

# The effect of repetitive bilateral arm training with rhythmic auditory cueing on motor performance and central motor changes in patients with chronic stroke

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## Objective

The aim of this study was to compare the effects of bilateral arm training with auditory cueing (BATRAC) versus control intervention on motor performance of the upper extremity (UE) and to explore the central neurophysiological mechanism underlying this effect in moderately impaired chronic stroke patients.

## Design

This was a randomized-controlled clinical trial.

## Materials and Methods

Overall, 76 chronic stroke patients (mean age = 50.2 ± 6.2 years), 6–67 months after the onset of the first stroke were enrolled. They received either BATRAC (with both UE trained simultaneously in symmetric and asymmetric patterns) or control intervention (unilateral therapeutic exercises for the paretic UE). Each session lasted for 1 h, scheduled as three sessions/week (on an alternate day) for 8 successive weeks. Outcome measures included the Fugl-Meyer motor performance test for the UE (FMUE) and percutaneous transcranial magnetic stimulation to elicit motor-evoked potential (MEP) in paretic abductor pollicis brevis muscle.

## Results

Group comparisons indicated a significantly better improvement in the MEP parameters (transcranial magnetic stimulation threshold, central motor conduction time, and MEP amplitude) in the BATRAC group. The FMUE scores increased in both groups, but there was no significant difference between groups in the FMUE scores.

## Conclusion

These findings recommend the use of BATRAC in chronic stroke patients not only to improve motor performance but also to induce central neurophysiological effects.

## Keywords:

auditory cueing, central plasticity, chronic stroke, repetitive bilateral arm training

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## Introduction

Upper extremity (UE) hemiparesis is the most common poststroke disability and its recovery is often limited. It has been reported that 30–66% of individuals with hemiparesis have poor arm function 6 months after stroke [1]. Nevertheless, traditional therapeutic intervention results in continued impairment in 50–95% of stroke patients [2]. However, there is evidence that a specific rehabilitation intervention can improve UE motor performance in chronic stroke survivors [3].

Systematic reviews of treatment interventions for the paretic UE suggest that participants benefit from exercise programs in which functional tasks are directly trained, with less benefit if the intervention is impairment focused [4]. Repetitive task practice combines elements of both the intensity of practice and functional relevance. Most daily living activities rely on bilateral arm use; thus, unilateral UE paresis affects the patients' ability to perform bimanual tasks. Therefore,

bilateral retraining is necessary. Bilateral arm training (BAT), which includes a number of different training techniques with the use of both UE to complete a task, has been used in treating stroke survivors at all levels of arm impairment with a positive overall outcome [5]. The BAT with rhythmic auditory cueing (BATRAC) protocol uses a device that provides assistance to the paretic UE and provides both inphase (symmetrical) and antiphase (asymmetrical) movement training accompanied by rhythmic auditory cueing [3,6–9]. BATRAC is based on motor learning principles including repetition, feedback, and goal setting with the aim of overcoming learned nonuse and relative inactivity [10,11]. It includes the use of the nonparetic UE as a fundamental component of the training, on the basis of interlimb coupling theory, where the two UE act to form a neurofunctional unit [12].

Uncontrolled studies with BATRAC showed functional improvement [3], and two controlled studies suggested cortical activation associated with improved

UE function after BATRAC [6,7]. However, there are inconsistent findings across bilateral movement studies [5,13]. Although several studies [3,6,14,15] showed benefits of BAT in improving movement performance after stroke, some other researches [16–19] failed to show these benefits. Besides, the overall findings of the Whitall *et al.* [3] study suggested that BATRAC might be a better approach than conventional rehabilitation to improve UE motor impairment and enhance motor control. However, it involved no control group for comparison, and thus failed to provide compelling evidence to support this suggestion.

This study aimed to investigate the efficacy of BATRAC versus a unilateral UE rehabilitation program (UUPERP), as a control intervention (CI), on both UE motor performance and motor-evoked potential (MEP) changes in moderately impaired chronic stroke patients.

## Materials and Methods

### Design

This was a randomized pretreatment and post-treatment control group study.

### Participants

Participants were recruited for screening and 76 patients were enrolled according to the following criteria: (a) first ever-unilateral cortical or subcortical ischemic stroke of more than 6 months duration; (b) the ability to follow two-step commands (i.e. to follow simple instructions); (c) no previous experience with BATRAC; and (d) moderate UE impairment [Fugl-Meyer [20] UE (FMUE) motor performance scores between 26 and 50] [21]. The study was carried out on moderately impaired stroke patients who would have the potential to use the arm as a stabilizer or as a functional assist [21]. Thus, these patients would be able to participate in BATRAC and most probably would have obtainable MEP.

### Exclusion criteria

Patients with cerebellar or brainstem involvement, symptomatic heart disease, uncontrolled hypertension (>180/100 mmHg), significant orthopedic or painful UE disorder, severe pulmonary disease, excessive spasticity in the affected arm (Modified Ashworth Scale [22] score >2 in any UE joint), history of other neurological disease and/or emotional disorders (as these may preclude the UE function), those who participated in a rehabilitation program during the last 3 months before participation in the study as well as patients with contraindication to transcranial magnetic stimulation, for example seizures, pacemaker,

and metallic implant at the head or neck were excluded from the study.

Among the patients recruited, there were 39 men and 37 women; their mean age was  $60.73 \pm 5.38$  years and their stroke duration was 6–67 months (mean =  $33.06 \pm 20.84$  months). Patients were randomized through a computer-generated randomization code to receive either BATRAC (group I,  $n = 40$  patients) or UUPERP (group II,  $n = 36$  patients). All patients were blinded to the study hypothesis. All patients signed written informed consent forms to participate in the study, which was approved by Faculty of Medicine — Alexandria University Local Ethical Committee.

### Outcome measures

Assessment was performed immediately before intervention (baseline assessment) and immediately after completion of the 8-week intervention program (BATRAC or UUPERP). The first author enrolled patients and provided both treatment interventions. Measurements were performed by the second author who was blinded to patients' grouping. These included the following.

#### *Functional assessment*

The FMUE [20] motor performance scale (33 items, maximal score = 66) was used. Each item is rated on a three-point ordinal scale (0 = cannot perform, 1 = performs partially, and 2 = performs fully). A higher FMUE score indicates less motor impairment. Test–retest reliability, inter-rater reliability, and validity have already been established in stroke patients [23].

#### *Neurophysiological evaluation*

This was done using percutaneous transcranial magnetic stimulation of the corresponding cortical motor upper limb area to record MEP. MEPs were recorded from the affected paretic abductor pollicis brevis (APB) muscle using surface recording electrodes connected to a conventional electrophysiological apparatus (Nihon Kohden; Neuropack 2, Tokyo, Japan). The filter was set to 3–30 KHz. Gain was varied according to the MEP amplitude. Time base was set at 5 ms/division. Magnetic stimulation was performed using a Magstim 200 single pulse stimulator (Magstim Company, Whitland, UK), equipped with a high-power 90 mm circular coil, that generated 2 T maximum field intensity. The testing protocol was carried out according to the International Federation of Clinical Neurophysiology criteria for magnetic stimulation of the brain [24]. MEP was considered unobtainable if 10 successive discharges failed to elicit a response from the APB muscle

at the maximum output (100%) intensity. Resting threshold intensity (%), MEP maximum peak to peak amplitude (mV), and shortest MEP cortical latency in milliseconds were recorded. Central motor conduction time was calculated for APB muscle by subtracting peripheral latency (PL) from the cortical latency after recording the F-wave and M-wave neurographically following median nerve supramaximal stimulation at the wrist according to the following formula:  $PL (ms) = [\text{minimal F-wave latency (ms)} + \text{motor distal latency (ms)} - 1] / 2$ , where 1 is the estimated turnaround time (in ms) of the antidromic volley at the anterior horn cell [25]. The amplitude of MEP was expressed as the ratio of the M-wave amplitude recorded from the APB muscle to cancel the effect of muscle bulk on the MEP amplitude.

### Interventional training protocols

Both groups participated in an 8-week training protocol. Patients in both groups received three training sessions (each of 1 h duration) per week for 8 successive weeks. Thus, each patient received 24 h of training. If a session was missed during any given week, an extra session was added to the following week or at the end of the 8 weeks. At least 24 h elapsed between each two consecutive training sessions.

#### Group I (BATRAC group)

During BATRAC [26], participants were seated comfortably at a table in front of the training apparatus, which consisted of two independent T-bar handles attached to nearly frictionless linear tracks in the transverse plane (plane perpendicular to the patient). The handles were adjusted according to the shoulder width of each patient. The patient grasped the handles or the affected hand was strapped to the corresponding T-bar handle if the patient was unable to grasp the handle independently. If necessary, antigravity arm support was provided to avoid an improper arm position during the training. Participants completed 5 min of training with the arms moving symmetrically (inphase) by pushing the handles away from the body by both hands and then pulling the handles toward the body by both hands in time to an auditory stimulus. This was followed by 10 min of rest. Then, training was continued for another 5 min with the arms moving asymmetrically (antiphase), pushing one handle away from the body by one hand and pulling the other handle toward the body by the other hand in time with an auditory cueing. This was followed by 10 min of rest. Auditory cueing was set at the patient's preferred speed; this was established at the first session by asking the patient to assume a comfortable speed that he/she could continue for 5 min (frequencies ranged from

0.25 to 1.0/s). Alternate inphase and antiphase training blocks were repeated, achieving a total of 20 min of active BATRAC (which was completed in about 1 h for each participant). Participants were instructed to produce the forward and backward motions actively and to reach as far as they could with their paretic arm throughout the training period.

#### Group II (UUERP group)

This group received unilateral therapeutic exercises for the paretic UE. Training was based on neurodevelopmental principles. It included assisted range of motion exercises, strengthening exercises, and fine motor tasks practice [27]. Training was interrupted by a period of rest similar to that in group I. Thus, training was equivalent in intensity and duration to BATRAC training.

### Statistical analysis

The change in FMUE scores and MEP parameters in each group was calculated and used in data analyses. The Wilcoxon signed rank test was used to test the pre-post training effect within each group. Comparison between the two studied groups was carried out using the Mann-Whitney test. All analyses were carried out using the software package SPSS 17.0 Inc., Chicago, Illinois, USA. Significant difference was considered if the *P* value was less than 0.05.

## Results

All participants completed the study without dropouts. The baseline characteristics of the participants are shown in Table 1. There was no significant difference between groups in age, sex, duration of stroke, side affected (left/right), or preintervention FMUE scores. Also, there was no significant difference between groups in the baseline MEP parameters (Table 1).

**Table 1 Demographic and preintervention clinical characteristics of the participants in the two groups studied**

	Mean ± SD		<i>P</i>
	Group I ( <i>n</i> = 40)	Group II ( <i>n</i> = 36)	
Age (years)	61.4 ± 5.52	62.7 ± 3.1	0.36
Sex (men/women)	21/19	19/17	0.43
Stroke duration (months)	31.5 ± 21.6	35.6 ± 19.5	0.12
Stroke side (right/left)	17/23	15/21	0.08
FMUE score	40.5 ± 6.2	38.5 ± 6.1	0.31
MEP resting threshold (%)	85.7 ± 11.5	83.4 ± 16.1	0.35
CMCT (ms)	12.0 ± 2.4	10.7 ± 2.3	0.77
MEP amplitude ratio	0.09 ± 0.11	0.13 ± 0.12	0.10

CMCT, central motor conduction time; FMUE, Fugl-Meyer motor performance test for the upper extremity; MEP, motor-evoked potential.

### Changes in FMUE scores

On intragroup comparison, the postintervention FMUE scores were significantly higher than the preintervention scores (Table 2). However, intergroup FMUL changes were not significantly different. The FMUE change ranged from -1 to +13 ( $2.45 \pm 2.62$ ) in group I and from -4 to +15 ( $3.30 \pm 4.33$ ) in group II.

### The changes in MEP parameters

The changes in MEP parameters were significantly better in group I than group II; a significant postintervention increase in MEP amplitude and a significant decrease in MEP threshold and central motor conduction time were found in group II (Table 2).

## Discussion

This study showed that: 8 weeks of BATRAC is not superior to unilateral therapeutic exercises (CI) in improving FMUL scores as both interventional modalities improved the paretic UE motor performance without any significant intergroup difference. However, only 8 weeks of BATRAC intervention induced significant changes in MEP parameters, suggesting better cortical reorganization and/or increased central excitability following BATRAC.

Luft *et al.* [6] reported improvement in the FMUE in six out of nine stroke patients who had undergone BATRAC when compared with discrete movement training, which was correlated with an increase in contralesional sensorimotor cortex activation as documented by functional MRI [28]. No single pattern of central nervous system change is observed during recovery; rather, the results for upper limb function and pattern of neuroplasticity seemed to depend on the type of training intervention [29]. Our findings support the differential neuroplastic processes resulting from the two different training programs.

Through an interlimb coupling effect, the beneficial effects of BATRAC on UE impairment appeared to be mediated by an increase in

bihemispheric — mainly contralesional — activation of the premotor cortex, recruitment of the ipsilateral corticospinal pathways, and normalization of intrahemispheric and interhemispheric inhibitory mechanisms of the ipsilesional and contralesional hemispheres [6,16,26,30–32]. Supramarginal gyrus was found to be one of the brain regions where changes in brain activation correlated with improved arm function after BATRAC [30]. The supramarginal gyrus may be involved in attention [33]. Activation changes in this region during BATRAC may be related to the participant paying more attention while moving the paretic UE, causing an additional facilitation in the affected hemisphere and positive after effects for reducing the motor impairment of the affected UE [5,9,30]. Besides, synchronized movement to a beat in BATRAC might produce a generalized increase in cortical excitability, not exclusive to the cortical areas associated with the muscle being trained [34]. The increased cortical excitability during rhythmic movement may result in longer-term improvement in synaptic efficacy in the motor cortex and may possibly lead to the use of dependent plasticity. These neural changes provide optimal conditions for learning a motor task [3,7,35], whereas CI seemed to be associated with smaller increments in brain activation; distributed among different brain regions. Therefore, despite similar improvements in arm performance, CI appeared to use adaptations that are outside the brain or not measured by MEP. These differences may be a result of the different circuitry used in bilateral and unilateral arm movement [3,7].

In this study, the lack of a significant intergroup difference in motor performance gain is inconsistent in part with some previous studies. It was reported that stroke patients achieved greater gains in FMUE scores following BAT than following unilateral training [3,14]. However, in some other studies, BAT has not been shown to be better than other training approaches [6,17]. The lack of a significant intergroup difference (between BAT and unilateral training intervention) can be attributed to the small sample size, degree of initial impairment, time since stroke onset, or intensity of treatment [6,17,36–38]. To overcome these

**Table 2 Preintervention and postintervention outcome measurements in the two groups studied**

	Group I ( <i>n</i> = 40) (mean ± SD)			Group II ( <i>n</i> = 36) (mean ± SD)			
	Preintervention	Postintervention	<i>P</i> <sub>1</sub>	Preintervention	Postintervention	<i>P</i> <sub>2</sub>	<i>P</i> <sub>3</sub>
FMUE score	40.5 ± 6.2	42.4 ± 7.4	0.001*	38.5 ± 6.1	41.4 ± 6.4	0.003*	0.93
MEP resting threshold (%)	85.7 ± 11.5	79.7 ± 12.3	0.001*	83.4 ± 16.1	82.8 ± 15.1	0.10	0.001*
CMCT (ms)	12.0 ± 2.4	10.9 ± 2.6	0.003*	10.7 ± 2.3	10.6 ± 1.1	0.10	0.001*
MEP amplitude ratio	0.09 ± 0.11	0.14 ± 0.11	0.001*	0.13 ± 0.12	0.13 ± 0.15	0.16	0.001*

CMCT, central motor conduction time; FMUE, Fugl-Meyer motor performance test for the upper extremity; MEP, motor-evoked potential. *P*<sub>1</sub>, probability (preintervention to postintervention comparison in group I); *P*<sub>2</sub>, probability (preintervention to postintervention comparison in group II); *P*<sub>3</sub>, probability (postintervention change in group I vs. group II). \**P* ≤ 0.05, significant.

limitations, a large sample and an intense long training protocol (8 weeks) were used for both groups in this study. Also, there was no significant difference between groups in this study in the degree of initial impairment and stroke duration. The lack of a significant difference in motor performance gain between groups in this study could probably be because of the fact that the patients studied had moderate UE impaired (FMUE scores = 26–50); thus, patients in both groups might had enough motor control to participate well in the training program irrespective of the modality. Summers *et al.* [38] found a significant improvement in a short-term bilateral versus unilateral training study carried out on stroke patients with mild impairment; our results also suggest a superior outcome with long-term BATRAC training than unilateral training for moderately impaired chronic stroke patients.

Among the limitations of the present study is the lack of follow-up data to address persistence of gains after BATRAC. A follow-up study is required to investigate this point. In order to predict recovery after BATRAC, future research may consider a larger patient sample who differ in severity of motor impairment not only to evaluate functional benefits but also to understand precisely which factors are associated with cortical reorganization following BATRAC (e.g. baseline motor performance level, stroke duration and training bilaterality, rhythmicity, or intensity).

## Conclusion

BATRAC is effective in improving motor performance in chronic stroke patients with moderate UE motor impairment. BATRAC can also induce reorganization in the motor cortex. These findings recommend using BATRAC in chronic stroke patients. Besides, BATRAC requires less interaction between the physiotherapist and the patient and might be relatively easier to translate into self-directed training in home.

## Acknowledgements

### Conflicts of interest

None declared.

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