Journal of Magnetics 27(4), 506-513 (2022)

ISSN (Print) 1226-1750
ISSN (Online) 2233-6656
https://doi.org/10.4283/JMAG.2022.27.4.506

A Comparative Study of 5 Hz Repetitive Transcranial Magnetic Stimulation on Cortical Activity and Upper Limb Function in Chronic Stroke Patients with Different Stroke Etiologies: A Case Study

Jung-Woo Jeong[1], Byung-Il Yang[2]*, and Bo-Kyoung Song[3]*

[1]*Department of Occupational Therapy, Bobath Memorial Hospital, Seongnam 13552, Republic of Korea*
[2]*Department of Physical Therapy, Sangji University, Wonju 26339, Republic of Korea*
[3]*Department of Occupational Therapy, Kangwon National University, Samcheok 25949, Republic of Korea*

(Received 19 October 2022, Received in final form 23 December 2022, Accepted 24 December 2022)

The purpose of this study was to investigate the effect of 5Hz repetitive transcranial magnetic stimulation (rTMS) on cortical activity and upper limb function in the etiology of chronic stroke patients. 2 patients with ischemic stroke and 2 patients with hemorrhagic stroke who satisfied the selection criteria were selected using the ABA' single subjective design. The study period was applied 18 times in all 4 patients: 3 times at baseline (A), 12 times in intervention period (B), and 3 times in baseline (A'). During intervention period(B), 5Hz rTMS was applied 4 times a week for 3 weeks, and no intervention was performed during the 3 baseline (A) and baselines (A'). Electroencephalography (EEG), box and block test (BBT), and fugl-meyer assessment (FMA) were performed to investigate changes in cortical activity and upper limb function. As a result, EEG and BBT were changed after intervention (B) in ischemic stroke patients than in hemorrhagic stroke patients, and there was no difference in FMA of all stroke patients. Through this, it is thought that 5 Hz r TMS can help to improve cortical activity and upper limb function in ischemic stroke rather than hemorrhagic stroke.

Keywords : repetitive transcranial magnetic stimulation, ischemic stroke, hemorrhagic stroke, cortical activity, upper limb function

1. Introduction

Stroke is a vascular disease in which the supply of oxygen and nutrients is interrupted due to the abrupt blockage or bursting of some cerebral blood vessels, leading to necrosis of the brain tissue. It can largely be classified into ischemic and hemorrhagic stroke [1, 2]. Previous studies have emphasized that early ischemic and hemorrhagic patients should be provided with neurorehabilitation at an early stage because it may not only strengthen the neurological response due to neuroplasticity, but also activate a dynamic response with the spontaneous recovery of the brain [3]. Recently, non-invasive brain stimulation has been proposed as a method to activate the cerebral cortex and promote upper limb function in stroke patients, and repetitive transcranial magnetic stimulation (rTMS) using a magnetic field has been applied to achieve this [4]. rTMS is an approach that promotes the depolarization of neurons in the cerebral cortex by applying magnetic stimulation to the outermost part of the skull using an electromagnetic coil that creates a magnetic field within a short space of time. The generated magnetic field wave applies an electric current directly to the brain cells [5]. In 1831, Faraday suggested that a time-varying current could create a magnetic field, thereby inducing an electric field as well as a secondary current in a nearby conductor. Barker established the basic theory of transcranial magnetic stimulation (TMS) that could be applied to patients using the magnetic field principle and proposed the first magnetic stimulator that could stimulate the human brain using magnetic fields [6]. rTMS promotes cortical activity excitability or inhibition through stimulation of neural synapses. High frequency rTMS (HF-rTMS) increases cortical excitability by decreasing the motor threshold (MT) and increasing the amplitude value of the motor evoked potential (MEP),

*Corresponding author: Tel: +82-33-738-7674
Fax: +82-33-738-7652, e-mail: bobathyang@naver.com
Tel: +82-33-540-3483, Fax: +82-33-540-3489
e-mail: bksong@kangwon.ac.kr

whereas low frequency rTMS (LF-rTMS) inhibits the excitability of the cerebral cortex and has the opposite effect on MEP and MT [5]. Lomarev *et al.* (2007) confirmed the improvement of electroencephalography (EMG) and finger strength by applying HF-rTMS to chronic stroke patients [7], while Ameli *et al.* (2009) applied 10 Hz HF-rTMS to stroke patients and used functional magnetic resonance imaging (fMRI) to confirm the differences in the cerebral cortex [8]. Khedr *et al.* (2009) applied HF-rTMS, LF-rTMS, and sham-rTMS to 36 patients with early ischemic stroke and confirmed the activity and motor function of the cerebral cortex [9]. In particular, by confirming the positive effect of LF-rTMS on the motor cortex, it was suggested that LF-rTMS rather than HF-rTMS could be beneficial in the functional recovery of early stroke patients. In the Framingham study, cerebral infarction due to arterial thrombosis and embolism occurred in 84.6 % of people with strokes, and cerebral hemorrhage, including subarachnoid hemorrhage, occurred in 14 % of people with strokes. Ischemic stroke accounts for 70 %-80 % of all strokes, and different treatment methods, such as antithrombotic drugs, are used due to differences in the major risk factors of hemorrhagic stroke [10, 11]. Although previous studies have suggested the rTMS effect by focusing on the onset of stroke patients, a few studies have noted the rTMS effect according to the cause of stroke. Through a single case study of four people, the purpose of applying 5 Hz rTMS according to the cause of the chronic stroke was therefore to determine how it helps the cortical activity and upper limb function and to confirm the effects of rTMS.

2. Materials and Methods

2.1. Subjects

In this study, two patients with ischemic stroke and two patients with hemorrhagic stroke who were admitted to the Department of Rehabilitation Medicine at B Hospital in G area were selected for this study based on the results of magnetic resonance imaging (MRI). The inclusion criteria were patients who actively consented to participate in the study, chronic stroke patients with an onset period of more than six months but less than 24 months after stroke diagnosis, and a Korean-Montreal cognitive assessment (K-MoCA) score of 23 or higher for normal cognitive level and communication. The patients were also required to understand the study instructions. On the other hand, those with contraindications to the application of rTMS and those with clinically unstable medical disorders such as seizures were excluded from the study. The subjects who participated in the study underwent physical and occupational therapy, followed by the intervention for an additional four weeks and evaluations.

2.2. Study design

In this study, a single-subject research design was applied as ABA'. A full treatment course consisted of 18 sessions.: The baseline phase (A) with 3 sessions, the intervention phase (B) with 12 sessions, and the baseline phase (A') with 3 sessions. No intervention was performed in the baseline phases (A and A'). In the intervention phase, 5 Hz HF-rTMS treatment was administered 3 times a week over the course of four weeks. Each treatment session lasted for 15 minutes. For the evaluation of upper limb function, the box and block test (BBT) and fugl-meyer assessment (FMA) were used, and the evaluations in the baseline phases (A) and (A') were performed three times each and 12 times after the intervention. Electroencephalography (EEG) was used to measure cortical activity. The first measurement was performed at the baseline, the second measurement was performed in the 15th session of the experiment, and the third measurement was performed in the 18th session (Fig. 1).

2.3. Assessment methods

In this study, EEG, BBT, and FMA were performed to investigate changes in activity in the cerebral cortex and upper limb function.

2.3.1. EEG

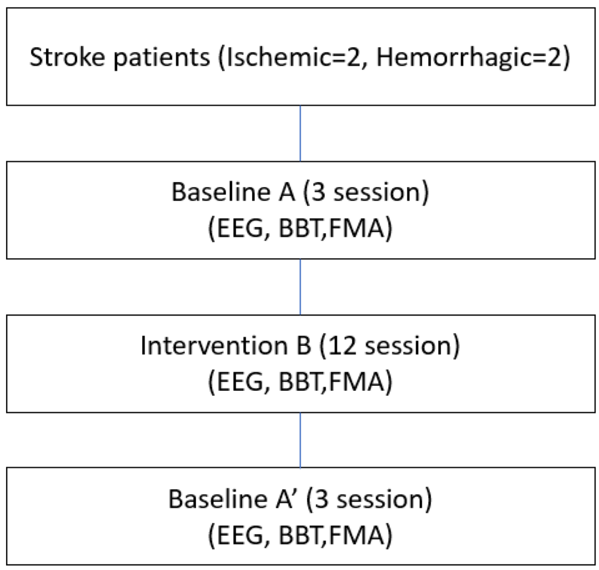


Fig. 1. Flow chart of the study process in patients with ischemic stroke and hemorrhagic stroke. EEG, electroencephalography; BBT, box and block test; FMA, fugl-meyer test.

EEG is a method used to measure electrical signals caused by nerve excitability between the neurons in the cerebral cortex [12]. EEG is known as a neuroimaging technique that measures the activity of electrical signals generated in the cerebrum through the placement of a terminal on the scalp and can measure the electrical activity of normal and damaged brains [13]. Unlike other neuroimaging techniques, EEG is a non-invasive method that does not harm the human body. It has the further advantages of allowing functional changes in the brain to be observed within a short period of time and of providing various data that can be analyzed after the examination, so it is widely used by clinicians [14]. EEG is divided into various areas from low frequency (LF) to high frequency (HF) depending on the frequency, namely, delta wave (δ-wave), theta wave (θ-wave), alpha wave (α-wave), beta wave (β-wave), and gamma wave (γ-wave) [15]. In this study, the sensorimotor rhythm (SMR) was set to 12-15 Hz for the β-waves measured. SMR occurs when a subject opens their eyes, and the activity of the cerebral cortex is passive. The subject pays attention to external stimuli in a relaxed and stable manner, including when solving a problem that requires sustained attention [16]. In this study, a total of 21 channels were assessed using the 10/20 international electrode arrangement method (Fig. 2). A computerized brain wave analyzer QEEG-21 (LXE5208, Laxtha Inc, Korea) was used for the measurement. For the EEG measurement, the subjects were allowed to rest for three minutes before the measurement, and when it started, they were asked to look at the action image presented on the 13-inch monitor in front of them for one minute and 30 seconds. To minimize any noise caused by frontal lobe eye movements during the measurement, the subjects were controlled not to blink frequently (Fig. 2). The raw data were collected using TeleScan version 3.2.9.0 (Laxtha Inc, Korea), which is a real-time data collection program, and the relative SMR wave value for each channel was visualized, and a relative power analysis was performed.

2.3.2. BBT

BBT is an evaluation tool used to measure hand agility and to evaluate patients with physical disabilities. The method requires the subject to move a one-inch-sized block from one box to the other, and the number of blocks moved by each hand in one minute is scored [17]. The test-retest reliability is reportedly r = 0.98 for the right hand and r = 0.94 for the left hand, while the inter-examiner reliability has been established as r = 1.00 for the right hand and r = 0.99 for the left hand [18]. In this study, only the injured hand was examined.

2.3.3. FMA

The FMA is performed to evaluate the degree of recovery of upper limb function in stroke patients. The evaluation items are given 0-2 points depending on the degree of performance, where 0 = not performing, 1 = performs partially, and 2 = performs fully. Thirty-three items corresponding to upper limb function are tested to evaluate the hemiplegic side. The total score is 66 points, and the degree of recovery is expressed as a percentage [19]. The items consist of the shoulder, elbow, and forearm (18 items), the wrist (five items), the hand (seven items), and upper extremity coordination ability (three items). The inter-inspector reliability of the test has been reported as 0.96 [20].

2.3. Procedure

2.3.1. 5 Hz HF-rTMS

The rTMS equipment used in this study was ALTMS® (Remed, Korea, 2018) and consisted of a 70 mm Fig. 8 coil device. While seated, the subject was asked to fix their head on the headrest, place both arms comfortably on a pillow or cushion, keep the forearms in a neutral

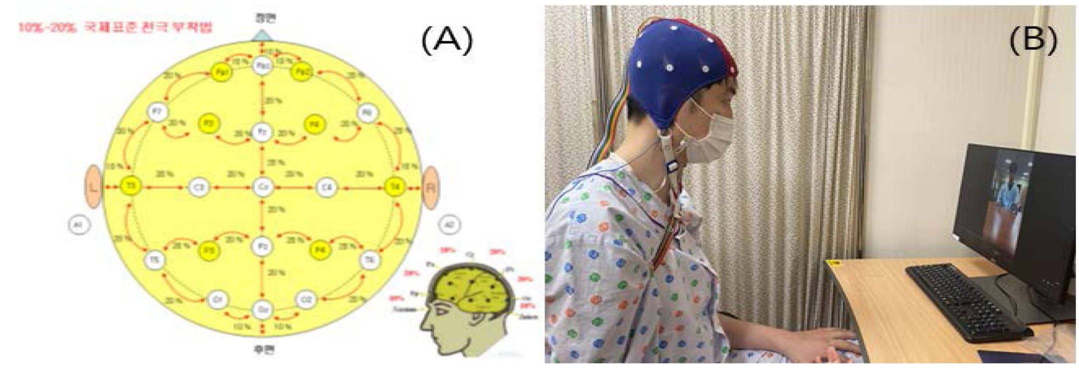


Fig. 2. (Color online) A total of 21 channels measured with the International 10/20 system for the area of EEG measurement in this study (A), and EEG measured using the motion observation image of the front 13-inch monitor (B).

state, and position themselves with the forearm propped up and the fingers extended. The coil stimulator was placed on the subject's head over the injured cerebral hemisphere and 2 cm lateral to the center line at an angle of 45°. When measuring the MEP, the position of the motor area was confirmed through the first dorsal interosseous muscle. During the MEP measurement, the resting motor threshold (RMT) was set as the stimulus intensity at which an MEP of 50 μV or more was recorded in at least five out of 10 stimuli. A frequency of 5 Hz was applied to activate the cerebral cortex on the injured side with an intensity of 120 % RMT at 900 pulses [21].

2.4. Data analysis

The general characteristics of the subjects were described in this study, and the K-MoCA and MFT results were indicated as scores. The BBT and FMA, which were conducted to investigate the subjects' upper limb function before and after the intervention, were analyzed by converting them into graphs using descriptive statistics. In addition, the treatment effect was determined to be improved when the average value and standard deviation were measured twice consecutively during the intervention period based on the average value obtained from the baseline of the existing study. The lasting effect of the intervention was set to be significant when the average value of the baseline (A') was higher than the average value of the baseline (A) [22, 23]. To investigate the activity of the cerebral cortex, EEG was used to measure baseline (A), the intervention period (B), and the baseline (A') three times. The measured values were converted to brain mapping using Telescan software, and the cerebral cortex activity was then compared.

3. Results

3.1. General characteristics of the subjects

Subject 1 was a 52-year-old male who complained of a sudden severe headache after stroke onset and was diagnosed with left hemiplegia due to ischemic stroke. Subject 1 had no specific diseases and had no difficulty with the therapist's instructions or their implementation. He had a K-MoCA score of 29 points. The subject scored 9/32 points on the left and 30/32 points on the right in the MFT. Subject 2, a 60-year-old male who had an ischemic stroke, complained of sudden muscle weakness. Although his pronunciation was slurred, his communication was not limited. He scored 25 points on the K-MoCA, which indicated that he had no difficulty understanding or carrying out the therapist's instructions. His MFT scores were 31/32 points on the left and 15/32 points on the right. Subject 3 was a 55-year-old male who had an onset period of 20 months and was diagnosed with left hemiplegia due to cerebral hemorrhage. No other diseases were present, and the subject had no difficulty understanding or carrying out the examiner's instructions. His K-MoCA score was 24 points. The subject had an initial unilateral neglect symptom, but that subsequently improved, and the results of the MFT showed that the left side was 11/32 points and the right side 32/32 points. Subject 4 was a 43-year-old female who had been diagnosed with left hemiplegia due to a cerebral hemorrhage following a sudden loss of consciousness 14 months prior. With a score of 28 points on the K-MoCA, the subject had no difficulty understanding or carrying out the examiner's instructions. The subject's scores on the MFT were 14/32 points on the left side and 29/32 points on the right side (Table 1).

3.2. Comparison of changes in cerebral cortex activity before and after the intervention

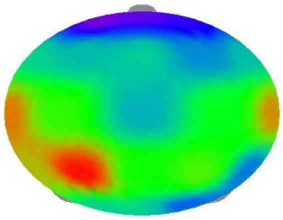
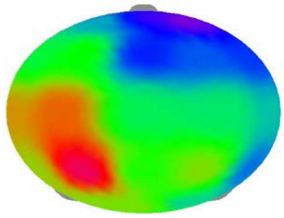
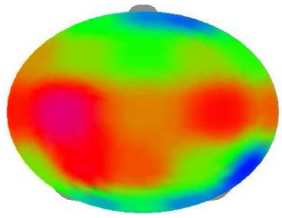
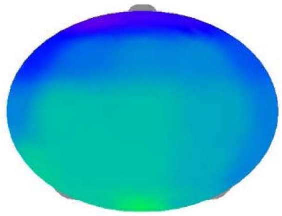
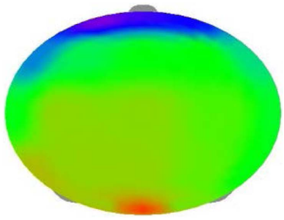
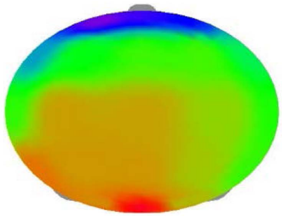
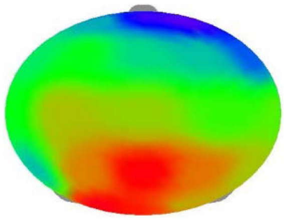
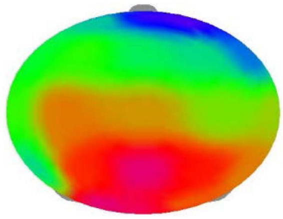
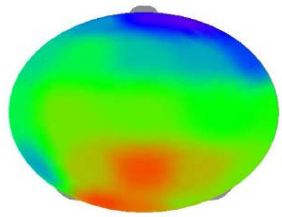
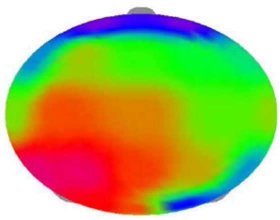
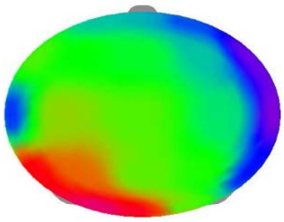
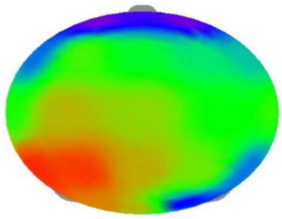
Differences in the regions F3, Fz, C3, Cz, C4, P3, and T3 were noted in the EEG conducted to investigate cortical activity before and after the intervention in subject 1. In subject 2, differences were evident in the regions C3, Cz, and C4, while for subject 3, only a difference in Cz was apparent. Subject 4 showed a difference in Cz and Pz (Table 2).

Table 1. General haracteristics of subjects.

Variables	Subject 1	Subject 2	Subject 3	Subject 4
Sex/age	M/52	M/60	M/55	F/43
Side of stroke	Left	Right	Left	Left
Type of stroke	Ischemic	Ischemic	Hemorrhagic	Hemorrhagic
Lesion	Parietal lobe	Basal ganglia	Thalamus	Parietal lobe
Time from stroke to rehab (months)	12	8	20	14
K-MoCA (score)	28	25	24	28
MFT (Rt/Lt, score)	9/30	31/15	11/32	14/29

K-MoCA: korean-montreal cognitive assessment, MFT: manual function test

Table 2. Comparison of EEG changes at baseline (A) intervention (B) baseline (A') of study subjects.

Variables		Baseline A	Intervention B	Baseline A’
Ischemic stroke	Subject 1			
	Subject 2			
Hemorrh-agic stroke	Subject 3			
	Subject 4			

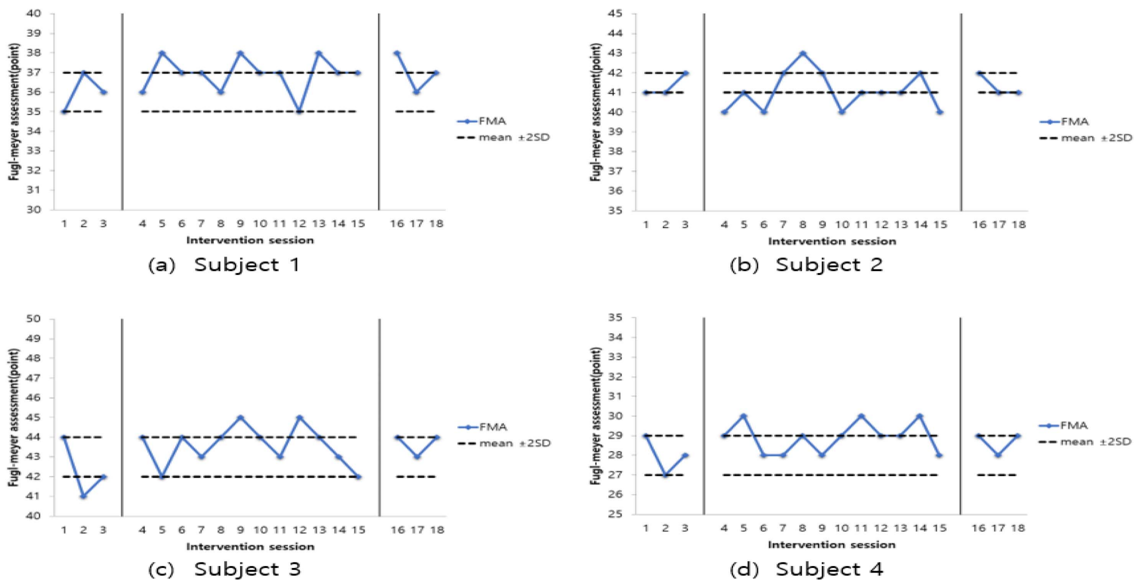


Fig. 3. (Color online) Comparison of BBT changes at baseline (A) intervention (B) baseline (A') of study subjects.

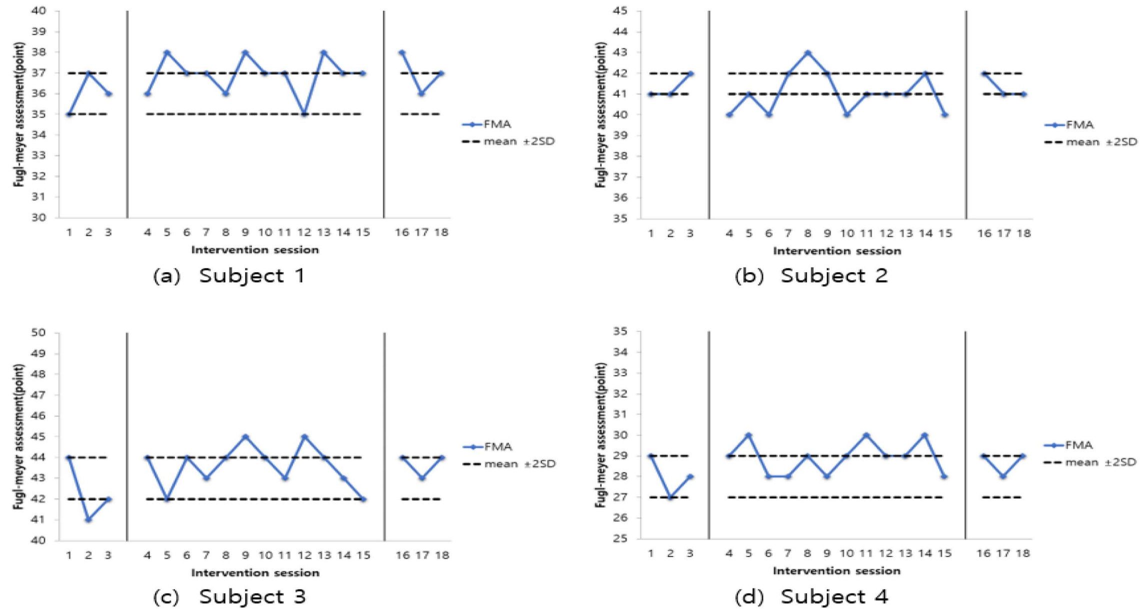


Fig. 4. (Color online) Comparison of FMA changes at baseline (A) intervention (B) baseline (A') of study subjects.

3.3. Comparison of changes in upper limb function before and after the intervention

For the BBT, which was applied to examine changes in upper limb function, the ischemic stroke subject 1 showed improvement: baseline (A) = 11.000 ± 1.00 points, intervention (B) = 12.583 ± 0.99 points, and baseline (A') = 12.666 ± 0.57 points. In subject 2, who had an ischemic stroke, there was improvement in baseline (A) (23.333 ± 0.57 points), intervention (B) (24.166 ± 0.93 points), and baseline (A') (25.000 ± 1.00 points). Subject 3, who had a hemorrhagic stroke, showed no improvement in baseline (A) (16.333 ± 1.15 points), intervention (B) (15.500 ± 0.79 points), and baseline (A') (16.333 ± 0.57 points). Similarly, there was no improvement in subject 4 (hemorrhagic stroke patient) for baseline (A) (22.333 ± 0.57 points), intervention (B) (21.333 ± 0.98 points), and baseline (A') (22.000 ± 1.00 points) (Fig. 3).

The results of the FMA showed no improvement in any of the subjects (Fig. 4): subject 1 (ischemic stroke), baseline (A) = 36.000 ± 1.00 points, intervention (B) = 36.919 ± 1.08 points, baseline (A') = 37.000 ± 1.00 points; subject 2 (ischemic stroke), baseline (A) = 41.333 ± 0.57 points, intervention (B) = 41.083 ± 0.99 points, baseline (A') = 42.333 ± 0.57 points; subject 3 (hemorrhagic stroke), baseline (A) = 42.333 ± 1.52 points, intervention (B) = 43.183 ± 0.99 points, baseline (A') = 43.166 ± 0.57 points; subject 4 (hemorrhagic stroke), baseline (A) = 28.000 ± 1.00 points, intervention (B) = 31.750 ± 4.26 points, baseline (A') = 28.666 ± 0.57 points.

4. Discussion

Ischemic stroke occurs when a part of the brain that is supplied with blood is damaged due to the blockage of blood vessels by arterial thrombus or embolism, while hemorrhagic stroke occurs when blood pools in the brain, or the brain is damaged by the rupture of a cerebral blood vessel, for example, via a subarachnoid or cerebral hemorrhage [24]. And Diabetes, atrial fibrillation, previous myocardial infarction, previous stroke, and intermittent arterial claudication can be the main causes of ischemic stroke or cerebral hemorrhagic stroke [25]. The limitations in functional movement in stroke patients may result from ischemic or hemorrhagic damage to the motor cortex, premotor cortex, motor pathways, or related descending pathways of the cerebrum or cerebellum. Among these types of stroke, cerebral infarction (84.6 %) and cerebral hemorrhage (14 %), including subarachnoid hemorrhage, have ischemic rather than hemorrhagic causes. It has been reported that the prognosis for motor function after the onset of ischemic stroke is more positive than that for hemorrhagic stroke [26]. In general, compared to ischemic stroke, hemorrhagic stroke is associated with a considerable increase of mortality in the early period after stroke onset, which is highly correlated with the hemorrhagic nature of the lesion. These different pathophysiologies have different long-term cerebral and functional implications [27]. After stroke onset, improvements through decreased edema and reperfusion of the ischemic penumbra not only affect the reorganization of the ischemic region of the brain, but rapidly applied neurorehabilitation after onset can also greatly help patients with rapid recovery and neuroplasticity. In addition, differentiated neurorehabilitation programs and various interventions are required for effective function recovery after stroke. Various interventions are applied to improve the movement restrictions that occur after stroke. In addition, methods such as constraint-induced movement therapy, sensory biofeedback, mental practice with motor imagery, and robotic assisted therapy have been suggested to restore upper limb function during neurorehabilitation [26]. However, very few studies have applied the pathophysiological differences of stroke patients, and many studies have been conducted with the onset period of ischemic stroke. In a previous study, rTMS was applied to recover upper limb function in stroke patients [28]. The effect of upper limb function was confirmed by comparing HF-rTMS, LF-rTMS, and sham-rTMS in ischemic stroke. Based on the results, it was suggested that rTMS can help activate the motor area of the cerebral cortex and improve upper limb function in stroke patients. rTMS may play an important role in improving the prognosis and cerebral activity of stroke patients [29]. In particular, rTMS induces depolarization and action potential generation in the stimulated regions of the cerebral cortex, which can modulate cortical excitability and induce positive neuroplasticity depending on the characteristics of the stimulus, such as the frequency, coil direction, and stimulus intensity [30]. In this study, four subjects were designed as a single case, and it was to investigate the difference in cortical activity and upper limb function of 5 Hz rTMS based on the pathophysiological differences of stroke patients. First, EEG was applied to determine the activity of the cerebral cortex. In subject 1, an ischemic stroke patient, there were differences in the regions F3, Fz, C3, Cz, C4, P3, and T3, while in subject 2, also an ischemic stroke patient, differences were seen in C3, Cz, and C4. In subject 3, a hemorrhagic stroke patient, a difference was evident in Cz, and in subject 4, who was also a hemorrhagic stroke patient, the differences were in Cz and Pz. An improvement in cerebral cortex activity was confirmed in all the subjects, and cortical activity was confirmed in all four subjects in Cz, which corresponds with the motor area. Activation was observed in a wider area of the cerebral cortex in the ischemic subjects than the hemorrhagic subjects. Khedr *et al.* (2010) reported the recovery of upper limb function in an early stroke patient as a result of applying HF-rTMS for 10 days at 3 Hz and 120 % RMT intensity to the damaged motor area [31]. With the exception of the patients with infarcts in large areas of the cerebral cortex, it was possible to confirm the initial effects of rTMS on cortical excitability by following the patients for one year. Ameli *et al.* (2009) applied 10Hz HF-rTMS to 29 stroke patients with damage to the middle cerebral artery, including either the primary or secondary cortical sensorimotor areas, and used fMRI to assess index finger and hand tapping movements [8]. Improvements in cerebral cortex activity and hand function were confirmed. In addition, in a systematic review of four studies conducted to determine whether the application of HF-rTMS to the ipsilateral hemisphere would recover upper limb movement in ischemic stroke patients compared with sham rTMS, 10 Hz HF-rTMS was used for the damaged upper limbs and was confirmed to increase motor function [26]. It is thought that rTMS can promote cerebral cortex activation not only in early stroke patients, but also in chronic stroke patients and that it may be more effective in cerebral activation, especially in ischemic stroke patients. In this study, activation was observed in the Cz, C3, and C4 regions of the ischemic subjects. These regions are adjacent to the primary sensorimotor cortex and may affect hand function. As a result, the application of rTMS according to pathophysiological differences requires a more diverse approach to treatment strategies according to stroke diagnosis. In addition, it is judged that neurorehabilitation according to the cause of stroke patients can have a positive effect on cerebral cortex activity in stroke patients in connection with treatment strategies and HF-rTMS. In addition, using the neurorehabilitation approach with HF-rTMS and classifying the causes of chronic stroke in patients may help restore upper limb function. The positive effects of HF-rTMS can be confirmed through the recovery of hand function in subjects 1 and 2 who both had ischemic stroke and were assessed via the BBT, which was conducted to investigate changes in upper limb function [32]. Notwithstanding, Kim *et al.* (2006) showed an improvement in the MEP by applying 10 Hz HF-rTMS to 15 chronic stroke patients, but no significant change in upper limb function could be confirmed [33]. These results may suggest that the linkage of neurorehabilitation via occupational therapy for the recovery of upper limb function is important. This study has limitations in generalizing the results due to the case study design, and it is necessary to make the equipment that evaluates hand function improvement more objective. In future studies, the effectiveness of the rTMS intervention could be assessed by considering different variables, such as the onset period and lesion site as well as the cause of the disease, in many subjects.

5. Conclusion

This case study, which was based on an ABA' design, investigated the effect of 5 Hz HF-rTMS on cerebral cortex activity and upper limb function based on the cause of chronic stroke in four subjects. Two subjects with ischemic stroke and two subjects with hemorrhagic stroke were selected for the study. Baseline (A) was measured three times, the intervention period (B) 12 times, and baseline (A') three times. rTMS at 5 Hz was performed four times a week for three weeks. As a result, EEG confirmed that the ischemic stroke subjects gained more cerebral activity than the hemorrhagic stroke subjects. Meanwhile, BBT, which was performed to examine upper limb function, revealed a difference in the ischemic stroke patients, but no difference was apparent with FMA in any of the subjects. It can therefore be confirmed that 5 Hz HF-rTMS produced differences in cortical activity and upper limb function depending on the cause of the stroke.

References

[1] N. Chaudhary, A. S. Pandey, and J. J. Gemmete, Postgraduate Medical Journal **87**, 714 (2011).
[2] T. V. Azizova, M. B. Moseeva, E. S. Grigoryeva, and N. Hamada, Radiation and Environmental Biophysics **61**, 5 (2022).
[3] C. Gorman and L. Gustafsson, Disability and Rehabilitation: Assistive Technology **17**, 409 (2022).
[4] T. H. Cha and H. S. Hwang, Brain Sciences **12**, 994 (2022).
[5] R. Jalinous, J. of clinical neurophysiology: official publication of the American Electroencephalographic Society **8**, 10 (1991).
[6] A. T. Barker, R. Jalinous, and I. L. Freeston, Lancet Lond. Engl **1**, 1106 (1985).
[7] M. P. Lomarev, D. Y. Kim, S. P. Richardson, B. Voller, and M. Hallett, Clinical Neurophysiology **118**, 2072 (2007).
[8] M. Ameli, C. Grefkes, F. Kemper, F. P. Riegg, A. K. Rehme, H. Karbe, and D. A. Nowak, Annals of Neurology: Official Journal of the American Neurological Association and the Child Neurology Society **66**, 298 (2009).
[9] E. M. Khedr, M. R. Abdel-Fadeil, A. Farghali, and M. Qaid, European Journal of Neurology **16**, 1323 (2009).
[10] S. H. Suk, Annals of Geriatric Medicine and Research **3**, 5 (1999).
[11] H. T. Meza, J. A. Roy, C. P. Lázaro, M. B. Cardiel, O. A. González, C. T. Juste, and J. M. Moreno, Neurología (English Edition) **37**, 434 (2022).
[12] J. C. Eliassen, E. L. Boespflug, M. Lamy, J. Allendorfer, W. J. Chu, and J. P. Szaflarski, Topics in Stroke Rehabilitation **15**, 427 (2008).
[13] M. Teplan, Measurement Science Review **2**, 1 (2002).
[14] C. D. Binnie and P. F. Prior, J. of Neurology, Neurosurgery & Psychiatry **57**, 1308 (1994).
[15] P. N. Friel, Alternative Medicine Review **12**, 146 (2007).
[16] M. de Zambotti, M. Bianchin, L. Magazzini, G. Gnesato, and A. Angrilli, Experimental Brain Research **221**, 69 (2012).
[17] V. Mathiowetz, G. Volland, N. Kashman, and K. Weber, The American Journal of Occupational Therapy **39**, 386 (1985).
[18] F. S. Cromwell, Primary Prevocational Evaluation **1**, 21 (1976).
[19] M. V. Radomski and A. A. T. Latham, Lippincott Williams & Wilkins **332**, (2008).
[20] D. J. Gladstone, C. J. Danells, and S. E. Black, Neurorehabilitation and Neural Repair **16**, 232 (2002).
[21] P. M. Rossini, D. Burke, R. Chen, L. G. Cohen, Z. D. Daskalakis, R. Di Iorio, and U. Ziemann, An updated report from an IFCN Committee. Clinical Neurophysiology **126**, 1071 (2015).
[22] K. J. Ottenbacher, Williams & Wilkins **141**, (1986).
[23] I. Marklund and M. Klassbo, Clinical Rehabilitation **20**, 568 (2006).
[24] W. Johnson, O. Onuma, M. Owolabi, and S. Sachdev, Bulletin of the World Health Organization **94**, 634 (2016).
[25] K. K. Andersen, T. S. Olsen, C. Dehlendorff, and L. P. Kammersgaard, Stroke **40**, 2068 (2009).
[26] P. Langhorne, F. Coupar, and A. Pollock, The Lancet Neurology **8**, 741 (2009).
[27] R. Perna and J. Temple, Behavioural Neurology **1** (2015).
[28] N. Kubis, Frontiers in Neural Circuits **1**, 56 (2016).
[29] N. Takeuchi, Int J Phys Med Rehabil **1**, 2 (2013).
[30] M. A. Dimyan and L. G. Cohen, Neurorehabilitation and Neural Repair **24**, 125 (2010).
[31] E. M. Khedr, A. E. Etraby, M. Hemeda, A. M. Nasef, and A. A. E. Razek, Acta Neurologica Scandinavica **121**, 30 (2010).
[32] F. Khan and F. Chevidikunnan, Turkish Journal of Physical Medicine and Rehabilitation **63**, 193 (2017).
[33] Y. H. Kim, S. H. You, M. H. Ko, J. W. Park, K. H. Lee, S. H. Jang, and M. Hallett, Stroke. Stroke **37**, 1471 (2006).