Effect of Lower Extremity Robotic Therapy Combined with 5 Hz High Frequency Repetitive Transcranial Magnetic Stimulation on BBS, TUG and 10 Walk in Stroke Patients

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Purpose This study sought to investigate the effects of lower-extremity robotic therapy combined with 5 Hz high-frequency repetitive transcranial magnetic stimulation on the Berg Balance Scale (BBS), Timed Up & Go Test (TUG) and 10 m walk in stroke patients. ***Methods*** A total of 14 stroke patients participated in the study—namely, seven persons in the lower-extremity robotic therapy group who used 5 Hz high-frequency repetitive transcranial magnetic stimulation on the cerebral hemisphere on the damaged side (5Hz-rTMSRG) and seven persons in the general robotic walking therapy group (GRG). The subjects' training period was 30 min/day, 3 days/week, for 4 weeks, and both groups performed functional evaluations related to balance and walking before and after the intervention. ***Results*** A comparison of the results obtained by the two groups revealed that those in the 5Hz-rTMSRG showed significant differences in the BBS, TUG, and 10 m walk results after the intervention ($p<0.05$). In addition GRG showed significant differences in the BBS, TUG, and 10 m walk results ($p<0.05$). When comparing the balance and gait evaluations after the intervention between the two groups, significant differences were found in the 5Hz-rTMSRG and GRG in terms of the BBS, TUG, and 10 m walk results ($p<0.05$ and $p<0.001$, respectively). ***Conclusion*** These results revealed that lower-limb robotic therapy combined with 5 Hz high-frequency repetitive transcranial magnetic stimulation had a more positive effect on the BBS and TUG results of stroke patients than general lower-limb robotic therapy.

Key words Robotic therapy, 5 Hz high-frequency repetitive transcranial magnetic stimulation, Berg Balance Scale, Timed Up & Go Test, 10 m walk test.

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Ⅰ. Introduction

Stroke is a disease caused by a sudden hemorrhage or infarction in the cerebral blood vessels. According to the World Stroke Organization (2022), more than 10 million strokes occur every year, making it the second leading cause of death worldwide[1)]. Stroke has various causes, including atherosclerosis, hypertensive intracerebral hemorrhage, aneurysm, embolism, and vascular malformation. Moreover, hypertension, diabetes, smoking, drinking, and family history are all reported to be risk factors for cerebrovascular diseases such as stroke[1)]. When the supply of oxygen and glucose to the brain tissue is blocked due to a stroke, it can cause disorders in various nerve pathways. In particular, the descending and ascending nerve tracts are the central nervous pathways that transmit information to the brain and spinal cord structures, and they are the major neural pathways that transmit sensory information from the outside environment and motor information from the cerebral cortex and brainstem[2)].

The descending nerve tract, which is part of the central nervous system, is largely divided into the pyramidal tract and the outer pyramid, and it is involved in motor functions. The pyramidal tract is a motor nerve tract involved in human voluntary movement, which begins in the cerebral cortex and transmits in-

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formation from the motor neurons of the spinal cord through the brainstem. This information is involved in the sophisticated voluntary movements of the peripheral nervous system, notably hand and foot movements[3)].

Recently, innovative changes have occurred in the field of rehabilitation medicine as a result of the Fourth Industrial Revolution. Advanced, cutting-edge medical technology is now being used in both the medical and rehabilitation fields, including robotic surgery and robotic rehabilitation. In the rehabilitation field in particular, customized upper- and lower-extremity rehabilitation training for patients is being introduced that involves the use of rehabilitation robots[4)].

Robotic therapy can control abnormal movement patterns stemming from problems in the descending nerve tracts, such as the corticobulbar, corticospinal, reticulospinal, and vestibulospinal tracts, due to stroke. This kind of therapy improves movement patterns by controlling the range of various joints involved in the patient's damaged movement and helping the patient perform precise movements by setting the appropriate range of motion of the joints. In addition, it can provide patients with improved concentration, magnetic confidence, and motivation through encouraging voluntary movement by assisting them with motor skills they can no longer perform on their own[5,6)].

The lower-extremity rehabilitation robots currently used in clinical settings can be broadly divided into treadmill gait trainers, stationary gait trainers, foot-plate-based gait trainers, and overground gait trainers, with the most commonly used robots being of the treadmill type. An example of the treadmill-type robot is the Walkbot(P&S Mechanics), which allows the patient to control the movement of their joints on the treadmill via reducing the weight load through a weight-bearing system. It is also possible to train not only the hip and knee joints but also the ankle joints, which cannot be controlled by one therapist at the same time[7)]. The most widely used Walkbot is a robot-assisted fixed-exercise device that serves as a walking aid in cases of lower-limb functional losses. Improving the walking function of stroke patients is among the most important goals of rehabilitation treatment. In this regard, walking patterns can be improved by allowing patients to experience the ideal gait intensively and repeatedly for the purpose of social reintegration[8)].

Research is currently being actively conducted to induce neuroplasticity by means of non-invasive magnetic stimulation in the nerve cells of the damaged area in patients who exhibit motor and sensory impairment as a result of brain lesions[9)]. Magnetic stimulation was first developed by Anthony Barker in 1985, and the first related study sought to demonstrate the effect of relieving depression through transcranial magnetic stimulation (TMS) in patients with depression[10)]. Since then, TMS has been applied to patients with various neurological disorders worldwide, and research is now being conducted on its impact in terms of pain relief, auditory hallucinations, cognitive impairment, psychiatric disorders such as obsessive-compulsive disorder, stroke, Parkinson's disease, and central and peripheral axonal damage. Since 2010, studies have shown that TMS treatment with different stimulation frequencies, such as low-frequency, high-frequency, and theta-burst magnetic stimulation, can be applied to patients with various brain lesions and damage types to excite and inhibit the brain's nerve cells[11)].

Repetitive magnetic stimulation in stroke rehabilitation is largely applied in two forms: low-frequency repetitive transcranial magnetic stimulation (LF-rTMS) using a stimulation frequency of 1 Hz or less and high-frequency repetitive transcranial magnetic stimulation (HF-rTMS) using a stimulation frequency of 5 Hz or more. Depending on the utilized stimulation frequency, the activity of the cerebral cortex and the motor-evoked potential (MEP) value, which causes the voluntary contraction of the corresponding muscles, can be either increased or decreased. Additionally, in recent years, theta-burst stimulation (TBS)—that is, continuous stimulation that can be divided into intermittent TBS (iTBS) and continuous TBS (cTBS)—has been introduced based on the difference in frequency. This TBS has been reported to have an excitation effect on the cerebral cortex in the case of iTBS and an inhibitory effect on the cerebral cortex in the case of cTBS[12]. According to a previous study, it was reported that HF-rTMS combined treadmill training improved effective on the walking performance of chronic stroke patients[13].

In light of the above, the present study sought to determine whether there is any difference in gait between patients who undergo robotic therapy combined with HF-rTMS using a stimulation frequency of 5 Hz and patients who undergo simple robotic therapy.

Ⅱ. Methods

Ⅱ.1. Subjects

In this study, 14 people who were hospitalized at C Rehabilitation Hospital in Seoul and receiving robot rehabilitation treatment for lower-extremity walking were selected as subjects for less than 12 months after the onset of their disease. The conditions for selecting subjects were as follows. All had a score of 24 or higher on the Korean version of the Mini Mental State Examination test, 2 or higher on the Functional Ambulation Category, 21 or higher for membership of the severe fall group according to the Berg Balance Scale (BBS), and a Timed Up & Go Test (TUG) result indicating them to be eligible for the intervention. The 14 subjects who participated in the experiment were randomly divided into two groups—namely, the experimental group and the control group—by flipping a coin. All the patients voluntarily agreed to participate in the study.

Ⅱ.2. Evaluation tools

Ⅱ.2.1. Assessment of balance ability

This study used the BBS, an indicator of gait evaluation, to determine the difference in the subjects' balance ability before and after 5 Hz high-frequency repetitive transcranial magnetic stimulation in the experimental group (5Hz-rTMSRG) and general robotic walking therapy in the control group (GRG). The BBS is an evaluation scale developed for balance evaluation in the elderly. Each item can be scored on a five-point scale ranging from 0 to 4, with the total score ranging from 0 to a maximum of 56. In the present experiment, the evaluation items were fully explained to the subjects before the evaluation, meaning that the evaluation was performed after familiarizing them with the evaluation method. The BBS was used twice for each subject, before and after the intervention. Liston and Brouwer (1996) reported the test–retest reliability of the BBS to give an intraclass correlation coefficient of .98[14].

Ⅱ.2.2. Timed Up & Go Test

The TUG evaluates the walking ability of elderly persons. In clinical practice, it measures the time taken for a patient with a walking disorder to get up from a chair, walk 3 m, return to their original position, and sit down again. The test evaluates the subject's walking mobility, with agility being the most important aspect. For the evaluation in this study, all the subjects were taught the evaluation method, required to practice it once, and then asked to perform the TUG evaluation. This test was performed twice by each subject, once before the intervention and once after all the training was completed. The TUG used in this study had an intraclass correlation coefficient of .99 within the raters and an intraclass correlation coefficient of .99 between raters[15].

Ⅱ.2.3. 10 m walk test

The 10 m walking test involves the patient walking a total distance of 14 m, with an extra distance of 2 m before and after for the purpose of acceleration and deceleration, and the time taken to travel the 10 m distance in the middle is recorded in seconds. In this study, the average value of the measurements after being repeated three times was used. The 10 m walk test for stroke patients shows high inter-rater reliability at both comfortable walking speeds (intraclass correlation coefficient [ICC] = .94) and fast walking speeds (ICC = .97)[16].

Ⅱ.3. Experimental procedure

Ⅱ.3.1. Robotic walking therapy for the lower extremities

The lower-extremity robot walking therapy used in this study involved a skeleton-controlled robot (Walkbot,

Figure 1. WalkBot

P&S Mechanics, Korea), which is a state-of-the-art walking robot that helps patients learn lost walking patterns by reducing the fatigue burden and inducing patients with walking disabilities to repeatedly learn accurate movements(Figure 1). The skeleton-controlled robot trains on the treadmill and reduces its own weight in real time, thereby enhancing various walking elements, such as the range of motion (ROM), stiffness, and force according to the robot's intervention.

II.3.2. Repetitive transcranial restimulation

In this study, 5 Hz high-frequency repetitive transcranial magnetic stimulation was applied to the M1 foot area of the cerebral cortex on the damaged side of the patients to increase the excitability of the lateral corticospinal tract. The measuring equipment in this study used an 8-shaped coil in the MagPro R30 body(Figure 2). The 8-shaped coil was placed on the hemisphere of the affected side at an angle of approximately 45° from the central zone for the magnetic stimulation. A total of 900 pulses of magnetic stimulation were applied at an intensity of 90% of the motor threshold to excite the lateral corticospinal tract on the affected side using a frequency of 5 Hz for 15 min at a time, 3 times per week, for 4 weeks, giving a total of 12 sessions. The control group received 30 minutes of general robotic therapy.

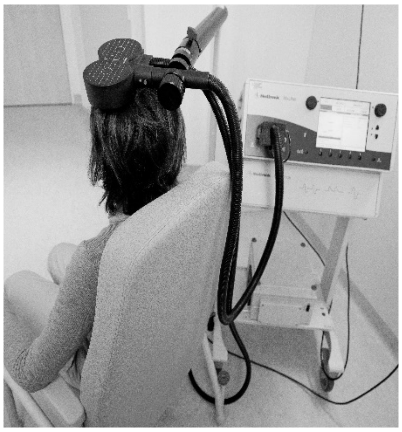

Figure 2. MagPro R30 TMS

II.3.3. Intervention method

In addition to central nervous system development therapy, the subjects in both groups received general robotic walking therapy for 30 min at a time, 3 times a week, for 4 weeks, giving a total of 12 sessions (figure 1). In the 5Hz-rTMSRG, this therapy was administered for 15 min at a time before the gait training with the skeletally controlled robot, while the patients in the GRG performed the conventional lower-extremity robotic therapy for 30 minutes.

II.3.4. Analysis method

In this study, the collected data were analyzed using SPSS 22.0 for Windows software. Descriptive statistics were used to determine the general characteristics of all the subjects. The Wilcoxon signed-rank test was used to determine any changes in the gait variable before and after the intervention in both groups. The Mann–Whitney U test was used to compare the gait variable between the situation before the intervention and that after the intervention. All the statistical significance levels were set at $p<0.05$.

III. Results

III.1. General characteristics of the subjects

The general characteristics of the subjects who participated in this study can be summarized as follows (Table 1). The 5Hz-rTMSRG included four men and three women, with an average age of 60.57±6.97

years. In terms of their injury type, there were three cases of cerebral hemorrhage and four of cerebral infarction. The GRG included three men and four women, with an average age of 61.42±8.62 years. With regard to their injury type, there were three cases of cerebral hemorrhage and five of right hemiparesis. The mean disease duration after onset in the 5Hz-rTMSRG was 13.43±4.66 months, while in the GRG it was 14.71±5.56 months(Table 1).

III.2. Comparison of the changes in balance and gait ability before and after the intervention in both groups

The BBS scores evaluating the balance ability within the two groups showed that the subjects in the 5Hz-rTMSRG increased their scores from 23.875±4.79 points before the evaluation to 46.000±8.20 after the evaluation, while the subjects in the GRG also increased their scores from 24.625±3.70 points to 29.125±5.25 ($p<0.05^{*}$)(Table 2). In terms of the TUG to evaluate walking ability, the subjects in the 5Hz-rTMSRG decreased their results from 41.133±7.83 seconds before the intervention to 40.535±4.59 afterwards, while the subjects in the GRG also decreased their results from 35.878±8.28 seconds to 33.431±8.35 ($p<0.05^{*}$)(Table 2). Concerning the 10 m walk test, the time taken also decreased from 32.749±6.50 seconds to 15.696±3.95 in the 5Hz-rTMSRG and from 26.9.00±4.30 to 24.500±4.36 in the GRG ($p<0.05^{*}$) (Table 2).

III.3. Comparison between the groups concerning the changes in balance and gait ability after the intervention

A comparison of the BBS scores evaluating the balance ability between the two groups revealed that the subjects in the 5Hz-rTMSRG showed a change of 22.125±6.243 points and those in the GRG showed a change of 4.500±4.175 points after the intervention, indicating a significant difference between the groups ($p<0.001^{**}$)(Table 3). The difference in terms of the TUG results evaluating walking ability between the

Table 1. General characteristics of subjects (N-14)

Variables		5Hz-rTMSRG (N=7)	Robotic G (N=7)
Gender	Male	4	3
	Female	3	4
Age		60.57±6.97	61.42±8.62
Lesion type	Hemorrhage	3	2
	Infarction	4	5
Time from stroke to rehab (months)		13.43±4.66	14.71±5.56

M±SD: mean±standard deviation
5Hz-rTMSRG: 5Hz repetitive transcranial magnetic stimulation robotic group, GRG: general robotic group

Table 2. Comparison of changes in gait ability within groups (N-14)

Variables		Groups	Pre-test	Post-test	Z	P
Functional ability	BBS (point)	5Hz-rTMSRG	23.875±4.79	46.000±8.20	-2.533	0.011*
		GRG	24.625±3.70	29.125±5.25	-2.375	0.018*
	TUG (sec)	5Hz-rTMSRG	41.133±7.83	40.535±4.59	-2.521	0.012*
		GRG	35.878±8.28	33.431±8.35	-2.521	0.012*
	10M (sec)	5Hz-rTMSRG	32.749±6.50	15.696±3.95	-2.521	0.012*
		GRG	26.9.00±4.30	24.500±4.36	-2.521	0.012*

M±SD: mean±standard deviation, 5Hz-rTMSRG: 5Hz-rTMSRG: 5Hz repetitive transcranial magnetic stimulation robotic group, GRG: general robotic group, BBS: burg balance scale, TUG: timed up & go test, 10M: 10 M walk test, $^{*}p<.05$

Table 3. Comparison of changes in gait ability between groups after post test (N-14)

	5Hz-rTMSRG (N=7)	GRG (N=7)	z	p
	M±SD	M±SD		
BBS (point)	22.125±6.243	4.500±4.175	-3.518	.002**
TUG (sec)	17.231±5.453	2.446±1.501	-2.310	.021*
10M (sec)	17.053±3.693	2.403±1.615	-2.941	.003**

M±SD: mean±standard deviation

5Hz-rTMSRG: Robotic High frequency Repetitive Transcranial Magnetic Stimulation Group, Robotic G: robotic therapy group ,BBS: Burg Balance Scale, TUG: timed Up & Go Test,10M: 10 M walk test

*p<.05, **p<.01

two groups was also significant, showing a decrease of 17.231±5.453 seconds in the 5Hz-rTMSRG and of 2.446±1.501 seconds in the GRG ($p<0.05^{*}$)(Table 3). In the 10 m walk test, the time taken was also shortened, with a decreased of 17.053±3.693 seconds in the 5Hz-rTMSRG and 2.403±1.615 in the GRG, indicating a significant difference ($p<0.001^{**}$)(Table 3).

Ⅳ. Discussion

Walking ability is important if humans are to function independently in their daily lives. Indeed, walking is important not only for motor skills and sensory integration but also for cognitive skills. Walking ability should be preceded by balance ability, which entails the ability to maintain the center line of the body on the base of support, as balance ability is necessary to improve walking ability. When a stroke occurs, it can cause asymmetric motor ability during walking, which can be said to result from the loss of motor control ability due to the resultant damage to the descending tract[17,18].

The descending tract can be broadly divided into the ventromedial system and the dorsolateral system. Damage to these systems is prominent due to stroke. Moreover, when the vestibulospinal and reticulospinal tracts included in the ventromedial system are damaged, the trunk stability is reduced. As a consequence, there is a decline in the patient's trunk and balance ability. Additionally, when the pyramidal tract associated with the dorsolateral system is damaged, the patient's distal movement is significantly impaired, resulting in precise movement disorders. The extrapyramidal tract has also been reported to be involved in automatic movement and both trunk and posture control[19]. Stroke patients exhibit noticeable gait difficulties due to the damage to their pyramidal tracts. This causes a decrease in their postural control and ability to maintain their balance due to the related damage to the extrapyramidal tract. Hence, recovery of the function of these two tracts is highly important in the field of rehabilitation following stroke.

The purpose of this study was to determine how robot therapy affects patients' balance and walking when combined with 5 Hz high-frequency repetitive transcranial magnetic stimulation. Currently, in most gait treatments, the gait training is conducted via one or two therapists participating per patient. Gait training is limited due to the inability to perform motor learning through accurate repetitive training patterns because the patient's gait training is different for each therapist. However, due to advancements in medical science, robot gait training has been suggested as a model for new treatment methods. This type of robotic therapy can both accurately and repeatedly provide different exercise training patterns for each therapist. Furthermore, robotic therapy can apply motor skills intensively via standardizing movements. Thus, robotic gait training is attracting attention as an ideal treatment method for enhancing the kinematic movement and muscle strength of the joints through analyzing the most ideal movements during human walking and then repeating accurate and rhythmic walking patterns. In addition, walking robots can be used for treatment purposes by combining auditory, visual, and tactile stimulation, with the major advantage being that there is no risk of falling while walking[20)].

According to a study by Kim et al(2022), the activation of damaged primary sensorimotor areas, supplemental motor areas, and premotor cortices was increased after robot-assisted gait training for 30 min/day, 5 days/week, for 4 weeks. Additionally, the Fugl–Meyer Assessment (FMA), TUG, and 10 m walk test scores were all improved after the training[21)]. Moreover, Moucheboeuf et al(2020) reported improvements in the functional ambulation category, TUG, and BBS scores as a result of a meta-analysis of robot-assisted gait training in stroke patients[22)]. However, these robotic treatments exhibit limitations in directly activating neurons in the primary motor area for commanding ankle movement. Most rehabilitation treatments provide sensory feedback to the lower centers within the treatment room and training in the hope of changing the nerve cells in the higher centers of the brain. Still, rTMS can activate the damaged lateral corticospinal tract more easily by directly reducing the motor threshold via non-invasive magnetic stimulation without pain.

This study was more progressive than that by Kim et al(2022) and confirmed there to be a difference in the walking effects indicated by the BBS, TUG, and 10 m walk scores before and after the robot training involving direct rTMS to the damaged cerebral hemisphere[21)]. Given the results presented in tables 2 and 3, when the robot therapy was combined with magnetic stimulation, there was a significant difference in the results between the groups before and after the intervention, with the 5Hz-rTMSRG showing better results when compared with the GRG.

These research results indicate that increasing the excitability of neurons prior to training via non-invasive magnetic stimulation improves the learning effect during robotic therapy when compared with conventional robotic therapy. This is likely because activation of the damaged cerebral hemisphere through repetitive magnetic stimulation improves the efficiency of the synaptic connections in the brain's nerve circuit and promotes nerve regeneration. Additionally, it is believed that neuroplasticity is promoted via the cortical reorganization of damaged areas of the cerebral cortex.

According to previous studies, HF-rTMS can easily induce the action potential of motor cells in the damaged cerebral cortex, induce the cortical excitability of cortical neurons, and induce positive neuroplasticity through various factors, such as the coil size, shape, frequency modulation, and stimulation intensity[23,-24)]. Thus, rTMS can be considered a new model when used in combination with robot training in rehabilitation, and it is believed that patients' quality of life can be improved by improving their muscle strength and function through learning more sophisticated movements involving more joints and more muscle participation[25)].

It must be acknowledged that study has some limitations. The GRG group did not perform sham magnetic stimulation for 15 minutes to confirm whether there was a pure effect of rTMS, meaning that the conditions of the subjects were not the same. Moreover, it is difficult to generalize the rTMS effect of the robot therapy due to the small number of subjects. In the future, additional studies involving the same conditions, more subjects, and the effect of magnetic stimulation based on frequency are required to confirm and extend the present findings.

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