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High vs. Low Frequency Stimulation Effects on Fine Motor Control in Chronic Hemiplegia: A Pilot Study

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Abstract

Introduction—The optimal parameters of neuromuscular electrical stimulation (NMES) for recovery of hand function following stroke are not known. This clinical pilot study examined whether higher or lower frequencies are more effective for improving fine motor control of the hand in a chronic post-stroke population.

Methods—A one-month, 4x/week in-home regimen of either a high frequency (40Hz) or low frequency (20Hz) NMES program was applied to the hemiplegic thenar muscles of 16 persons with chronic stroke. Participants were identified a priori as having a low level of function (LF) or a high level of function (HF). Outcome measures of strength, dexterity, and endurance were measured before and after participation in the regimen.

Results—LF subjects showed no significant changes with either the high or the low frequency NMES regimen. HF subjects showed significant changes in strength, dexterity and endurance. Within this group, higher frequencies of stimulation yielded strength gains and increased motor activation; lower frequencies impacted dexterity and endurance.

Conclusions—The results suggest that higher frequencies of stimulation could be more effective in improving strength and motor activation properties and that lower frequencies may impact coordination and endurance changes; results also indicate that persons with a higher functional level of recovery may respond more favorably to NMES regimens, but further study with larger patient groups is warranted.

Keywords

cerebrovascular accident (CVA); dexterity; hand; hemiplegia; neuromuscular electrical stimulation; rehabilitation; stroke

Introduction

Hemiplegia is one of the most debilitating conditions following stroke, and the loss of motor function of the upper extremity is a significant burden that can impair or prevent

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independent living [1]. Six months after a stroke, half of all stroke survivors reported persistent hemiplegia and almost a third were institutionalized [2].

Until recently, much of the research dedicated to upper extremity rehabilitation following stroke has focused on those persons in the acute phase of recovery (1-6 months following onset) who tend to demonstrate quicker motor gains and a more rapid resolution of symptoms [3]. Rehabilitation therapies are usually implemented immediately following the stroke, but average inpatient rehabilitation stays typically last only 23.5 days [4]. To date, less scientific inquiry has been directed toward interventions specifically for persons living with stroke who are beyond 6 months since onset (chronic stroke) and have enduring motor deficits. By the sixth month, most therapies have ended and further intervention is usually not offered or available [5]. Current evidence regarding neuroplasticity of the cortex [6] indicates that post-stroke motor recovery can continue to occur months and even years following the onset of disability [7-8]. Few rehabilitation efforts have been identified as being effective for this chronic segment of the stroke survivor population, yet these are the individuals who are most in need of novel, innovative strategies that restore movement.

Current traditional treatment options for persons who demonstrate severe hand dysfunction associated with chronic stroke have shown limited effectiveness and have been largely inadequate: Constraint-induced movement therapy has proven quite effective for increasing movement in the affected upper extremity, but approximately 80% of stroke survivors are not eligible to participate due to the active movement needed (10° of wrist extension and 20° of finger extension [9]). Neurodevelopmental treatment (Bobath method), while popular with practicing therapists, has little empirical evidence to support its advantage over other interventions [10-11]. Even less evidence exists on superior patient outcomes when other traditional methods such as Brunnstrom treatment [12] or proprioceptive neuromuscular facilitation (PNF) are used [13]. Recently, neuroprosthetics and robotics have been developed that activate grasp and release or reaching abilities in the hemiplegic extremity [14-15] but these still remain largely cost-prohibitive for the consumer.

Neuromuscular electrical stimulation (NMES) is a modality used by therapists to enhance motor recovery following stroke. NMES has been effective in a variety of applications used in both acute and chronic post stroke recovery including improvement in arm and hand movement for function [16-17], reduction of spasticity [18-19], minimization of post stroke shoulder pain [20-21], and re-education of muscle for specific movement patterns [22-23]. Benefits in sensory awareness following NMES have been reported as well [24-26].

Because NMES can induce a high rate of muscular fatigue [27-28], constant low frequency stimulation is often used to produce a smooth contraction at low force levels [29]. Typical frequencies used in clinical applications for motor recovery following stroke range from 20-50 Hz [30]. Interestingly, lower frequencies of stimulation have been shown to impart a long-lasting depression of force output known as “low-frequency fatigue,” first described by Edwards, Hill, Jones and Merton [31]. These researchers observed that fatigued muscle stimulated with lower frequencies (10-30Hz) could exhibit a depression in force output lasting 24 hours or longer when the same effect was not seen at higher frequencies. Investigators are currently calling for more investigation into the optimal parameters of

NMES that will maximize force output while minimizing fatigue, thereby allowing successful performance of rehabilitation regimens [32-33].

The contribution of stimulation frequency in rehabilitation regimens has been previously studied. When NMES was delivered to the knee extensors of seven healthy participants and the influence of frequency, pulse width and amplitude on fatigue was studied, investigators found that fatigue was impacted most when *frequency* was modulated; varying other parameters had no appreciable effect on reducing fatigue [34]. We previously examined a group of chronic post stroke individuals when the hemiparetic thenar muscle group was stimulated with a 3-minute fatiguing protocol and found that stimulation programs that incorporated higher frequencies (40Hz) and varying pulse patterns were more effective in maximizing force output than 20Hz constant-pattern stimulation programs [35]. Based on these outcomes, we hypothesize that the use of higher frequencies of stimulation may be more effective in maximizing force output and improving fine motor skills following stroke. Additionally, keeping stimulation frequencies high, e.g., at approximately 40 Hz, would serve to maximize force production yet offset fatigue effects seen in 60 Hz and higher frequency applications.

The purpose of our pilot study was to compare the effects of using a high frequency NMES protocol (40 Hz) versus a low frequency NMES protocol (20 Hz) to improve fine motor control in the affected hands of a chronic stroke population. We chose to focus intervention on the thenar muscle group as these muscles contribute significantly to functional grip and release skills, pinch movements and prehensile digit patterns [36]. Outcome measures included changes in muscle strength, dexterity, and endurance of the affected hand following implementation of the 1-month in-home program. This information will be extremely useful in identifying effective clinical intervention strategies and determining the optimal frequencies of NMES that facilitate improved fine motor control in the chronic post-stroke population.

Methods

Participants

Sixteen persons with chronic stroke were recruited from the Austin, TX, vicinity through a local newspaper advertisement. Individuals were selected if the following criteria were met:

- Stroke onset of at least 6 months prior to start of study involvement
- Full discharge from any inpatient, outpatient, or home health therapies and not receiving any co-interventions to confound the effects of NMES during the period of study
- No significant cognitive impairment as documented by physician
- Upper limb paresis with at least 20° of wrist extension, 20° wrist flexion, 30° MCP extension, and active grasp/release intact in the affected extremity (this was necessary to perform the pre- and posttesting batteries and to position the extremity in the testing apparatus)

- Able to comprehend objectives of study and follow study-related directions

Participants were required to have been discharged from other therapies so as not to confound the results of the study. All research procedures were approved by the University of Texas (UT) Institutional Review Board (IRB) in accordance with the Declaration of the World Medical Association (www.wma.net); all subjects signed informed consent forms per protocol by the UT IRB.

Procedure

Participants were a priori designated as high functioning (HF) or low functioning (LF) as determined by their score on the upper extremity subsection of the Fugl-Meyer Motor Assessment (FMA). Because of the extreme variability of functional levels and functional performance present in chronic stroke survivors, researchers often separate participants with stroke into high and low functional groups in study designs. This is typically done a priori using scores from motor performance tests such as the Fugl-Meyer or other standard motor assessments [37, 38, 39]. The Fugl-Meyer is a reliable and valid assessment of movement and function used extensively in research and clinical applications [40]. Total possible score on this measure is 66. Participants scoring 60 or above were classified as high functioning (HF); those scoring below 60 were classified as low functioning (LF).

In the LF group, scores on the FMA averaged 45.62 ± 11.09; in the HF group, the average was 62.62 ± 1.76. Within each recovery level group, participants were randomly assigned to receive either the low frequency stimulation regimen (20 Hz) or the high frequency stimulation regimen (40 Hz); therefore, 4 subjects received the low frequency regimen and 4 subjects received the high frequency regimen within each group. Table 1 shows subject demographics, Fugl-Meyer scores, and stimulation frequency regimens administered to the two groups.

Participants also provided documentation of medical clearance from their personal physician verifying that they had no current medical condition that would preclude them from participation (e.g., presence of a pacemaker or lesions at the site of stimulation application). All participants provided informed consent and then attended an initial orientation/assessment session where they completed a short hand-use questionnaire to determine typical hand use.

Rehabilitation Training Program

All participants received supervised in-home training 4 times a week for 4 weeks. The duration of treatment was chosen based the typical length of an outpatient or inpatient therapy program. The eight participants in the low frequency regimen received NMES at 20Hz to the thenar muscle group for 40 minutes via a portable electrical stimulation unit (300PV Empi, Inc.). The frequency ramped up from 0 Hz to 20 Hz over a 1 second period, held at 20 Hz for 10 seconds, then ramped down to 0 Hz over a 1-second period. A rest period of 10 seconds followed. This pattern was repeated for the duration of the program. The eight participants in the high frequency regimen received NMES at 40Hz to the thenar muscle group for 20 minutes via the same portable electrical stimulation unit described above. This pattern ramped up from 0 Hz to 40 Hz over a 1 second period, held at 40 Hz for

5 seconds, then ramped down to 0 Hz over a 1-second period. A rest period of 5 seconds followed.

The high frequency regimen matched the low frequency regimen such that the total number of pulses delivered per session was the same for both groups. That is, for the low-frequency regimen, 200 pulses were delivered every 20 seconds for 40 minutes (10 seconds “on”, 10 seconds rest). This yielded a total of 24,000 pulses in total. For the high-frequency regimen, 200 pulses were delivered every 10 seconds for 20 minutes (5 seconds “on”, 5 seconds rest) also yielding a total of 24,000 pulses delivered.

For all participants, the current was adjusted to an appropriate intensity level at each session so as to elicit a tetanized contraction of 30% of the subjects' maximal voluntary contraction (MVC). As strength changes occurred over the treatment period, intensity of stimulation was increased to maintain a 30% MVC for each training session, thereby controlling the effects of muscle work load.

Instruments

Fine motor skill was measured using outcomes of manual dexterity, grip and pinch strength, and motor endurance. Pre and post-intervention measures included the Minnesota Manual Dexterity Test (MMDT; American Guidance Service, 1969) that measured manual dexterity; The MMDT measures the ability to grasp multiple 3 cm discs from indentations on the main test board and place the discs accordingly in an identical test board positioned directly below the upper test board (placing test). The test is performed in standing, with the boards on a tabletop, and is timed.

Grip and pinch strength dynamometry (Jamar, Inc.) were used to measure lateral, palmar, and tip pinch force as well as grip strength. Thumb adductor strength and motor endurance were measured using a customized upper extremity apparatus with transducers positioned to record force output; electromyography (EMG) during muscle contractions was also recorded to measure motor activation. Participants sat in a high-back armless chair with their affected arm placed in a pre-fabricated metal splint (North Coast Medical Progress elbow hinge splint, NC25658) that stabilized the elbow in 100° of flexion, the forearm in pronation and the thumb abducted and extended against the force transducer. The custom-designed force recording device (Mechanical Engineering Shop, University of Texas at Austin) consisted of a vertical surface that measured forces of thumb adduction (x), and a horizontal surface that measured forces of thumb extension (y). The contact area spanned from the thumb tip to midway between the IP and MCP joint. Using this device, the participants performed three maximal voluntary isometric contractions (MVCs) of thumb adduction for thumb strength measures, and a voluntary isometric contraction of 30% MVC of thumb adduction held until endurance limit as a measure of motor endurance. The resultant force, R, ($R=\sqrt{x^2+y^2}$) was calculated, displayed on the computer monitor, and recorded using commercially-available software (Spike 2, Version 5.14, Cambridge Electronics Design). The force output signal was amplified by 100 (Bridge 8 Amplifier System, Model 74030, World Precision Instruments) sampled at 1000 Hz and low-pass filtered at 1 kHz.

During the isometric contractions, the electromyographic (EMG) signal was recorded through two adhesive pre-gelled Ag/AgCl$^-$ bipolar surface electrodes 5mm in diameter (Danlee Medical Products, Inc. USA). The active electrode was placed over the thenar eminence slightly medial to the metacarpal-phalangeal joint of the thumb and the reference electrode, approximately 1cm medial to the active electrode, both targeting the thenar muscles. The EMG signal obtained from the thenar muscles during contractions was amplified by 100 (Coulbourn Instruments Isolated Bioamplifier with Bandpass Filter, Model V75-04), high-pass filtered above 8 Hz, sampled at 2000 Hz, and digitally converted (Micro 1401 mkII 500kHz 16-bit Analog-Digital Converter with ADC 12 Expansion, Cambridge Electronics Design).

All data were recorded on computer and analyzed offline using Spike 2 for Windows (version 5) software package (Cambridge Electronic Design). All experimental procedures were repeated following the 4 week training program for post-intervention measures.

Statistical Analysis

A two-way mixed method analysis of variance (ANOVA) tests with factors of frequency (high frequency stimulation regimen or low frequency stimulation regimen) and time (repeated measure; pre or post-intervention) for each recovery condition. Outcome measures were strength (grip; lateral, palmar, and tip pinch; thumb adductor strength), dexterity (Minnesota Dexterity test scores), motor endurance, and RMS of thumb adductor MVC. Holm-Sidak tests were used for post hoc pairwise comparisons. An alpha level of 0.05 was used for all statistical tests and significance accepted when $p \leq 0.05$. Data are presented as means ± standard deviation.

Results

Strength

For grip strength changes in the LF group, there was no significant difference from baseline when high or low frequencies were used; however, for the HF group, the higher frequency regimen resulted in significantly greater gains in grip strength than the low frequency regimen (avg. grip strength change for low frequency regimen 100.75 ± 10.05 lbs. pre, 102.75 ± 13.72 lbs. post; high frequency regimen 54.50 ± 11.62 lbs. pre, 67.00 ± 17.57 lbs. post).

Prehensile strength measures included lateral, palmar, and tip pinches obtained with dynamometry and thumb adductor MVC strength obtained with equipment setup described above. Although there were no significant changes before and after intervention for either the LF or HF group when the palmar and tip pinches were considered, a notable difference was found in lateral pinch changes in the HF group. Those participants who received the high frequency regimen in this group demonstrated a statistically significant change following intervention when compared to those receiving the low frequency regimen (average lat pinch, low frequency, 20.00 ± 4.76 lbs. pre, 19.25 ± 3.77 lbs. post; average lateral pinch, high frequency, 14.25 ± 2.87 lbs. pre; 17.00 ± 2.45 lbs. post). No significant changes in thumb adductor MVC strength were observed in either the LF group or the HF group.

Dexterity

Dexterity scores as measured by scores on the timed Minnesota Dexterity Test (placing subtest) showed a change from pre-intervention to post-intervention for the HR group only; those who received the low frequency regimen showed a significantly greater reduction in time to perform the test after intervention than those who received the high frequency regimen (low frequency 4.07 ± 0.46 min. pre, 3.83 ± 0.42 min. post; high frequency, 3.27 ± 0.73 min. pre, 3.17 ± 0.69 min. post).

Endurance

The HR group again showed changes in thumb adduction motor endurance whereas the LF group did not. Endurance time in participants receiving the low frequency regimen was significantly greater after the regimen than in those receiving the high frequency regimen (low frequency pre, 452.50 ± 204.47 sec. pre, 619.50 ± 349.24 sec. post; high frequency, 281.37 ± 116.89 sec. pre, 236.50 ± 40.12 sec. post).

Motor Activation

The root mean square (RMS) of EMG amplitude is an indicator of muscle power or energy. For MVC thumb adduction, there were significant changes from pre- to posttesing in the HF group, but not in the LF group. The high frequency regimen within the HF group resulted in a greater increase in RMS of the EMG than in the low frequency group. Changes from pre to posttesing were as follows: low frequency, 0.23 ± 0.02 mV pre, 0.19 ± 0.03 mV post; high frequency, 0.18 ± 0.02 mV pre, 0.21 ± 0.03 mV post. See Table 2 for a summary of outcome measures.

Discussion

The purpose of this pilot study was to compare the changes in fine motor control in the affected hands of a chronic stroke population when a high frequency NMES protocol was implemented versus a low frequency protocol. Based on previous work within our laboratory, we hypothesized that the use of higher frequencies of stimulation would be more effective in maximizing force output and improving fine motor skills following stroke. Participants in the high function group (HF) showed significant improvement in many of the post-intervention measures; however, participants in the lower function group (LF) did not show meaningful differences on outcome measures. Within the high function group (HF), the data suggested that high frequency electrical stimulation regimens may facilitate changes in strength and motor activation and that lower frequency stimulation may enhance gains in dexterity and endurance.

Sensorimotor recovery is typically rapid in acute stroke [41], but less predictable in the chronic, lower functioning population such as those in our LR group; few effective interventions exist for these individuals [42]. Stroke sequelae such as severe sensory impairment and spatial neglect are related to longer lengths of hospital stay and usually coexist with lower overall functional levels [43]. Deficient sensation may also limit the effectiveness of NMES in persons with chronic stroke; in a recent study of 140 stroke survivors over a year post infarct, severe sensory impairment and spasticity were determined to be the primary factors for persisting lack of dexterity in the upper extremity [44].

Our work confirms results found by previous investigators demonstrating that strength can be facilitated through the use of higher stimulation frequencies. Shin et al. [45] employed electromyography (EMG)-triggered stimulation on 14 chronic post-stroke patients at 35 Hz over 10 weeks; persons in the stimulation group performed notably better than the control group on tasks of strength and dexterity and improvement in muscle activation properties were noticeable through EMG measures following the intervention. Additionally, increased activation areas and cortical representation were apparent through fMRI in the experimental group. Dean, Yates and Collins [46] found that higher frequencies of stimulation (80-100 Hz) used on the ankle plantarflexors could activate motorneurons in the spinal pool through a volley of impulses resulting in higher centrally-generated torque output. Therefore, higher frequencies of stimulation applied peripherally may have the ability to impact central structures, potentially reinforcing motor learning.

Participants in the HR group receiving low frequency stimulation improved their rate of manipulation on the Minnesota Dexterity Test. Other researchers showed that a low frequency stimulation program (1.7 Hz) delivered to the elbow and wrist extensors of 26 persons with stroke 5 days/week, 60 minutes/day for 3 months improved upper extremity motor function when compared to a control group; 23% of the treatment group showed increases specifically in hand and wrist function [47]. Similarly, a program of 20 Hz NMES was delivered to the adductor pollicis muscle of 30 post-stroke individuals 3 times daily for 8 weeks; these participants made gains in their ability to grasp and manipulate items [33].

Participants in the HR group receiving low frequency stimulation also improved motor endurance of the thenar muscle group more so than those receiving high frequency stimulation. A chronic stimulation program using a pulse rate of 30 Hz resulted in greater endurance in the quadriceps of paraplegics; however, when an even lower rate (16 Hz) was used, the amount of neuromuscular fatigue was significantly reduced [48]. Chronic low frequency stimulation has been suggested to modify the contractile property of muscle in animal models [49] as well as in human subjects [50] from fast-twitch to slow twitch. The mechanisms behind this transition have been identified as direct alteration of muscle proteins and isoforms within the filaments and decreases in protein levels within the T-tubules of the sarcoplasmic reticulum; this is said to occur as a result of the uniform and slowed stimulation of motor unit activity continually produced during the low frequency regimen [51].

Heightened sensory perception could also influence motor performance on the dexterity tests. Fingertip force coordination and gradation are skills modulated by sensory and haptic awareness, processes which have been repeatedly found to improve following training with NMES [26, 52]. The reduction in time to perform the Minnesota Dexterity Test seen in our participants following training could have resulted from improved brain organization, enhanced sensory awareness and/or changes in grip processes as well.

Individuals in the high frequency group showed a decrease in motor endurance in pre to post-intervention measures. The reason for this decrement in performance is unclear, although variability in motor unit firing rates and accompanying force variability have frequently been observed in older adults [53-54]. Kurillo, Bajd and Tercelj [55] also found older adults to have significantly greater variability in controlling a lateral pinch grip when compared to younger adults; however, a recent study now indicates that strength training of the wrist and hand may improve finger and pinch forces and decrease this variability often seen in older individuals [56].

Conclusions

The results of this pilot study begin to suggest that specific electrical stimulation frequencies selected for use in rehabilitation regimens may directly impact skills gained. Whereas clinical frequencies typically used for rehabilitation intervention are in the 20 to 50 Hz range [30], our outcomes indicate that higher frequencies of stimulation may prove to be more effective for improving hand strength in higher functioning chronic post-stroke individuals. Additionally, the results also suggest that lower frequency stimulation programs may have a greater impact on hand dexterity and endurance; however, additional work with larger patient groups and more comprehensive investigations are needed to statistically confirm this trend.

Limitations of our pilot study included the small number of participants; additional work with this population should expand these findings and incorporate larger numbers. Subjects were classified as high or low functioning based on Fugl-Meyer scores, therefore, age and time post stroke varied greatly and could have confounded the results. Because of the extreme variability in the motor presentation of post-stroke individuals, baseline pretesting scores on some measures showed differences between groups; further testing with larger patient groups and a wider variety of recovery levels and stimulation frequencies is recommended to reduce these confounders, improve test power, and capitalize on these initial findings. Gains achieved were not tested at a follow-up to determine if effects were lasting. This additional information would strengthen subsequent studies on this topic.

Our pilot investigation explored the possible benefits of high frequency NMES to enhance specific motor function in the hand when used with a chronic stroke population; this information will be extremely useful to begin to design effective therapeutic interventions for this population and enhance client outcomes.

Abbreviations

CVA	Cerebrovascular accident
NMES	neuromuscular electrical stimulation
MVC	maximal voluntary contraction

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Table 1

Participant demographics and characteristics

Subject	Age	Gender	TPS (mos.)	Dominant UE	Affected UE	Fugl-Meyer	Stimulation Regimen
Low Function Group (LF)							
1	73	M	41	R	R	32	Low Freq
2	74	M	247	L	L	43	Low Freq
3	73	M	33	L	L	45	Low Freq
4	76	M	52	R	L	58	Low Freq
5	65	M	180	R	R	34	High Freq
6	64	M	54	R	R	37	High Freq
7	65	M	93	R	L	58	High Freq
8	70	M	78	L	R	58	High Freq
High FunctionGroup (HF)							
9	58	M	120	L	R	59	Low Freq
10	58	M	108	R	R	64	Low Freq
11	79	M	11	R	R	64	Low Freq
12	65	M	20	R	L	64	Low Freq
13	47	F	7	R	R	60	High Freq
14	67	M	91	R	R	62	High Freq
15	60	F	27	R	R	63	High Freq
16	47	F	14	R	R	64	High Freq

TPS = Time post stroke; UE = Upper extremity.

Table 2

Optimal frequencies within the high function [HF] group for specific outcome measures studied. Low function [LF] group showed no significant changes when pre and post intervention measures were compared

Measure	**Frequency**	**Significance (P)**
Grip	High (40 Hz)	< 0.001[*]
Lateral Pinch	High (40 Hz)	0.04[*]
Palmar Pinch	High (40 Hz)	0.36
Tip Pinch	High (40 Hz)	0.08
Minnesota Dexterity	Low (20 Hz)	0.02[*]
Endurance	Low (20 Hz)	0.02[*]
MVC	High (40 Hz)	0.75
RMS	High (40 Hz)	0.02[*]

MVC - Maximal voluntary isometric contraction of thumb adduction; RMS - Root mean square of EMG during maximal voluntary isometric contraction of thumb adduction;

[*] significant at the alpha ≤ 0.05 level.