduction velocity (effect size 1.00 for both) (Table 2).

DISCUSSION

High-frequency rTMS is known to have control effects on motor and sensory functions[8)] and the fact that high-frequency rTMS increases primary motor cortex excitability has been well established. Summers et al.[9)] reported when high-frequency rTMS was applied to the primary motor cortex, sensory and pain threshold values increased in normal adults and in patients with central or peripheral nerve damage. However, the mechanism responsible for sensory nerve network reactions induced by stimulating the motor cortex has not been clearly identified. Repeated administration of rTMS pulses can induce long-lasting changes in the excitabilities of the corticospinal tract, M1, and spinal cord structures and result in significant improvements in aspects of sensory and motor functions in patients with motor disorde[10)]. The present study was conducted to investigate the effect of active rTMS on sensory recovery of the lower extremities in patients with subacute SCI. According to our results, the SNCV was more enhanced after the intervention in the experimental group than in the control group. Furthermore, active rTMS was found to be more effective at improving sensory recovery than sham treatment. rTMS could reduce corticospinal inhibition and thus induce motor improvements in SCI, and it is possible that motor score improvements induced by rTMS in SCI could be due to enhancement of descending corticospinal projections and reductions in corticospinal inhibition[7)]. Notably, Caria et al.[11)] reported a direct relation between motor and sensory nerves. Ragert et al.[12)] reported that 5 Hz rTMS induced sustained increases of somatosensory cortex excitability, and Pleger et al.[13)] found that rTMS of the somatosensory cortex improved tactile discrimination and enhanced somatosensory cortex activation and that changes in

Table 1. General and medical characteristics of the subjects (N=20)

	EG (n=10)	CG (n=10)
Gender (male/female)	6/4	7/3
Age (years)	41.0 ± 8.1	43.3 ± 9.6
Time since injury (months)	3.8 ± 1.6	3.7 ± 1.1
AIS (C/D)	3/7	5/5
Cause (F/TA)	4/6	4/6

EG: Active rTMS and conventional physical therapy group; CG: Sham rTMS and conventional physical therapy group; AIS: American Spinal Cord Injury Association Impairment Scale; F: fall; TA: traffic accident

Table 2. Comparison of changes in characteristics of the experimental group and control group with values presented as mean (standard deviation)

		EG (n=10)	CG (n=10)
Amplitude (μV)	Pre	31.1 ± 14.2	30.4 ± 15.2
	Post	35.0 ± 15.9**	32.2 ± 15.5**
Latency (ms)	Pre	3.6 ± 1.0	3.6 ± 0.7
	Post	3.2 ± 0.7*	3.3 ± 0.4*
SNCV (m/s) a,b	Pre	43.3 ± 7.6	43.7 ± 10.7
	Post	49.1 ± 4.4**	45.6 ± 10.7*

Values are shown as the mean ± SD. *Significant difference from the pre-intervention value ($p<0.05$).
**Significantly difference from the pre-intervention value ($p<0.01$). [a]Significant difference in gains between the two groups ($p<0.05$). [b]Effect size greater than >0.70.
EG: Active rTMS and conventional physical therapy group; CG: Sham rTMS and conventional physical therapy group; SNCV: sensory nerve conduction velocity

primary motor cortex were negatively correlated with gains in discrimination ability. These results support the notion that rTMS augments sensory recovery in subacute -stage patients when they are treated within 6 months of SCI[14, 15]. The present study has some limitations. First, the small sample size may have adversely influenced the analysis and impacted our results, and thus, our findings cannot be generalized to all SCI patients. Second, the absence of follow-up after the end of the active rTMS prevented determination of the durability of the effects of this intervention. Further studies, including a long-term follow-up assessment, are needed to evaluate the long-term benefits of rTMS.

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