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ORIGINAL REPORT

ELECTROMYOGRAPHIC BRIDGE FOR PROMOTING THE RECOVERY OF HAND MOVEMENTS IN SUBACUTE STROKE PATIENTS: A RANDOMIZED CONTROLLED TRIAL

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Objective: **The electromyographic bridge (EMGB) detects surface electromyographic signals from a non-paretic limb. It then generates electric pulse trains according to the electromyographic time domain features, which can be used to stimulate a paralysed or paretic limb in real time. This strategy can be used for the contralateral control of neuromuscular electrical stimulation (NMES) to improve motor function after stroke. The aim of this study was to compare the treatment effects of EMGB vs cyclic NMES on wrist and finger impairments in subacute stroke patients.**

Methods: **A total of 42 hemiplegic patients within 6 months of their cerebrovascular accidents were randomly assigned to 4-week treatments with EMGB or cyclic NMES. Each group underwent a standard rehabilitation programme and 10 sessions per week of hand training with EMGB or cyclic NMES. Outcome measures were: Brunnstrom stage, upper extremity components of the Fugl-Meyer Assessment, Motor Status Scale, voluntary surface electromyographic ratio and active range of motion of the wrist and finger joints.**

Results: **The EMGB group showed significantly greater improvements than the cyclic NMES group on the following measures: Brunnstrom stages for the hand, upper extremity – Fugl-Meyer Assessment, Motor Status Scale, and the voluntary surface electromyographic ratio of wrist and finger extensors. Eleven and 4 participants of the EMGB group who had no active wrist and finger movements, respectively, at the start of the treatment could perform measurable wrist and finger extensions after EMGB training. The corresponding numbers in the cyclic NMES group were only 4 and 1.**

Conclusion: **In the present group of subacute stroke patients, the results favour EMGB over cyclic NMES for augmenting the recovery of volitional wrist and finger motion.**

Key words: stroke; hemiplegia; neuromuscular electrical stimulation; electromyographic bridge; upper extremity rehabilitation.

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Stroke is a leading cause of disability, both in China and around the world (1). Upper extremity hemiplegia is the primary impairment underlying stroke-induced disabilities and 80% of stroke survivors have incomplete upper extremity function 3 months post-stroke (2, 3).

Neuromuscular electrical stimulation (NMES) has received increasing attention as a therapeutic option for post-stroke rehabilitation because it can improve voluntary motor control by strengthening muscles, reducing spasticity, decreasing pain, increasing range of motion and reorganizing damaged corticocerebral circuits after stroke (4). For the success of NMES therapy, it is vital that stimulation-induced movements are augmented with concurrent volitional effort (5, 6). New NMES strategies, including electromyography (EMG)-triggered NMES (7), proportional EMG-controlled NMES (8), and brain-machine interface (BMI)-controlled NMES (9) encourage repetitive, voluntary, and functional movement of impaired upper extremities. However, EMG-triggered or EMG-controlled NMES requires residual volitional movements to acquire control signals, and these approaches are thus not applicable to severely paralysed patients, especially during the early phase of rehabilitation post-stroke (<3 months post-stroke) (7, 8). The neurobiological mechanisms that probably underlie recovery during the initial weeks after stroke include cell genesis, functional plasticity, and structural adaptations, which have been characterized using animal models and, to a lesser extent, in studies of human subjects (10, 11). It has been shown that the most rapid recovery of volitional motor activation occurs during the first month after stroke. More gradual recovery continues for the next 2 months, but a motor recovery plateau was found in most stroke patients by 6 months post-stroke (12, 13). Therefore, NMES strategies that enable voluntary controlled movements during the early phase of motor rehabilitation are essential for exploiting acute neuroplasticity (3).

Contralaterally controlled functional electrical stimulation (CCFES) developed by Knuston et al. is an emerging development in sensor-controlled NMES (5). It uses the finger joint angle of the non-paretic hand to control the intensity of stimulation of the paretic hand. Because the patient can control the timing and degree

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of hand opening and utilize the rehabilitation mechanisms of bilateral symmetrical movement, CCFES has been shown to be more effective than cyclic NMES. The authors reported the largest treatment difference in maximum voluntary finger extension, with a 94% confidence interval favouring CCFES. However, no statistical significance was found due to the small sample size (CCFES: $n=9$, Control: $n=8$).

Recently, we reported a novel self-controlled NMES system called the electromyographic bridge (EMGB) (14, 15). Instead of a joint angle measured by the bend sensor, the surface EMG (sEMG) of the muscles on the non-paretic side is transformed to control the relevant stimulation pulse duration and frequency applied to the corresponding paralysed muscles. Therefore, the activation status of the controlling muscle can better mimic and further enhance the coupling of motor intention to motor response while performing simultaneous bimanual movements (14).

The aim of this randomized controlled trial (RCT) was to evaluate the effects of 4 weeks of EMGB training on the upper extremity impairment of subacute hemiplegic patients by comparing EMGB with cyclic NMES. Cyclic NMES was adopted as a control treatment to confirm the added value of controlling NMES with non-paretic EMG (5). Compared with Knutson's study, a larger number of participants was selected in order to increase the statistical power. This is the first RCT study of contralaterally controlled NMES in a Chinese stroke population.

METHODS

Participants

This study was approved by the Human Subjects Review Board of Southeast University. Participants were recruited from the inpatient stroke rehabilitation programme of ZhongDa Hospital affiliated with Southeast University (Nanjing, China). Each participant provided written informed consent prior to their eligibility assessment. Inclusion criteria were: (*i*) first haemorrhagic or non-haemorrhagic stroke 2 weeks to 6 months prior to the study; (*ii*) lesions located in the territory of the middle cerebral artery (MCA), including the subcortical regions of the corona radiata, internal capsule, and the basal ganglia (mainly the putamen and the globus pallidus, as well as the overlying cortex, diagnosed using either computed tomography (CT) or magnetic resonance imaging (MRI); (*iii*) a Brunnstrom score between stages I and IV for the upper extremities; (*iv*) ability to understand and follow simple verbal instructions; (*v*) visible hand opening in response to NMES; and (*vi*) ability to sit unsupported for 40 min. Exclusion criteria were: (*i*) severe heart, liver, kidney or infectious diseases; (*ii*) lesions in the cerebellum or brainstem; (*iii*) a history of other neurological diseases or psychiatric disorders; (*iv*) shoulder-hand syndrome; (*v*) uncompensated hemineglect; (*vi*) intramuscular botulinum toxin injections in any upper-extremity muscles within 3 months; (*vii*) severe cognitive disorders (Mini-Mental State Examination score ≤ 24) (16); or (*viii*) severe depression (Hamilton Rating Scale for Depression >24) (17).

Recruited patients were randomly assigned to either the EMGB or cyclic NMES groups using a computer-generated random number. All assessments were performed by the same therapist who was blinded to the treatment assignment. To avoid interfering with the regular rehabilitation programme, participants were enrolled at least one week before their rehabilitation treatment. A flow chart of the participant groups in the study is shown in Fig. 1. After inclusion, 42 patients completed the baseline tests. As seen in Fig. 1, 6 patients discontinued participation, and the data from 36 patients (18 EMGB, 18 cyclic NMES) who completed all of the study assessments were analysed.

Sample size

The required sample size was determined using the pooled estimate within-group standard deviation of Fugl-Meyer Assessment - upper extemities (UE-FMA) scores from the previous study by Knutson et al. (5). A power analysis indicated that a sample size of 13 patients for each group is required to detect a minimal clinical important difference of UE-FMA (10-point increase of UE-FMA) (18) with a probability (power) of 0.80 and $\alpha=0.05$ (type I error rate).

Neuromuscular electrical stimulation systems

For the EMGB group, a double-channel EMGB system was used to generate stimulation pulse trains with the MAV/NSS dual-coding algorithm (MAV/NSS Dual Coding (MNDC), MAV and NSS refer to mean absolute value and number of slope sign changes, respectively), which simultaneously modulated the stimulation pulse duration with MAV of sEMG and the pulse frequency with NSS of sEMG. In our previous studies with 8 healthy subjects, the MNDC algorithm reproduced voluntary muscle force with high fidelity and was more fatigue-resistant than the sEMG amplitude-modulated NMES methods (14). The sEMG signals were detected from the non-paretic limb over the extensor carpi ulnaris (ECU) for wrist extension and extensor digitorum communis (EDC) for finger extension using double differential Ag-AgCl electrodes. In the current version of the system, the modulation range of pulse duration and frequency

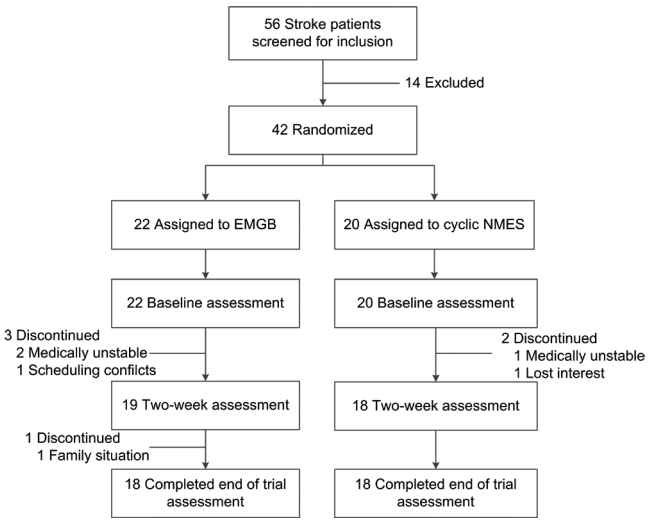

Fig. 1. Flow chart of study participants. EMGB: electromyographic bridge; NMES: neuromuscular electrical stimulation.

are 150–750 μs and 23–60 Hz, respectively, the maximum/minimum compliance voltage is ±34 V, and the maximum output peak current is up to 30 mA. Before each training session, the current amplitude was first determined and set to elicit maximum wrist extension or hand opening without pain using a stimulation train with a pulse duration of 750 μs and a frequency of 60 Hz. An asymmetrical, charge-balanced waveform was used to allow better control of electrochemical reactions at the electrode sites and to suppress undesirable muscle reactions (19).

For the cyclic NMES group, the ITO ES-420 system (ITO Co. Ltd, Tokyo, Japan) was used and a pre-programmed stimulation protocol was applied automatically. The stimulator delivered biphasic rectangular current pulses at a frequency of 50 Hz with a pulse duration of 500 μs. The stimulation current was set to elicit maximum wrist extension and hand opening in a range up to 40 mA. The time for ramping up and down was 1 s each, and a duty cycle of 5 s on and 5 s off was applied.

For both groups, gelled stimulation electrodes (4×4 cm^2) were fixed to the motor point of ECU of the paretic limb, with a reference electrode of the same size positioned approximately 4 cm from the stimulation electrode for wrist extension. For hand opening, a pair of stimulation electrodes (4×4 cm^2) was used to activate the EDC and the extensor pollicis longus (EPL) simultaneously, similar to the previous study by Keller (20). The proper positions of the electrodes were photographed for each participant to assist with consistent and repeatable positioning.

Interventions

Both groups participated in a 4-week training protocol. All patients received the same amount of standard treatments, including 40 min physical therapy and 40 min occupational therapy for 5 days each week. In addition, participants in each group received 2 sessions of EMGB or cyclic NMES training for wrist extension and hand opening (finger extension). A training session consisted of 10 min of wrist extension training and 10 min of hand opening training separated by 5 min of rest. For the EMGB group, participants were asked to perform simultaneous bilateral movements with a duty cycle that included 5 s extension and 5 s relaxation under the guidance of a rhythmic sound cue generated by a metronome. Participants were also encouraged to gaze at the paretic hand and imagine generating equal forces bilaterally. For the cyclic NMES group, a similar routine of unilateral movements was elicited passively by pre-programmed NMES without sound cues or observing the paretic hand. A flow chart of a training session of the 2 groups is shown in Fig. 2a.

In this study, wrist extension and hand opening were separated during training for 2 reasons. First, most moderate or severe paresis exhibits abnormal flexor synergy patterns or hypertonia (21). Isolated extension of the wrist and finger movements may improve recovery of the lost fractionated movements (3). Secondly, during wrist extension, the stretched muscle spindle of the finger flexors enhances the stretch reflex that leads to greater

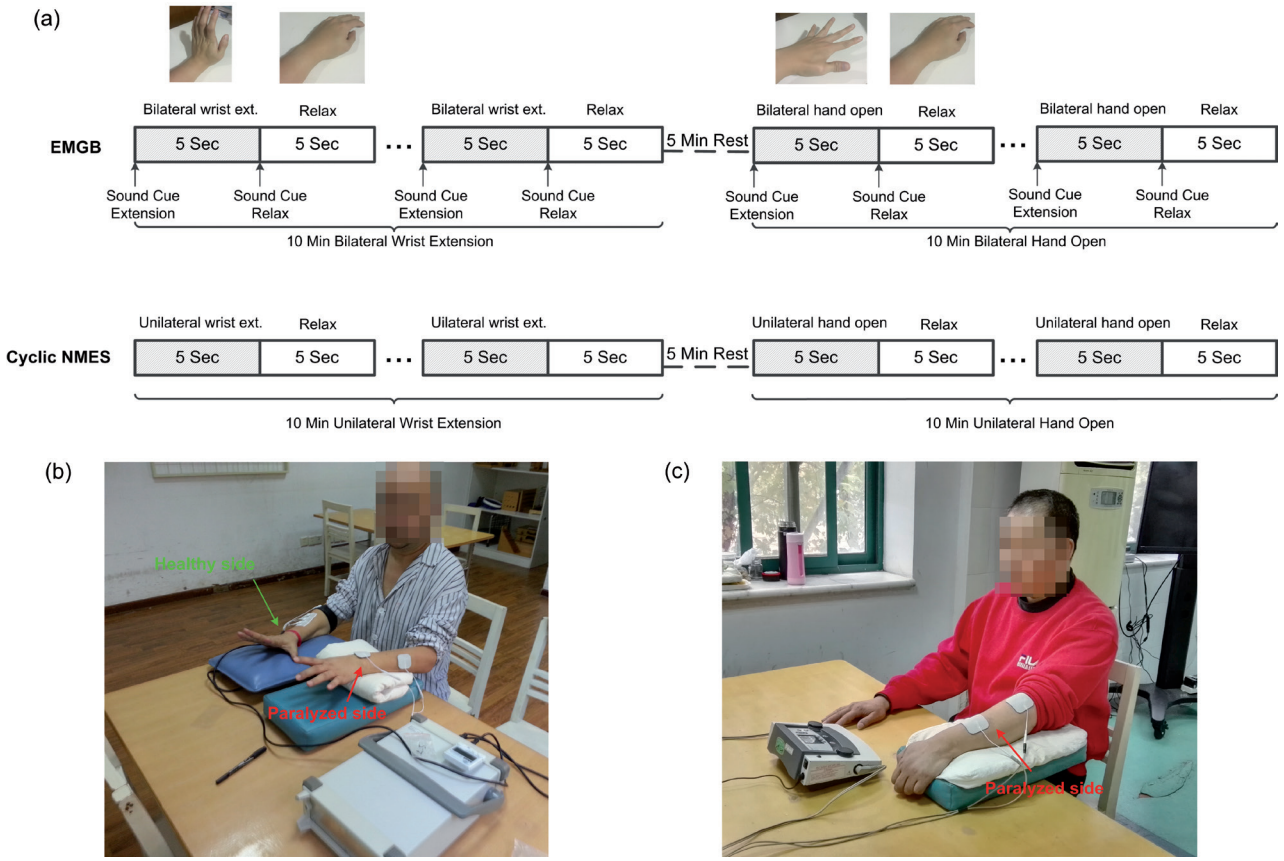

Fig. 2. (a) Flow chart of a training session and the experimental set-up for the 2 groups. The training procedure: (b) set-up for the electromyographic bridge (EMGB) group, and (c) set-up for the cyclic neuromuscular electrical stimulation (NMES) group.

activation of the finger flexors (22). Thus, full extension of the fingers becomes much more difficult during wrist extension. In the hand opening training, the participants were asked to relax their wrist on a cushion to facilitate sufficient finger extension. Fig. 2b and c show the set-up for the training tasks for the 2 groups, respectively.

Outcome measurement

All assessments were made at baseline, at the midpoint (2 weeks), and at the end of treatment (4 weeks) by a blinded therapist. The primary outcome measures included Brunnstrom's stages, the upper extremity components of the UE-FMA, and the motor status scale (MSS). The Brunnstrom stages qualitatively assessed motor recovery of hemiplegic arms and hands after stroke. The UE-FMA score is a reliable clinical assessment of upper extremity recovery of stroke survivors, which includes 18 items regarding shoulder/elbow/forearm, 5 items regarding wrists, 7 items regarding hands, and 3 items dealing with coordination (23). Although the MSS is based on the UE-FMA and the correlation between the scales is high, the MSS focuses on isolated movement regardless of synergy (24). The MSS was included in this study because the wrist and hand movements were separated during training and the MSS examines hand and wrist movement with more specificity than the UE-FMA.

In addition, the sEMG ratio of the ECU/EDC, and the active range of wrist/finger extension were assessed as secondary outcome measures. The Noraxon MyoSystem™ (Noraxon Inc., Scottsdale, AZ, USA) was used to detect the sEMG of ECU and EDC with single-differential sEMG electrodes. Subjects were seated while relaxed with the forearm on an arm brace in a neutral posture and attempted 5 times to achieve maximum wrist extension and finger extension for 3–5 s. Because the individual differences in volume conductor characteristics and the cross-talk generated by abnormal muscle synergy influence the root mean square (RMS) value of the agonist muscles, the sEMG ratio was calculated as shown in Equation [1] for wrist extension (wEMG) and in Equation [2] for finger extension (fEMG). This is a similar concept to that of the signal-to-noise ratio and the denominator of the RMS of signals detected in a neutral posture of the wrist joint reducing the differences in volume conduction properties associated with tissues under the skin and other peripheral factors within the pick-up volume of the electrodes (25).

$$\text{wEMG ratio} = \frac{RMS_{\text{wristExt}}}{RMS_{\text{neutral}}}$$

$$\text{fEMG ratio} = \frac{RMS_{\text{fingerExt}}}{RMS_{\text{neutral}}}$$

The mean active range of motion (AROM) (in °) of the wrist joint and finger joint (metacarpophalangeal (MPJ) and proximal interphalangeal (PIPJ)) were measured and calculated during the 5 maximum extension attempts with a goniometer (Baseline® Evaluation Instruments, Fabrication Enterprises Inc., Elmsford, NY, USA).

Statistical analysis

The data were analysed with SPSS statistics 19.0 software (Chicago, IL, USA). A 2-factor repeated measures analysis of variance using the baseline data as a covariate (ANCOVA), with a between-subject factor at 2 levels (2 groups) and a within-subject factor at 2 levels (time: 2 weeks, 4 weeks), was performed to compare the treatment effects of the 2 NMES methods. Vickers (26) found that the ANCOVA with a baseline score as a covariate had greater statistical power than analysing only the post-treatment scores or the percentage change from baseline when correlation between baseline and post-treatment scores is high, and this applies exactly to the present study. Differences with $p \leq 0.05$ were considered significant.

RESULTS

Of the 42 participants, 4 in the EMGB group and 2 in the cyclic NMES groups discontinued the study during the treatment phase for reasons unrelated to the study, such as recurrent stroke or scheduling conflicts (Fig. 1). Descriptive demographic data and baseline characteristics of the 36 patients ($n = 18$ for each group) who completed the study are shown in Table I. Because the EMGB group had a greater score than the cyclic NMES group on some variables, such as UE-FMA, wEMG ratio and fEMG ratio at baseline, a general linear model (GLM) concerning the interactions between the baseline score and the group effect was performed (between-subjects design: baseline+ group+ group*baseline+ intercept) and the test results of between-subjects effects of outcome measurements are shown in Table SI[1] of the supplementary data. Because no significance for these interactions was found for all 5 measurements, a simplified model (between-subjects design: baseline+ group+ intercept) was adopted.

During the treatments, all measurements but one (fEMG ratio; $p = 0.859$) improved significantly over time (Brunnstrom stage hand: $p < 0.001$; UE-FMA: $p < 0.001$; MSS: $p < 0.001$; wEMG ratio: $p < 0.001$). The

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Table I. Demographic characteristics and baseline measurements

Characteristic	EMGB ($n = 18$)	Cyclic NMES ($n = 18$)
Age, years, mean (SD)	50.9 (13.8)	56.9 (10.0)
Males, *n* (%)	13 (72.2)	12 (66.7)
Days post-stroke, mean (SD)	74 (55)	75 (49)
Paresis of dominant, *n* (%)	6 (33.3)	10 (55.5)
Right hemisphere lesion, *n* (%)	12 (66.7)	8 (44.4)
Ischaemic stroke, *n* (%)	9 (50.0)	11 (61.1)
Brunnstrom stage (UE), mean (SD)	2.9 (0.4)	2.8 (0.7)
Brunnstrom stage (hand), mean (SD)	2.4 (0.7)	2.2 (0.7)
UE-FMA, mean (SD)	20.8 (8.0)	15.2 (8.6)
MSS score, mean (SD)	18.1 (10.1)	13.8 (11.9)
Participants with voluntary wrist extension before treatment, *n* (%)	3 (16.7)	2 (11.1)
Participants with voluntary finger extension before treatment, *n* (%)	1 (5.6)	0 (0)
wEMG ratio, mean (SD)	4.5 (4.5)	1.7 (1.7)
fEMG ratio, mean (SD)	2.5 (2.2)	1.0 (0.0)

EMGB: electromyographic bridge; NMES: neuromuscular electrical stimulation; UE: upper extremity; SD: standard deviation; wEMG: wrist electromyography; fEMG: finger electromyography; MSS: motor status scale; UE-FMA: Upper Extemity - Fugl-Meyer Assessment.

Table II. Adjusted mean±standard error and 95% confidence interval (95% CI) for treatment effect

	EMGB ($n=18$)	Cyclic NMES ($n=18$)	Treatment effect[a], 95% CI, and p*
Brunnstrom stage (hand)			
Mean at baseline	2.3±0.1		
2 weeks	2.9±0.1	2.4±0.1	0.41* [0.08, 0.75]
4 weeks (EOT)	3.4±0.2	3.0±0.2	$p=0.018$
UE-FMA (maxi score: 66)			
Mean at baseline	18.0±1.4		
2 weeks	28.5±1.3	23.8±1.3	6.66** [1.76,11.57]
4 weeks (EOT)	39.1±2.0	30.4±2.0	$p=0.009$
MSS (maxi score: 82)			
Mean at baseline	15.9±1.8		
2 weeks	31.2±1.9	22.9±1.9	10.97** [4.43, 17.51]
4 weeks (EOT)	46.2±2.7	32.4±2.7	$p=0.002$
wEMG ratio			
Mean at baseline	3.1±0.6		
2 weeks	6.6±0.9	4.0±0.9	3.56* [0.01, 7.11]
4 weeks (EOT)	10.2±1.6	5.6±1.6	$p=0.049$
fEMG ratio			
Mean at baseline	1.8±0.3		
2 weeks	4.5±0.8	1.7±0.8	3.37* [0.15, 6.59]
4 weeks (EOT)	6.7±1.3	2.8±1.3	$p=0.041$

*$p\leq0.05$ and **$p\leq0.01$ for repeated measures analysis of covariance (ANCOVA). [a]Treatment effect is the mean of the group difference across the 2 post-treatment time-points, and the positive values of treatment effects favour EMGB.EMGB: electromyographic bridge; NMES: neuromuscular electrical stimulation; UE: upper extremity; EOT: end of treatment; wEMG: wrist electromyography; fEMG: finger electromyography; MSS: motor status scale; UE-FMA: Upper Extemity - Fugl-Meyer Assessment.

failure to improve over time for the fEMG ratio could be attributed to the minimal improvement in the cyclic NMES group. There were also significant time-by-group interactions for UE-FMA ($p=0.008$) and MSS ($p=0.004$). In contrast, time-by-group interactions were not significant for Brunnstrom stage of the hand ($p=0.391$), wEMG ratio ($p=0.125$), and fEMG ratio ($p=0.251$). To illustrate the different rehabilitation effects of the EMGB and cyclic NMES more clearly, the baseline-adjusted measurements of Brunnstrom stage, UE-FMA, MSS and the EMG ratio at 2 and 4 weeks using an ANCOVA analysis are shown in Table II. The differences in the estimated margin means between the groups across the 2 post-treatment time-points (Treatment Effect) were significant ($p\leq0.05$) for Brunnstrom stage (hand), UE-FMA, MSS and the EMG ratio of wrist extension and finger extension. Moreover, the raw outcome measures are plotted in Fig. 3 and shown in Table SII.

Fig. 4 shows the detailed changes in the wrist and finger joint AROM. In the EMGB group, the number of subjects who could perform measurable wrist extension before ($n=3$) increased to $n=14$ after training. Seven of the 14 subjects were able to extend their wrist over 60° after training. The number of subjects who could perform measurable finger extension before ($n=2$) increased to $n=7$ after training. Three of the 7 subjects were able to extend their fingers (>80°) after training. In comparison, the corresponding numbers in the cyclic NMES groups were 5 vs 1 (wrist) and 1 vs 0 (fingers), respectively.

DISCUSSION

This study showed that EMGB combined with the standardized rehabilitation programme during the early phase of stroke is more effective than a similar treatment using cyclic NMES. Significant improvements

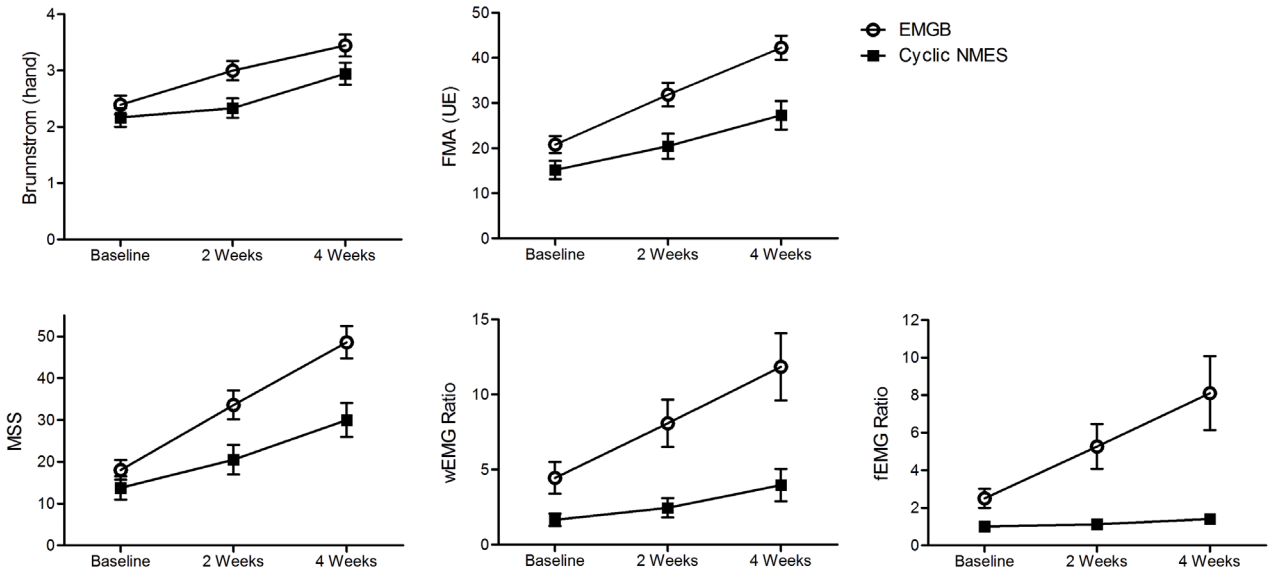

Fig. 3. Raw Brunnstrom, upper extremity components of the Fugl-Meyer Assessment (UE-FMA), motor status scale (MSS) and electromyography (EMG) ratio results. The results are shown as the mean and standard error. EOT: end of trial; wEMG: wrist electromyography; fEMG; finger electromyography.

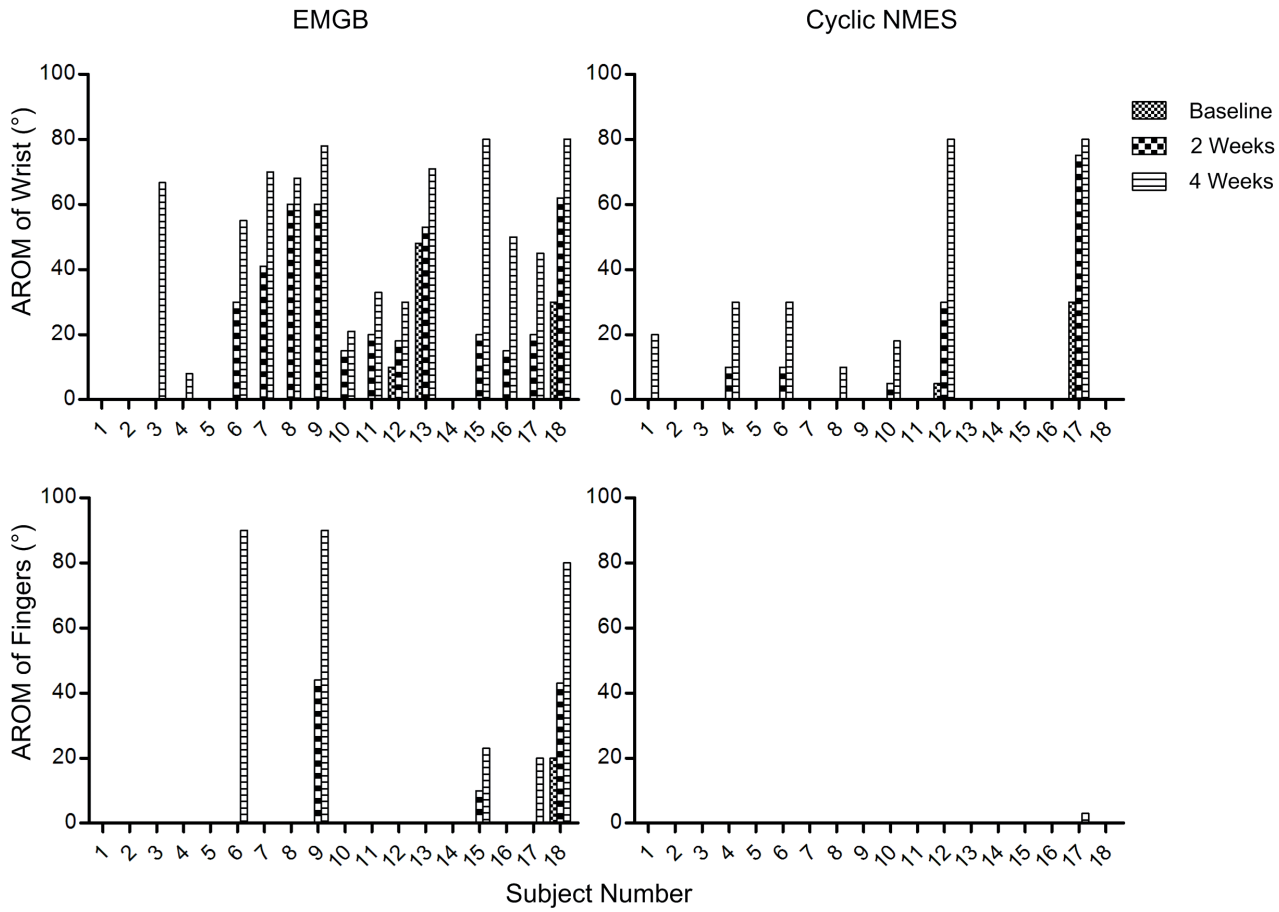

Fig. 4. Active range of motions (AROM) measures of the wrist and fingers for all 36 participants. EMGB: electromyographic bridge; NMES: neuromuscular electrical stimulation.

in most outcome measures support the hypothesis that the 4-week programme of EMGB enhanced motor recovery of the upper extremities, especially for hand impairment. The noted imbalance between groups, which was a result of the random assignment design of the study, dictated the treatment for the baseline scores as a covariance in the statistical analysis. The findings that 11 and 4 participants in the EMGB group, who had no active wrist and finger movements at the start of the treatment, could perform measurable wrist and finger extension, respectively, after EMGB training suggests the possibility of neuroplastic enhancement of the corticospinal motor network.

Attempts have been made to explain why EMGB training is effective. In the present study, similar amounts of non-invasive stimulations were used in both groups, which contributed to similar local effects, such as muscle strengthening or augmenting peripheral blood flow (27, 28). However, compared with cyclic NMES, the patient could control the timing and degree of movements during EMGB training, and this repetitive coupling of motor intention with motor response may induce synaptic remodelling and cortical reorganization (29, 30). In addition, faster resolution of hand impairment (indicated by the improved UE-FMA and MSS scores) may further enhance treatment effects of the more complex hand control training during routine therapy because the patients were more willing and more able to use their paretic hand actively (28).

The advantage of EMGB over unilateral control of NMES was extrapolated from bilateral arm training with a rhythmic auditory cue (BATRAC) by Luft et al (31). These authors showed a significant reorganization of corticocerebral circuits involving the contralesional motor cortex and ipsilesional cerebellum after BATRAC. In addition, disinhibition in bihemispheric motor cortices via transcallosal projections was found during BATRAC, which is beneficial for the reorganization of brain circuits. The EMGB training in the present study included the 2 major elements of BATRAC. First, practicing bilateral movements in synchrony with the EMGB may have facilitated transfer of volitional control from the non-paretic hand to the paretic hand, based on the knowledge that both hands are strongly linked as a coordinated unit in the brain (32, 33). The second important aspect of BATRAC, the rhythmic

repetitive auditory cue, was also used in EMGB training, and this has 3 advantages (33). First, the constant frequency ensures the same movement is repeated. Secondly, trying to match the sound with full extension of the wrist and fingers provides an attentional goal for the patients. Thirdly, receiving feedback has been shown to be fundamental for motor learning, which can be enhanced by the auditory cue and the sensation of electrical stimulation. Overall, EMGB training may take advantage of the rehabilitation mechanisms of BATRAC, which leads to a better recovery of volitional motor control compared with traditional cyclic NMES.

As another effective upper-extremity therapy for stroke patients, mirror therapy (MT) is also relevant to EMGB. MT can establish visual or mental feedback by superimposing the intact arm on the phantom limb via a mirror reflection (34). In the present study, patients in the EMGB group were told to gaze at their paretic hand and imagine generating equal forces bilaterally. Instead of a phantom hand in the mirror, participants observed the actual synchronized movements of the paretic hand. Currently, 2 mechanisms have been proposed to explain the effects of MT, which may also work during EMGB therapy. First, an fMRI study by Matthys et al. reported increasing activation within the superior temporal sulcus, which was linked to the mirror neurone system (MNS) during MT (35). This result supports the hypothesis that the effects of MT could be due to the activation of the MNS, since the observation of movements activates the motor areas in the affected hemisphere, which facilitates the excitability of the M1 area. Another theory suggests that the improvements induced by MT may depend on rebalancing the asymmetry of post-stroke hemispheric corticomotor excitability. A recent Magnetoencephalogram (MEG) study by Rossiter et al. found that MT could potentially aid stroke rehabilitation by normalizing an asymmetrical pattern of movement-related beta desynchronization in primary motor cortices during bilateral movement (36). When using EMGB for synchronized bimanual training, we would expect a similar or even stronger visual feedback that could induce the changes in cortex activity that are seen in MT. However, these hypotheses should be tested in future studies.

Study limitations

The present study has the following limitations:

- It focused on improving volitional control of wrist and finger extension. Although reducing these impairments are the fundamentals of hand function recovery, more attention should be paid in future studies to the overall hand function in activities of daily living (ADL). An ADL assessment, such as an arm motor abilities test (AMAT) (37) should be utilized and more complex movements, such as reaching and grasping, should be included in the EMGB training schedule, which may further take advantage of the self-control ability of EMGB to practice goal-oriented functional hand tasks (27).
- Patient drop-out and a relatively small sample size caused the heterogeneity of the baseline measurement. Adaptive randomization will be used in future studies to minimize group imbalances in key baseline measurements, such as severity of impairment (38).
- Treatment effects were limited because the treatment session was not long enough, due to the routine therapy schedule and limited hospital stay dictated by local medical insurance regulations. Studies of patients with severe motor loss of the upper extremity used 2–4 h of training over 12 weeks (39). Future EMGB training using extended treatment doses may be a better choice because the NMES treatment should be continued at a minimum until the patient achieves a threshold of upper extremity function (40).
- Follow-ups after treatment were not included in the present study due to financial limitations and scheduling conflicts for the therapist who conducted the assessments. The persistence of the treatment effects of EMGB therapy should be investigated with a longer follow-up period in the next RCT study.

Conclusion

After 4 weeks of treatment combining standardized therapy with EMGB, the group of moderately impaired subacute stroke patients in the current study showed better recovery of volitional hand movements compared with the control group treated with cyclic NMES and standardized therapy. However, the heterogeneity of the baseline measurements limits the generalization of the findings to clinical practice, especially as improvement in overall hand function was not investigated in the present study. Future studies should consider adaptive randomization to minimize group imbalances for key baseline measurements and include an assessment of ADL and follow-up retention data.

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