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Repetitive Transcranial Magnetic Stimulation Combined with Task Oriented Training to Improve Upper Extremity Function After Stroke

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The purpose of the present study was to investigate the effect of repetitive transcranial magnetic stimulation (rTMS) in conjunction with task oriented training, on cortical excitability and upper extremity function recovery in stroke patients. This study was conducted with 31 subjects who were diagnosed as a hemiparesis by stroke. Participants in the experimental (16 members) and control groups (15 members) received rTMS and sham rTMS, respectively, during a 10 minutes session, five days per week for four weeks, followed by task oriented training during a 30 minutes session, five days per week for four weeks. Motor cortex excitability was performed by motor evoked potential and upper limb function was evaluated by motor function test. Both groups showed a significant increment in motor function test and amplitude, latency in motor evoked potential compared to pre-intervention ($p < 0.05$). A significant difference in post-training gains for the motor function test, amplitude in motor evoked potential was observed between the experimental group and the control group ($p < 0.05$). The findings of the current study demonstrated that incorporating rTMS in task oriented training may be beneficial in improving the effects of stroke on upper extremity function recovery.

Keywords : repetitive transcranial magnetic stimulation, stroke, task oriented training

1. Introduction

Stroke is the leading cause of serious long-term disability in adults and approximately 70% to 80% of people after stroke have upper extremity impairments [1, 2]. Stroke survivors' impaired upper extremity function hampers their dexterity in everyday tasks, diminishing their quality of life [3]. Upper extremity function is important for gross motor skills, such as crawling, postural control, and body transfer, as well as fine motor skills for daily activities, such as feeding, dressing, and grooming [4]. Rehabilitation of the upper limb, many stroke survivors experienced reasonable motor recovery of their proximal upper limb but limited recovery at the distal [5]. Task oriented training provides intensive, meaningful, and progressive training regime, and it allows stroke patients to directly improve their motor disabilities with dynamic functional activities [6]. Advocates of task-oriented training conduct a training to engage systems. There is a growing body evidence that intensive task-oriented training can significantly improve walking competency in individuals with stroke [7].

But stroke patients currently experience little task-oriented training for their upper extremity during rehabilitation [8]. And the rate of recovery achieved with these studies may not be satisfying to the patients and their family. Repetitive Transcranial magnetic stimulation (rTMS) has a potential to maximize motor recovery in a short time. TMS is a powerful tool used to study brain function non-invasively. With TMS, a current carrying coil generates a pulsed magnetic field that can induce stimulating currents in the underlying neural tissue [9]. Low-frequency rTMS appears to cause a transient reduction in cortical excitability, as shown by the motor-evoked potential (MEP), whereas high-frequency rTMS increases the size of the MEP and cortical excitability [10]. Butler and Wolf [11] viewed rTMS as a tool that helps the brain to reach an optimal state of learning to facilitate subsequent training effects.

Thus, combining the effects of task-oriented training with those of rTMS conditioning is attractive. It is possible the rTMS application before task oriented training would enhance the therapeutic effect. The purpose of the present study was to investigate the effect of rTMS with task oriented training for 4 weeks, on cortical excitability and upper extremity function recovery in stroke patients.

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2. Materials and Methods

Patients ($n = 80$) with stroke were screened for this study from July 2013 to October 2013. The inclusion criteria were: (1) no significant cognitive deficit (a score of > 25 points in the Mini-Mental Status exam) [12]; (2) a lower than two grades on the Modified Ashworth Scale [13]; (3) no limited range of motion of the lower extremity; (4) a higher than fair score on the Manual Muscle test [14]; (5) no muscular-skeletal disorder and operation of the lower extremities; (6) no unilateral neglect, hemianopsia, or apraxia; (7) no phychological or emotional problems. Thirty patients with stroke met the criteria.

All procedures were reviewed and approved by the Institutional Ethics Committee of Eulji University Hospital (IRB file No.: EMC 2013-06-014-003). When the initial assessment was completed, the subjects were randomly assigned to either an experimental group ($n = 16$) or a control group ($n = 15$). The subjects were randomly assigned to the two groups according to their order of acceptance using a table of random numbers created with software Excel (Microsoft). The randomization was done by a third party totally unaware of the study content.

Participants in the experimental and control groups received rTMS and sham rTMS, respectively, during a 10 minutes session, five days per week for four weeks, followed by task oriented training during a 30 minutes session, five days per week for four weeks. The subjects' characteristics and all outcome measures before and after the treatment were assessed by Physician 1 who was blinded to the treatment allocations. The rTMS and task oriented training were conducted in a closed room by Physician 2 who was not involved in the assessment of the subjects. Both physicians were instructed not to communicate with the subjects about the possible goals or the rationale of either treatment.

Participants were seated in a stable chair with both arms resting comfortably on the lap. Transcranial magnetic stimulation was performed using a 70-mm figure-of-eight coil and a Magstim Rapid stimulator (Magstim Co, Ltd, Carmarthenshire, Wales, UK). The stimulator was placed in the subject's back so that they received no visual feedback about the stimulation parameters. The intensity of rTMS pulses was determined at 80% of motor threshold, which corresponded to the lowest intensity able to elicit a visible twitch of the first dorsal interosseous muscle of the hand in at least 5 out of 10 trials. Ten rTMS trains lasting 10s each were delivered during a 10 min period at a frequency of 10 Hz. Specifically, every 1 min, the subjects were given 5 s of TMS followed by a 55s rest period. Sham rTMS was applied over the identical cortical area and with rTMS frequency, but with zero stimulation output intensity.

Task-oriented training emphasized active participation and individualized and task-oriented functional training. Task oriented training was conducted with modified study of Song & Hwang [15]. The protocol of task-oriented arm training is consisted of 1) reaching, lifting, and placing plastic cans on shelves, 2) folding towels, 3) moving a set of rings, 4) stacking plastic cups, 5) turning over the pages of book, 6) writing. Each individual participated in 1-to-1 therapy. Progressions included increasing the number of repetitions completed within 5 minutes at a treatment room and increasing the difficulty of exercise performed at each treatment room.

The latency and amplitude of MEPs of the first dorsal interosseous muscle elicited by TMS were used to indicate corticomotor excitability [16]. The MEPs were recorded by an eletromyographic machine in response to TMS delivered through a figure-of-eight coil placed to be a sensitive measure for detecting residual corticospinal functions and to be predictive of motor recovery after stroke [17].

For evaluation of the motor function of the upper limb in stroke patients, we used the manual function test, which consists of "arm motion" and "manipulative activities". The arm motion was performed using four tasks: forward elevation and lateral elevation of the upper limb, touch the occiput and touch the dorsum with palm. The manipulative activities included four tasks: grip, pinch, carry cubes, and peg board. The total score of MFT for eight tasks is 32:0 indicates severe impairment and 32 indicates full function in the upper limb function. Test-retest reliability and inter-rater reliability of MFT are $r = 0.99$ and $r = 0.99$, respectively [18].

Differences in the general characteristics between the experimental group and the control group before the therapy were compared using independent t-tests and chi-square tests. Comparisons of measuring variables before and after the intervention within each group were made using paired samples t-test. Comparisons of pre- and post-test differences in measuring variables between the experimental group and the control group were done using the independent t-test. The statistical software SPSS 20.0 (SPSS, Chicago, IL, USA) was used for statistical analysis. The level of significance was chosen as 0.05.

3. Results

A summary of the clinical and demographic features of the sample ($n = 31$) is shown in Table 1, which also shows that there were no significant differences in the baseline characteristics observed between the two groups ($p > 0.05$).

Table 1. General and medical characteristics of subjects.

	EG (n = 16)	CG (n = 15)
Sex (Male/Female)	8/8	6/9
Age (years)	62.40 ± 7.50	61.80 ± 7.13
Height (cm)	164.00 ± 7.73	164.60 ± 10.96
Weight (kg)	62.60 ± 8.95	65.90 ± 8.80
Time since onset (months)	3.70 ± 1.25	4.89 ± 1.05

EG, experimental group; CG, control group
Values are expressed as mean ± SD

Table 2 shows the latency and amplitude in MEPs and MFT of the two groups (n = 31) before and after intervention. Both groups showed a significant increment in MFT and amplitude, latency in MEPs compared to pre-intervention ($p < 0.05$). A significant difference in post-training gains for the MFT, amplitude was observed between the experimental group and the control group ($p < 0.05$).

4. Discussion

This study was conducted to investigate the effect of rTMS on the improvement in the upper extremity function of patients with stroke. After four weeks of intervention, significant improvements in MFT, amplitude in MEPs were observed between the experimental group and the control group. This result supports the primary hypothesis of the study that rTMS would be beneficial to recovery motor of stroke patients. To our knowledge, ours is the first study to investigate the effects of rTMS on upper extremity motor recovery. The effect of task oriented training was already introduced by many researchers [19, 20]. And novel concepts are urgently needed to enhance the effectiveness of current treatment strategies early after stroke. Standard TMS instruments consist of a high-voltage capacitor that can be discharged through an insulated coil of wires [21, 22]. TMS is based on Faraday's principle of mutual induction. Electrical energy can be converted into magnetic fields and magnet fields can be converted into electric energy [23]. The rapid, time-varying magnetic field created around the coil, which passes unchanged through electrically resistant structures such as the skull, induces an electrical current in human brain tissue. When a TMS coil is placed on the scalp over the primary motor cortex (M1), the induced electrical current stimulates the neurons of the cortex [24]. It has the potential to improve dexterity of the affected hand after stroke [25]. The concept underlying the use of rTMS in the rehabilitation of hand function after stroke is based on the model of interhemispheric competition for sensory and motor processing [26]. We conducted high frequency repetitive transcranial magnetic stimulation to cerebral cortex of experimental group and as a result, MFT score of experimental group showed significant difference from the control group. Mally & Dinya [27] identified that rTMS application have a good effect on motor improvement of stroke patients.

The findings of the current study demonstrated that incorporating rTMS in task oriented training may be beneficial in improving the effects of stroke on upper extremity function recovery. The present study has some limitations. First, the small sample size may have influenced certain variables and impacted the results. Therefore, these results cannot be generalized to all stroke patients. Second, the absence of follow-up after the end of the intervention does not allow for determination of the durability of the effect of this therapy. Further studies, including a long-term follow-up assessment, are needed to evaluate the long-term benefits of mirror therapy.

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Table 2. Comparison of upper extremity function pre and post between each group (N=31).

	EG (n = 16)		CG (n = 15)	
	Pre-test	Post-test	Pre-test	Post-test
MFT	13.20 ± 5.00	22.20 ± 2.86*[a]	14.20 ± 2.82	16.90 ± 2.13*
Latency (ms)	29.79 ± 0.58	29.03 ± 0.63*	30.05 ± 0.36	29.75 ± 0.37*
Amplitude (mV)	1.10 ± 0.08	1.64 ± 0.21*[a]	1.06 ± 0.09	1.33 ± 0.30*

EG, experimental group; CG, control group
Values are expressed as mean ± SD
*significant difference from pre-test, $p < 0.05$
[a]significant difference in gains between two groups, $p < 0.05$

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