Immediate Effect of Repetitive Peripheral Magnetic Stimulation in Hemiplegic Patients with Arm Paresis: A Pilot Study

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ABSTRACT

Objectives: To compare the immediate effects of repetitive peripheral magnetic stimulation (rPMS) on upper extremity (UE) function of hemiplegic patients with different severity.

Study design: Experimental pilot study.

Setting: Rehabilitation Center at Ramathibodi Hospital, Mahidol University, Thailand.

Subjects: Thirteen participants (10 males and 3 females) with subacute to chronic UE paresis due to central nervous system lesion.

Methods: Each subject received one session of 12 minutes rPMS equally distributed over six hemiparetic shoulder-arm muscles (supraspinatus, infraspinatus, deltoid, biceps, triceps and pectoralis major). The train of stimulation was delivered to the affected arm with a figure eight coil at approximately 120% intensity of motor threshold at 20 Hz frequency in pulses of 4 seconds on alternating with 4 seconds of rest. Motor functions were assessed with upper extremity Fugl-Meyer motor (UE-FMA) scale, modified Ashworth Scale (MAS), and arm reach test (ART) before and then again 5 minutes after the stimulation. Patients with UE-FMA score of 16 or lower and those with score more than 16 were classified as more-severe and less-severe respectively. Statistical analysis was made comparing the difference between before and after of UE-FMA score, MAS, and ART of each group.

Results: The mean (SD) of UE-FMA score before and after rPMS stimulation were 21.6 (10.5) and 23.3 (8.9), respectively. Wilcoxon matched-pairs test confirmed that the results reached statistical significance (p = 0.018). The median (Q1-Q3) UE-FMA score before and after the stimulation in more-severe paresis group were 12.5 (9.3 to 13.3) and 16.0 (11.8 to 17.3), respectively. Wilcoxon matched-pairs test confirmed significant between group statistical difference (p = 0.027). The median (Q1-Q3) of UE-FMA score of the less-severe group before and after stimulation were 32.0 (24.0 to 35.0) and 32.0 (25.0 to 35.0), respectively. This difference has not reached significant level (p = 0.317). Analysis of the MAS and the ART, however, did not show any significances between groups.

Conclusion: The rPMS over six hemiparetic shoulder-arm muscles could result in immediate improvement of motor function in patients with severe upper extremity paresis, but not spasticity or arm and reach test.

Keywords: magnetic stimulation, hemiparesis, upper extremity

Introduction

Arm paresis is a common problem, but currently available treatments are not always satisfactory. Impaired upper extremity motor function and spasticity are two of the most common problems due to central nervous system pathologies. These lead to limited activities daily living (ADLs), increased pain symptom and poor quality of life.[1,2] Severe upper extremity paresis is also one factor indicating poor prognosis for motor recovery in stroke patients.[2] Even though there are many therapeutic interventions for rehabilitation of hemiparetic upper extremity, the recovery of upper extremity after severe stroke is in general less than satisfactory. Available supporting evidence for non-pharmacological treatments for this population were not strong.[1,3-5]

Repetitive peripheral magnetic stimulation (rPMS) to extremities is a novel therapy technique and may offer a new hope for better recovery as evidence were shown to improve motor recovery and to reduce spasticity.[3,6-8] Unlike direct electrical stimulation, magnetic pulses from rPMS could induce electrical current flow in deep neuromuscular tissues without stimulating the cutaneous nerve and receptors.[9,10] For this reason, it is possible to induce strong muscular contraction painlessly.[6,10] During alternating cycles of muscle contraction and relaxation numerous proprioceptive sensory receptors such as the muscle spindles, Golgi tendon organs, and other mechanoreceptors in the muscular and connective tissues can be strongly activated.[6,11] In addition to that, rPMS could also directly generate action potentials in the afferent nerve fibers. These two mechanisms combined, could generate a massive flow of afferent to the central nervous system.[6]

Previous research has shown that rPMS could modulate frontoparietal cortical motor control network activation,[12] in which increased unilateral activation of supplementary motor area (SMA), premotor cortex (PM), and parietal area (PA) during hand movement were observed.

However, existing evidence to support effectiveness of rPMS are still limited. Even though some studies had shown reduction of spasticity and/or improved motor control after rPMS in various groups of patients, the Cochrane review in 2019 demonstrated little evidence for the use of rPMS in stroke rehabilitation, probably due to small number of high quality research with more subjects, inhomogeneity of population, and differences of stimulation parameters among the rPMS studies might be another factor that diluted the positive outcome of treatment such as spasticity reduction or improvement of motor control.[9]

A new and different stimulation protocol may improve the effectiveness of rPMS. Recovery of motor function tends to follow stereotypical stages as described by Brunnstorm and Twitchell that recovery of proximal muscle tends to precede distal control.[13] In addition, flexor and extensor synergies precede movement of synergistic pattern.[13] Despite of these facts, all rPMS studies of hemiplegic patients, which were included in the Cochrane reviews delivered magnetic stimulation only to wrist and/or hand muscles[7,12,14] except for one single case experimental study which explored effects of EMG triggered rPMS to flexors and extensor muscles of the affected forearm and upper arm.[15] For these reasons, these authors postulated that a rPMS protocol which treated all major shoulder and arm muscle groups within one treatment session, might be a more effective way to induce upper extremity motor recovery of stroke patients.

Therefore, the primary objective of this study was to compare the immediate effect of a novel protocol of rPMS in patients with subacute to chronic hemiparesis. The secondary objective was to evaluate correlation between upper extremity Fugl-Meyer motor (UE-FMA) score improvement after rPMS, change of spasticity, and change of arm reach test.

Methods

The study was approved by the Ethics Committee on Human Rights Related to Research Involving Human Subjects, Faculty of Medicine Ramathibodi hospital, Mahidol University (approval number: 2014/324).

Participants

Patients with hemiparesis from various causes at the Department of Rehabilitation Medicine, Ramathibodi Hospital who gave informed consent and met the following inclusion-exclusion criteria.

Inclusion criteria

- Hemiparetic upper extremity of any severity due to a central nervous system lesion for at least 6 weeks prior to the study

- Stabilized neurological conditions for 6 weeks
- Stable medical conditions

Exclusion criteria

- On pacemaker or metal implanted devices around the stimulation area including chest region.
- History of seizure.
- Unstable fractures of the paretic upper extremity.
- Poor communication and co-operation.
- Received chemodenervation, or adjustment of anti-spastic medication dosage within 3 months prior to the stimulation date.
- Limited active shoulder motion due to pain.

The rPMS protocol

The participants were seated in a chair. They were instructed to relax and not try to initiate or imagine any specific movement of the limbs during the stimulation. A motor threshold of each muscle or the lowest magnetic pulse intensity which induced a visible muscle contraction was separately identified for supraspinatus, infraspinatus, deltoid, biceps brachii, triceps brachii and pectoralis major muscles. In order to save time and reduce unnecessary maneuvering of the stimulation coil, and to stimulate wide area of the muscles as possible, a specific stimulation protocol was designed. The stimulating magnetic coil was alternately placed and moved slowly along three paths over the affected arm (Figure 1).

The first sweeping path started from medial to lateral part of pectoralis major, and then continued distally along the biceps muscle group (Figure 1A). The second path ran along the length of supraspinatus muscles above the spine of scapular, from the medial part just lateral to the medial border of scapular toward the acromial process, and then further down along the length of either lateral, anterior, or posterior deltoid muscles until the insertion point of deltoid muscles on the humerus (Figure 1B). The last sweeping path went along infraspinatus muscles, starting from a point just lateral to the medial border of scapula toward the posterior axillary line, and then down along the triceps muscles toward the olecranon (Figure 1C).

Magnetic pulse was generated with a Neuro MS/D model Magnetic Stimulation which were manufactured by Neurosoft, Ivanovo, Russia 2020. A figure eight magnetic coil model FEC-02-100-C with liquid cooling system was used for all stimulations. The stimulation was delivered at 20 Hz frequency with 4 seconds pulse width and 4 second pause in between (Figure 2). Intensity of stimulation was arbitrarily set at 120% intensity of motor threshold level, to prevent loss of muscle contraction in case a slight change of coil orientation or distance from skin surface during stimulation. Since two muscles were stimulated within the same sweep, the motor threshold was determined from the higher value between each pair of muscles within each stimulation group.

The speed of stimulation coil movement was such that each sweep be completed within approximately 6 seconds. Once a sweep was completed, then the coil was placed back
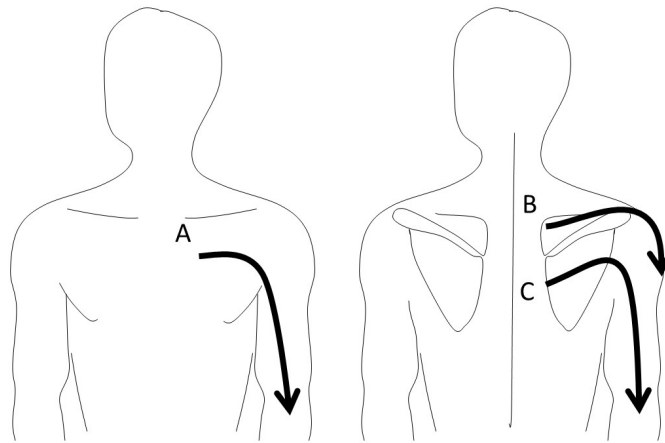
Figure 1. Three rPMS coil sweeping paths: A) pectoralis and biceps brachii, B) supraspinatus and deltoids, C) infraspinatus and triceps brachii

to restart next sweep without a pause. This continued for 4 minutes. Then the intensity was adjusted, and stimulation started again on the muscles of the next stimulation group. Each subject received 2,400 pulses in approximately 12 minutes treatment time (Figure 2).

Assessment tools

To assess the effect of rPMS, each patient underwent two assessments, before and immediately after the stimulation.

Assessment tools consisted of the motor part of upper extremity Fugl-Meyer Assessment (UE-FMA),[16,17] the modified Ashworth Scale (MAS),[18] and the arm reach test (ART). All assessments were done while the patients were in a seated position.

The FMA is a valid and reliable measurement of motor control impairment[16,17] which was designed according to brunnstorm's stage of motor recovery. For the purpose of this study, we only used scores from the UE-FMA, which has a highest possible maximum score of 66. A video recording of each patient during UE-FMA was scored by a blind assessor who was not aware which video was taken before or after therapy. Each of the 33 test items would be scored 0, 1, or 2 in the case that the patient was, completely not able to show the movement, partially do the movement, or show no impairment respectively. The total UE-FMA score was calculated from the sum of all test items.

The MAS is a valid and reliable tool for assessment of spasticity.[18,19] In order to test biceps muscle spasticity, the examiner, passively moves the elbow joint of the patient from fully flexed position to full extension over one second. Next, the elbow is brought from full extension to full flexion at the same speed to test for extensor spasticity. Scores of 0 up to 4 were given according to the well-known MAS scoring criteria.

The ART is a novel test invented by Wongphaet P and has been routinely used in the Rehabilitation Clinic at Ramathibodi Hospital as a tool for quick assessment of patient's ability to make upper extremity reaching motion free from primitive synergistic motor patterns. At the beginning of

the test, a helper passively places the patient's hand to the patient's own xiphoid process. A vertical support was then applied to the patient's forearm to keep the elbow and hand at the same height as the patient's xiphoid process, but no assistance or resistance were given to the movement in horizontal direction. The patient was then instructed to move his/her hand as far as possible forward without help from the opposite hand. The horizontal distance in millimeters or centimeters from the xiphoid process to the most distal part of the hand was then measured with a plastic measuring tape. All these three assessments were carried out twice by Sukhumvada T without any warm up. Average values were calculated for further analysis. The data was recorded at one decimal place.

Statistical analysis

The statistical analysis was performed using Minitab 19 and IBM SPSS Statistics Version 18. An alpha level of .05 was chosen for all analyses. Because of ordinal scale quality of the outcome parameters, the Wilcoxon matched-pairs test was used for the comparison of the UE-FMA and the MAS scores before versus after stimulation. Spearman's rank correlation coefficient was applied for the analysis of correlation between change of MAS score against change of UE-FMA. Kendall tau-b was applied to calculate correlation between change of ART score against change of UE-FMA.
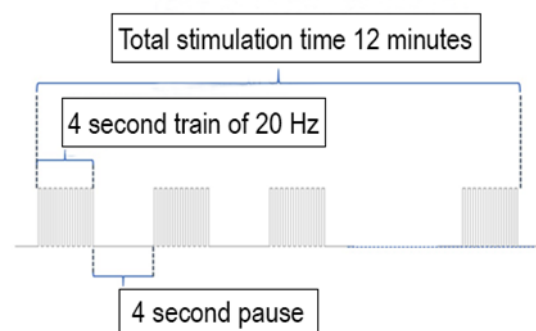

Figure 2. The rPMS stimulation pattern

These correlation coefficients of the whole patient group were calculated without separation between severity groups.

Results

Thirteen patients were included in the study. The clinical and baseline characteristics of the patients were demonstrated in Table 1.

Primary outcomes

The mean (SD) UE-FMA score before and after rPMS stimulation were 21.6 (10.5) and 23.3 (8.9), respectively. Wilcoxon matched-pairs test confirmed that the difference of UE-FMA between before and immediately after treatment reached statistical significance ($p = 0.018$). An additional subgroup analysis was done in order to see if severity of arm paresis impacted on responsiveness to therapy.

The median (Q1-Q3) UE-FMA score of the more-severe group, before and after the stimulation was 1.5 (9.3 to 13.3) and 16.0 (11.8 to 17.2), respectively. Wilcoxon matched-pairs test confirmed statistical significance at p value =0.027. On the other hand, the median (Q1-Q3) UE-FMA score of the less-severe group before and after stimulation was 32.0 (24.0 to 35.0) and 32.0 (25.0 to 35.0) respectively. This difference has not reached significant level ($p = 0.317$)

The increased UE-FMA score after stimulation was exclusively from the shoulder and arm motor section. No improvement of wrist, hand, or coordination sub section of FMA was seen in any subject. Individual UE-FMA scores of each subject before and after stimulation are shown in Figure 3.

The median (Q1-Q3) of MAS biceps and triceps muscles change in the more-severe group after stimulation was 0.0 (-0.6 to 0.0) and 0.3 (-0.6 to 1.1) and change of in the less-severe group was 0.0 (-5.0 to 5.0) and 0.0 (0.0 to 0.5). The mean (SD) of ART change of the more-severe and the less-severe groups after stimulation was 0.6 (5.9) cm and -1.1 (5.2) cm respectively. There was no statistically significant difference between all these parameters.

Table 1. Demographic data of all 13 participants

Age[1] (years)	54.23 (14)
Sex[2]	
Male	10 (77)
Female	3 (23)
Pathology	
Stroke	11 (85)
Traumatic brain injury	1 (8)
Progressive multifocal leukoencephalopathy	1 (8)
Seakness	
Right	5 (38)
Left	8 (62)

[1]Mean (SD), [2]number (%)

Secondary outcomes

The number of patients with unchanged, increased or decreased MAS of biceps and triceps muscles are shown in Table 2. Neither treatment nor severity group appeared to correlate with change of MAS. Spearman's correlation coefficient showed no significant correlation between UE-FMA change and MAS change of biceps and triceps muscles with correlation coefficient -0.77 ($p = 0.81$) and 0.31 ($p = 0.30$), respectively.

The difference of ART score showed no significant correlation against change of UE-FMA of the whole group at coefficient = 0.07 ($p = 0.77$). This lack of correlation can be observed from the scatter plot in Figure 4.

Table 2. Numbers of patients with changes in modified Ashworth Scale (MAS) scores of biceps and triceps muscles after stimulation

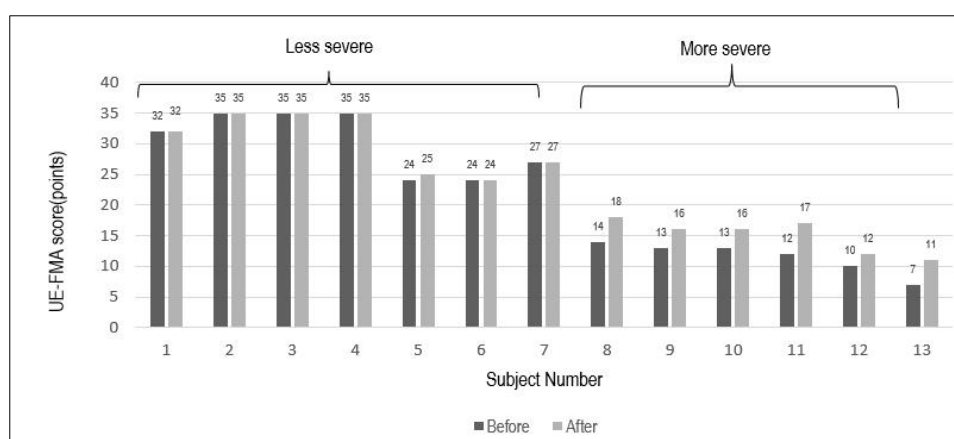|	MAS change (before-after)		
	Decrease (n)	Same (n)	Increase (n)
Biceps brachii			
Less severe[7]	3	2	2
More severe[6]	0	4	2
Triceps brachii			
Less severe[7]	2	4	1
More severe[6]	3	1	2

Figure 3. Individual UE-FMA scores of each subject before and after stimulation sorted according to initial FMA scores with the more severely affected cases to the right side.
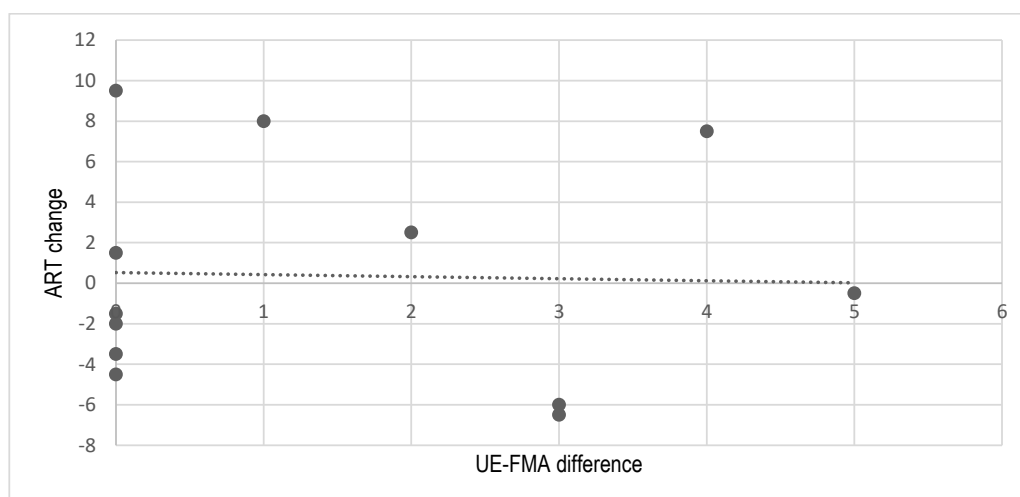
Figure 4. Scatter plot between ART changes versus differences of UE-FMA after stimulation

Discussion

Intensive and variable neural afferent signals, which resulted from this unique protocol of proximal upper extremity rPMS, as described in this research, has a potential to be an effective facilitator of motor recovery. This is the first rPMS study in hemiparetics, which specifically targets proximal upper extremity muscles. The target of rPMS in this study involved not only biceps and triceps muscles like many other previous studies, but also larger numbers of proximal muscles such as pectoralis major, supraspinatus and infraspinatus muscles which were not typical targets of previous studies[7,11,12,14] Movement of magnetic coil during treatment is another important factor because it increased areas of muscle tissues being stimulated. High intensity and variability of afferent input generated through such a stimulation technique is likely much greater than in other studies which stimulated only one or two distal muscle groups without moving the magnetic coil. This could possibly explain the immediate improvement of UE-FMA scores after rPMS in the current study.

Despite the improved UE-FMA score, we have found neither improvement of MAS nor ART. This finding is compatible with a previous study, which showed no change of neurophysiological markers of spasticity such as H-reflex and F-wave and Achilles tendon reflex after rPMS.[8] We speculate that improvement of FMA and spasticity after rPMS may indeed be independent from each other.

Both UE-FMA and ART are measurements of motor impairments. However, these measure different aspects of upper extremity functions. The ART measures only the ability to reach the arm forward away from the chest, which is considered a movement not within the primitive motor synergy pattern. On the other hand, the UE-FMA measures all types of motor patterns. Therefore, the lack of improvement in ART score, despite the improved UE-FMA, suggests that the improvement was likely due to increased ability to move within the primitive motor synergy pattern. Patients gained higher UE-FMA score after rPMS, because they could make bigger and more complete flexor synergy and extensor synergy pattern after rPMS. None of them showed increased selective single joint motor control ability.

So, why did more severely hemiparetic patients respond better to rPMS to proximal muscles than the less severe patients? Motor evoked response to cortical TMS studies has demonstrated that most, if not all of the hemiparetic patients such as the more severe group in this study, sustained a total loss of corticospinal tract on the affected side.[21-24] It is well known that this structure is essential for recovery of meaningful hand functions and perhaps as well as an ability to perform segmented control of a single joint motion.[23,25] All the observed increase of UE-FMA score after rPMS in this study were exclusively from the change of proximal part, (shoulder and arm) motor score. Therefore, the better recovery of UE-FMA scores in the more severe group as found here suggests that the improved function after rPMS may not depend on corticospinal integrity.

In this study we classified patients by their severity according to findings of a study of Woytowicz et al. which identified four distinctive subgroups among 247 subjects with chronic stroke who share a common level of deficit severity and a common residual motor pattern.[20] The FM score range of the groups were: severe (0-15), severe-moderate (6-34), moderate-mild (35-53), and mild (54-66). When such 4-group classification was used, no overlapping of severity group which was assigned by cluster analysis and severity group which was assigned according to UE-FMA score cut points were observed. To avoid confusion with the more commonly used three group classification, in which patients were separated into mild, moderate and severe according to their UE-FMA scores, the patients in this study were divided into two groups based on the pre-stimulation Fugl-Meyer scores. Those with score equal or more than 16, and those with score less than 16 were classified as less-severe and more-severe, respectively[20]

Even without active motor training, sensory stimulation alone can induce long term potentiation (LTP) of the neuron in the central nervous system.[26] Beauliu has proposed that the massive repetitive non-nociceptive proprioceptive afferent from movement related sensors could possibly facilitate greater activation of existing motor related neuronal circuits in recovering stroke patients.[6] We therefore, hypothesized that increased activation of the non-affected hemisphere[26] and/or subcortical motor centers[26-28] are potential contributors to motor recovery of proximal UE motor control in patients with severe UE paresis in this study. This difference of responsiveness to rPMS between the two severity groups, may explain the mixed results of previous rPMS studies in which analysis were not made separately for patients with different severity of arm paresis.[3]

With limited number of subjects, only imprecise estimation of effect can be expected. For example, a false-positive or overestimation of association can be produced.[29] Therefore, firm conclusions cannot be made. To confirm the finding of this small study with no control group, a future prospective randomized controlled trial with adequate number of subjects is needed. Such study should be designed to avoid mixture of different diagnosis and severity of arm paresis among the subjects. A longer treatment and follow up period should also be considered, to study the long-term effects of rPMS in a group of patients with a more homogenous diagnosis e.g., stroke only population.

Conclusion

An immediate effect of rPMS on proximal muscle group could improve motor impairment of hemiparetic patients with more severe upper extremity paresis but not in the less severe group.

Disclosure

The authors declare no conflict of interest with any financial organization regarding the material discussed in the manuscript

Acknowledgement

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