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Neurorehabil Neural Repair 2009 23: 67 originally published online 21 July 2008
DOI: 10.1177/1545968308317437

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Assisted Movement With Enhanced Sensation (AMES): Coupling Motor and Sensory to Remediate Motor Deficits in Chronic Stroke Patients

Paul Cordo, PhD, Helmi Lutsep, MD, Linda Cordo, BS, MSN, W. Geoffrey Wright, PhD, Timothy Cacciatore, PhD, and Rachel Skoss, PhD

Background. Conventional methods of rehabilitation in patients with chronic, severe motor impairments after stroke usually do not lessen paresis. **Objective.** A novel therapeutic approach (assisted movement with enhanced sensation [AMES]) was employed in a medical device phase I clinical trial to reduce paresis and spasticity and, thereby, to improve motor function. **Methods.** Twenty subjects more than 1 year poststroke with severe motor disability of the upper or lower extremity were studied. A robotic device cycled the ankle or the wrist and fingers at 5°/s through $\pm 17.5^\circ$ in flexion and extension while the subject assisted this motion. Feedback of the subject's active torque was displayed on a monitor. Simultaneously, 2 vibrators applied a 60 pps stimulus to the tendons of the lengthening muscles, alternating from flexors to extensors as the joint rotation reversed from extension to flexion, respectively. Subjects treated themselves at home for 30 min/day for 6 months. Every other day prior to treatment, the therapy device performed automated tests of strength and joint positioning. Functional testing was performed prior to enrollment, immediately after completing the protocol, and 6 months later. Functional tests included gait and weight distribution (lower extremity subjects only) and the Stroke Impact Scale. **Results.** Most subjects improved on most tests, and gains were sustained for 6 months in most subjects. No safety problems arose. **Conclusion.** The AMES strategy appears safe and possibly effective in patients with severe chronic impairments. The mechanism underlying these gains is likely to be multifactorial.

Keywords: Stroke; Vibration; Rehabilitation; Chronic; Movement

Paresis following stroke is defined as reduced or absent movement, yet many physiologically based factors may underlie the clinical findings. Among these factors is the inability to activate upper motoneurons on command or transmit the signals from upper motoneurons to the spinal motor nuclei, as well as complications such as spasticity, contracture, co-contractions, and muscle atrophy. Therapy following stroke may have to treat more than one of these factors to improve functional movement.

A common feature of these clinical factors is their dependence on somatosensation or, more specifically, proprioception. Coordinated activation of upper motoneurons depends in part on intact proprioception, as demonstrated by studies of deafferented patients.¹⁻³ Given the relationships between somatosensory deficits and motor disabilities,^{4,5} we hypothesized that, during rehabilitation, if voluntary muscle activity were coupled to enhanced sensation of motion, stronger connections might be formed between somatosensory neurons and functionally related motor output neurons in the cortex. For the sensorimotor system, "functional" implies an antagonistic

relationship, with motor activity from one side of a joint paired with the sensory input from the opposite side of the joint. We used tendon vibration to stimulate proprioceptive afferents⁶⁻⁹ in the lengthening muscles during voluntary contraction (ie, of the shortening muscles).

A robotic device was constructed to rotate the ankle or wrist and fingers while vibrating the tendons of the corresponding flexor and extensor muscles. The efficacy of assisted movement with enhanced sensation (AMES) as a treatment for spastic hemiplegia was assessed with strength and joint positioning tests as well as several clinically accepted tests of motor function. Safety and tolerability was based on the frequency of adverse events during ≈ 2000 hours of device usage by the subjects.

Methods

A total of 20 spastic hemiparetic individuals >1 year post-stroke (ages 31-69 years) were enrolled into the study after

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completing an informed consent procedure approved by the Oregon Health & Science University Institutional Review Board. Each subject was fitted to an AMES treatment device for the affected ankle or the wrist and fingers, and the device was then set up in the subject's home. Three subjects received both ankle and wrist and finger therapy devices, but not at the same time. Functional motor testing was conducted pretreatment, immediately posttreatment, and 6 months after treatment ended. In addition, the therapy device itself tested joint strength and position control every other day while the subject participated in the study.

Subjects

The principal investigator (PC) and the study coordinator (LC) screened each prospective subject to identify obvious characteristics that would preclude the individual's participation. Exclusion criteria considered at this stage consisted of stroke within last year, not the individual's first stroke, <18 or >75 years old, profound sensory loss from the limb, significant cognitive disability, and limb too large for the therapy device. The arm or leg of a prospective subject was also excluded from consideration if strength in the paretic limb exceeded 30% to 50% of contralateral strength or, conversely, if the individual could generate no active flexion and extension of the wrist and fingers or the ankle. Joint rigidity was not an exclusion criterion.

A total of 30 candidates were screened. Five candidates were excluded because of joint plegia, 3 because they were too high-level functioning, and 1 because of severe cognitive disability.

Subject enrollment followed a physical and neurological examination by the study physician (HL). Inclusion criteria included (1) sensory score on the NIH Stroke Scale (NIHSS) = 0 or 1, (2) motor score on NIHSS ≥ 1 , (3) total NIHSS ≤ 21 , (4) Rankin Disability score ≤ 3 , (5) no concurrent participation in another clinical trial, (6) no Botox in the last 5 months and none planned during this study, and (7) no concurrent unrelated health problems that could potentially interfere with the experimental treatment. If the examined individual met all criteria for inclusion, the study physician enrolled the subject into the study and informed the principal investigator whether to treat the subject's ankle and/or wrist and fingers. One subject was excluded at this stage due to rheumatoid arthritis. Table 1 lists descriptions of the subjects who completed the study. Three of these subjects were enrolled for both the upper and lower extremity.

Once enrolled, each subject was fitted for a therapy device (see Figure 1). Subjects enrolled for lower extremity treatment provided the investigators with an athletic shoe for the affected foot, and the shoe was attached to an aluminum plate that snapped into the therapy device. The most comfortable 35° range of joint movement for therapy was determined along with flexion and extension strength at the joint and the gain for the presentation of visual feedback of joint torque (ie, based on

strength). The subjects were then trained for 30 to 60 minutes to use the device, and the device was transported to their homes and set up for operation.

Therapy Device and Procedure

Nine therapy devices were constructed: 4 for either ankle (Figure 1A), 3 for the right hand (Figure 1B), and 2 for the left hand. The major components of each device were 2 tendon vibrators for the flexor and extensor tendons of the treated joint(s), a graphical interface (PC computer and screen) to present visual feedback and to provide device control, and a flexion–extension motion system (ie, motor and gear box). Motion was applied to the ankle by the ankle device and to the wrist and fingers (ie, wrist and metacarpophalangeal joint of all 4 fingers) by the hand device. The motions of the wrist and fingers were mechanically coupled. During therapy, the joint was ranged at 5°/s through a 35° arc.

The subject's only task during therapy was to assist the motion imposed by the device, that is, to exert flexion force on the device during imposed flexion and extension force on the device during imposed extension, such that the subject's force, minimal as it might be, was accompanied by a cyclical motion of $\pm 17.5^\circ$. The choice of $\pm 17.5^\circ$ was based on time and speed, providing sufficient time (7 s/half-cycle) for the subjects to recruit contraction in the paretic muscles and a slow enough speed (5°/s) to minimize recruitment of spasticity. A load cell, mounted between the gearbox and the limb, detected the active torque produced by the subject. The resulting active torque signal was displayed in real-time on the computer screen along with a torque target. For most of the therapy session, the flexion and extension torque targets were set at 40% of the subject's current maximum strength in the direction of motion. Feedback gains for flexion and extension were independently set and updated by the investigators as needed during the subject's 6-month treatment period. Six times during each 30-minute therapy session, the torque target increased from 40% to 80% of maximum for 1 minute 10 seconds (ie, 5 full flexion–extension cycles). On each half-cycle of joint motion, the subjects were instructed to hit the torque target and then to maintain a constant level of effort, even while their joint torque decreased due to the length–tension properties of muscle.¹⁰

At each reversal of movement direction, tendon vibration switched between the flexor and extensor tendons, always applying vibration to the lengthening tendon, that is, to the muscle antagonistic to the assisted joint motion. The vibration followed a pattern in which the rate of vibration spiked at 70 pps for 200 to 300 milliseconds and then dropped to 60 pps for the duration of the movement, mimicking the "initial burst" observed in muscle spindles in response to stretch.^{11,12} The vibrator probe applied a 2 to 3 mm peak-to-peak sinusoidal stimulus to the tendon on a background pressure of ≈ 1 to 2 N. If a subject had particularly sensitive skin, she/he wore a thin sock on the foot or sleeve on the forearm to decrease the friction between the Nylatron vibrator probes and the skin.

Table 1
Subject Demographics

Subject ID	Stroke Type	Stroke Location	Age at Enrollment	Years Poststroke	Usage
Upper extremity treatment					
2	I	Basal ganglia internal capsule	63	5.7	85.0
4	I	Insular, subinsular	42	4.9	40.2
5	I	Frontal, insular, putamen, external capsule, corona radiata	49	5.5	58.7
9 ^a	I	Frontal, temporal, parietal	33	2.4	75.9
11	I/H	Traumatic SAH-bifrontal, MCA	38	6.5	51.5
14	H	Lentiform, basal ganglia	56	10.2	65.0
16	I	Frontal, parietal	59	1.7	82.1
18	H	Post-sup, frontal, intraparenchymal	49	2.5	80.6
21 ^a	I	MCA, internal carotid artery	51	1.2	91.9
23 ^a	I	MCA	49	2.8	63.9
24	I	Basal ganglia	59	1.1	44.3
Average			49.8	4.0	67.2
Lower extremity treatment					
1	I	Post internal capsule	65	6.0	87.8
2	I	Basal ganglia, internal capsule	63	5.7	83.2
3	I	Anterior cerebral artery, MCA	45	1.9	48.0
6	I	Temp. mid-post parietal cortex	50	15.6	40.4
7	I	Frontal temp. and parietal cortex	75	12.7	95.7
10	I	Frontal temp. and parietal cortex	54	6.0	49.7
11	H/I	Traumatic SAH-bifrontal, MCA	38	6.5	76.8
12	I	Temp. parietal basal ganglia	58	2.0	59.1
15	H	Front-parietal, internal capsule, and basal ganglia	68	1.9	95.2
17	I	R MCA	55	2.3	57.0
18	I	Post-sup, frontal, intraparenchymal	49	2.5	66.1
22	I	Posterior limb internal capsule	74	5.8	79.3
Average			57.8	5.7	69.9

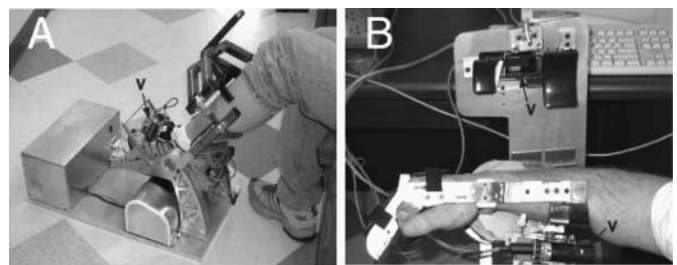
Abbreviations: SAH, subarachnoid hemorrhage; MCA, middle cerebral artery; I, ischemic; H, hemorrhagic

^aThese 3 subjects received electromyographic training during the treatment period and are not considered in the overall analysis of results.

Electromyographic (EMG) Training

Three subjects receiving therapy for the upper extremity could not generate any observable force in their wrist and finger extensors at the time of enrollment due to inadvertent co-contraction. As a consequence, the torque feedback presented during therapy was not useful for extension movements, and no improvement in extension strength and joint positioning was observed during the first weeks or months of therapy. To help these subjects resolve their co-contraction, each came to the laboratory for 3 to 5 sessions, 2 hours in duration, during which she/he received training with EMG feedback,^{13,14} while continuing to use the therapy device at home. Four pairs of surface EMG electrodes were adhered to the skin over the medial and radial aspects of the forearm to record EMG from the long finger flexors and extensors and from the flexor and extensor carpi radialis muscles. The raw EMG signals (amplification 5000×; bandpass filter 16-500 Hz) were displayed on a computer screen (Spike2 and μ 1401; Cambridge Electronic Devices, Cambridge, United Kingdom) while the experimenter

Figure 1
AMES Treatment Devices



Note: (A) A therapy device is shown for the ankle. (B) A device is shown for the wrist and fingers. Each "V" and arrow identifies a tendon vibrator.

requested the subject to produce isolated contractions of each of these 4 muscles, with and without concurrent passive manipulation of the relevant joints by the investigator. Passive manipulation consisted of assistive and resistive motion. As a

result of EMG training, 2 of the 3 subjects were able to reduce co-contraction of the finger and wrist flexors and extensors sufficiently to produce overt finger and wrist extension torque and, subsequently, to benefit from torque feedback during treatment with the therapy device. Because of the difference in treatment with these 3 upper extremity subjects, their data are treated separately from the main results of this article.

Testing

During each subject's 6-month treatment period, 2 tests were conducted every other day prior to the daily 30-minute therapy session. These tests were self-administered with the limb in the AMES device, using prompts from the graphical interface. The first test (strength test) measured the maximum voluntary torque produced by the subject in the flexion and extension directions. For subjects whose upper extremity was treated, the torque recorded was a composite of that produced by the finger and wrist muscles. For subjects whose lower extremity was treated, the torque recorded was from the ankle alone. During a strength test, the subject produced 3 maximum efforts in each direction, alternating between flexion and extension to control for fatigue. A 5-second rest period was provided between each maximum effort. During the strength test, the maximum torque achieved during a given effort was presented on the computer screen, in comparison to previous efforts during the ongoing test and to the subject's previous best effort since the beginning of the study. Joint torque was measured by a load cell that signaled ankle torque in the lower extremity device and a combination of wrist and finger torque in the upper extremity device.

The second test (joint positioning test) measured a composite of joint position control and active range of motion. During the joint positioning test, the ankle or hand positioning mechanism operated in a force-feedback mode with minimal resistance to movement. The subject was instructed to follow a graphically presented target by rotating the ankle or wrist and fingers in the therapy device through a 35° arc, with a staircase pattern of movement. Each direction of movement consisted of 6 equally spaced ramp-and-hold movements at a speed corresponding to joint rotation at 5°/s. Between each of these steps, joint position was held constant for 3 seconds. The range of motion employed in this test was identical to that used in the therapy. Projected on the graphical interface during the joint positioning test were a target window (ie, 2 red horizontal lines separated by the equivalent of 2°) and a single blue horizontal line, which indicated the subject's current joint position. To minimize spastic contractions induced by voluntary activation of the spastic muscles, the initial direction of motion was always dorsiflexion for the ankle or extension for the wrist and fingers. During the joint positioning test, the subject viewed an accumulating score on the computer monitor that incremented in real-time at a rate of 1 point for each contiguous 50-millisecond interval that the subject's joint was positioned inside the target.

Each subject was also tested for functional motor ability just prior to the beginning of the treatment period, immediately after the 6-month treatment period, and then again 6 months after the end of treatment. Most subjects were tested with the Stroke Impact Scale (SIS). Subjects receiving treatment for the lower extremity also participated in gait and weight distribution tests.

During the gait test, the subjects walked straight at a comfortable speed along a 5-meter path indicated on the floor by masking tape. During the pretreatment test, the subjects were allowed to use any assistive device (eg, walker, cane, ankle-foot orthosis) that enabled them to walk comfortably and securely. During the 2 subsequent testing sessions, the subject walked not only with the same assistive device (ie, for comparative purposes) but also without any devices that had become unnecessary as a result of the treatment. The subjects were instructed to walk at a "brisk," but comfortable rate. The relative motions of reflective markers adhered to the lower body were recorded by a video-based motion analysis system (Motion Analysis Corp, Santa Rosa, California), and these recordings were converted into measures of stride length, cadence, and ground speed. At least 3 gait trials (ie, up and back) were conducted for each subject in each testing session.

During the weight distribution test, the subject stood comfortably on 2 independent force plates while the weight supported by each leg was measured. These recordings were converted into an average measure of the left and right leg weight distributions. Two 10-second trials were conducted and averaged for each subject in each testing session.

The SIS questionnaire was also filled out 3 times by the subjects, but included only 5 of the 8 domains: Strength, Activities of Daily Living (ADL), Mobility, Hand, and Social.

Test data were not obtained or used from all subjects because (1) the test was added after the subject participated in the study, (2) the test could not be obtained at the appropriate time due to illness, (3) there were too few data points for that subject (<2 joint position control measurements/month), and (4) the load cell became uncalibrated during the treatment period. Table 2 shows how many subjects participated in each test.

Data Analysis

The data from subjects whose upper extremity was treated and that from subjects whose lower extremity was treated were analyzed separately.

Data from the SIS were quantified by averaging across subjects the normalized summed scores from each of the 5 domains.¹⁵ These data were compared among pretreatment, posttreatment, and 6-month follow-up testing sessions using analysis of variance with repeated measures.

Data from the gait test and weight distribution test for each subject were quantified by averaging the stride length, cadence, ground speed, and percentage weight supported by the paretic leg across multiple trials. These average measures were then compared between pretreatment and posttreatment and between

Table 2
Number of Limbs Tested

	Strength	Joint Position	SIS	Gait	Weight Distribution
Hand	8	7	5	NA	NA
Ankle	11	11	8	10	6

Abbreviations: SIS, Stroke Impact Scale; NA, not applicable.

pretreatment and follow-up (1-tailed paired *t* test) and between posttreatment and follow-up (2-tailed paired *t* test).

Data from the strength test were first quantified as peak torque, during each attempted maximal contraction in each direction, and averaging ($n = 3$) these peak values for flexion and extension from each test. Typically, subjects performed ≈ 60 strength tests during their 6-month participation in the study. To quantify the overall change in strength for a given subject, scores from the first 3 and last 3 tests were averaged and the difference determined. Second, the values from all strength tests were plotted versus the testing date, and depending on the shape of the resulting relationship, either an exponential or straight line was fit to the data points. In the case of exponential fits, the time taken to reach 90% of the asymptotic value of score was determined. A few plots could not be fit satisfactorily with either type of line, and were categorized as “no increase.” Data from the joint positioning test were treated essentially the same as the strength data, that is, determining the difference between the first 3 and last 3 scores and plotting exponential and linear regressions to the score as a function of time. Significant increases in strength and joint positioning were evaluated with repeated-measures analysis of variance. Correlation between the results of the strength test and joint positioning test was evaluated with the Pearson correlation coefficient. A significance level of $\alpha \leq .05$ was used as the criterion for a significant effect in all statistical tests.

Results

The average time poststroke for subjects receiving ankle treatment was 5.7 years, and the average time for subjects receiving wrist and fingers treatment was 4.0 years. Adequate data sets were not obtained from 5 enrolled subjects due to unrelated and prolonged illness ($n = 3$) or due to $<40\%$ compliance with the treatment regimen ($n = 2$), and these incomplete data sets were not included in the analysis. However, 2 of these excluded subjects later completed a full 6-month treatment with the other affected limb, and the latter data were included in the results.

Overall, the subjects were relatively compliant with the daily treatment protocol. During each treatment session, a computer attached to the therapy device registered the subject's usage of the device. If the duration of therapy was ≥ 15 minutes in any particular day, the subject was deemed compliant for that day. As shown in Table 1, the actual compliance with this protocol

was 67% for subjects using the upper extremity devices and 70% for those using the lower extremity devices.

Adverse Events

Over the course of the study, which involved ≈ 2000 hours of self-treatment by disabled subjects, we experienced one anticipated, nonserious adverse event in which the subject over treated himself (>3 h/day) for several days and developed a skin abrasion from one of the vibrator probes. After restructing the subject and removing the vibrator for 2 weeks to allow the lesion to heal, the subject continued his treatment without incident.

Strength

The subjects enrolled in the study were relatively weak. At the subjects' entry to the study, the average ankle plantarflexion strength was 8.6 ± 10.0 Nm and dorsiflexion strength was 11.6 ± 5.6 Nm ($n = 11$), which compares to an average in healthy elderly adults of 80 Nm and 42 Nm, respectively.¹⁶ In 2 subjects, ankle dorsiflexion strength was initially negative, that is, net torque during attempted dorsiflexion was in the plantarflexion direction. At the subjects' entry to the study, the average wrist and finger flexion strength was 5.5 ± 5.5 Nm and extension strength was 1.7 ± 3.5 Nm ($n = 8$). Similarly, 2 subjects produced a net flexion torque during attempted wrist and finger extension. In comparison, wrist strength in healthy adults is roughly 27 Nm in flexion (unpublished data) and, on average, 10 Nm in extension.¹⁷ In our study, we measured a combined finger and wrist torque, which would have been ≈ 5 to 10 Nm higher than that of the wrist alone (unpublished data). Over all subjects and joints tested, the average initial strength of subjects at enrollment ranged from $\approx 0\%$ to 50% of normal with an average of 10% to 25% of normal, depending on the joint.

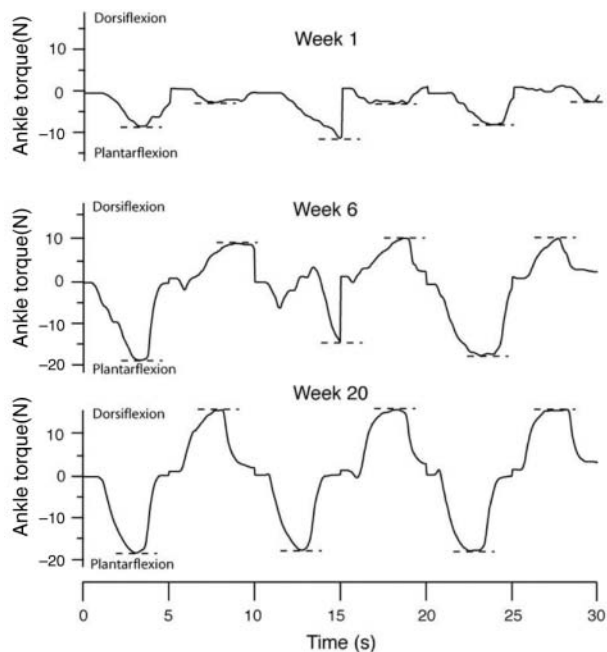
Strength increased $\geq 10\%$ in most subjects' ankles (8/11 in dorsiflexion and 10/11 in plantarflexion). In the hand, wrist and finger flexion strength improved $\geq 10\%$ in 7/8 subjects, and wrist and finger extension improved $\geq 10\%$ in 7/8 subjects (see Table 3). Torque recordings from 3 strength tests at different stages of the 6-month testing period are illustrated in Figure 2 for a representative spastic hemiplegic subject using a lower extremity therapy device. During the first week of therapy, the subject was relatively strong in plantarflexion (“P”), producing maxima of 8 to 12 Nm. However, during attempted dorsiflexion of the ankle (“D”), net torque was in

Table 3
Strength and Joint Positioning Tests

Type of Recovery	Waveform of Recoveries					
	Ankle (Number of SS)			Wrist and Fingers (Number of SS)		
	Flexion Strength	Extension Strength	Joint Position	Flexion Strength	Extension Strength	Joint Position
Exponential	5	7	10	5	4	5
Linear	3	3	1	2	3	2
No recovery	3	1	0	1	1	0
Percentage of subjects with $\geq 10\%$ improvement	73	91	100	88	88	100

Abbreviation: SS, stroke subject.

Figure 2
Improvement in Strength During AMES Treatment



the plantarflexion direction, suggesting that, during attempted dorsiflexion, this subject was inadvertently co-contracting the plantarflexor muscles. By the sixth week of therapy, plantarflexor strength had increased to 14 to 17 Nm, but more important, maximal dorsiflexion contractions produced dorsiflexion torque of ≈ 10 Nm. By the 20th week of therapy, plantarflexion strength increased an additional 1 to 2 Nm, but dorsiflexion strength had increased to 16 Nm. Therefore, in this subject, 6 months with the therapy device increased strength and reduced co-contraction.

Over the 6-month treatment period, the time course of strength increase most often followed a negative exponential

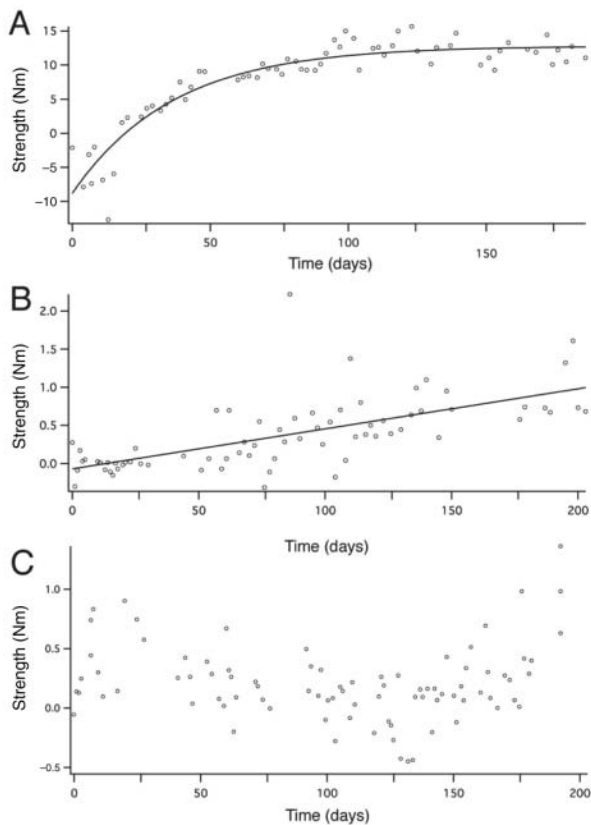
trajectory (ie, with a plateau), but other trajectories were also observed. A few subjects showed no strength increase, but conversely, other subjects showed no signs of a declining rate of strength improvement at the end of the 6-month treatment period. An example of each type of trajectory is shown in Figure 3A for flexion strength in the wrist and fingers, in Figure 3B for extension strength in the wrist and fingers, and in Figure 3C for dorsiflexion in the ankle. Table 3 summarizes the observed trajectories of strength change for all subjects, keeping in mind that each subject produced 2 trajectories, one for each direction of joint torque. There was no obvious tendency for subjects to produce similar trajectories in both directions of joint torque. For wrist and finger flexion and both directions at the ankle, strength trajectories were most often exponential in shape. The mean time to 90% of the projected asymptotic value was 73 days for ankle dorsiflexion, 83 days for ankle plantarflexion, and 111 days for wrist and finger flexion (Table 4). Projected asymptotic values could not be reliably determined for wrist and finger extension because the changes were small.

For each subject, strength change was quantified as the difference in average peak torque produced in the first 3 and last 3 strength tests. Average strength in the ankle increased by 3.7 Nm (31.8%) for dorsiflexion and by 7.9 Nm (91.9%) for plantarflexion. Average strength in the hand increased by 2.5 Nm (46.4%) in flexion and by 1.1 Nm (65.2%) in extension.

Strength and Co-contraction

Of the 11 subjects enrolled for upper extremity treatment, 7 could not produce any active torque in wrist and finger extension at enrollment (<0.1 Nm). Several of these subjects produced negative strength scores during their initial extension efforts, presumably due to flexor co-contraction. All enrolled subjects could voluntarily evoke some EMG activity in the wrist and finger extensors albeit, in a few subjects, only during attempted flexion. One additional subject, who began the trial with small, but measurable, finger/wrist extensor torque (0.76 Nm) was rendered

Figure 3
Time Course of Strength Recovery



Note: Three different patterns of strength recovery are illustrated for the wrist and fingers. (A) Recovery of flexion strength had a negative exponential trajectory. (B) Recovery of extension strength had a linear trajectory. (C) There was no recovery of extension strength. Data from 3 different subjects are shown.

incapable of generating extension torque by the end of treatment, presumably because of continued co-contraction with increasing flexor strength. To attempt to reduce co-contraction, 3 of these 7 subjects came to the laboratory for several EMG training sessions during the course of the 6-month treatment period. Because of this additional intervention, their data are not included in the overall analysis presented in this study. In these 3 subjects treated for the upper extremity, strength increased, on average, by 4.3 Nm (51%) in flexion and by -1.2 Nm in extension, although, of these 3 subjects, only 1 produced a negative score in extension, whereas the other 2 had small positive scores.

Strength and EMG data are shown in Figure 4 from 1 of the 2 subjects receiving EMG training who eventually produced a positive strength score in the extension direction. Initially, co-contraction occurred between extensor carpi radialis (Figure 4A, lower trace) and flexor carpi radialis (Figure 4A, upper trace) and between the finger flexors and extensors (not shown). During 4 attempted maximum contractions (Figure 4A) with the wrist and fingers—alternating between flexion and extension—the amplitude of wrist EMG decreased during attempted extension, but the ratio of flexion/extension muscle

activity appeared unaffected by the intended direction. This subject received EMG training at the end of 4 months of therapy, and Figure 4B shows the strength test results from this subject over 5 1/2 months of AMES treatment. Beginning with ≈ 0.5 Nm of flexion torque, this subject's flexor strength increased substantially over the treatment period with a negative exponential trajectory (solid trace). Extension strength, however, changed from 0 Nm to negative values (ie, net flexion torque) concurrently with the strengthening of the flexor muscles. Moreover, during AMES therapy, the subject was receiving no useful torque feedback during assisted movement in the extension direction. At the 4-month point of the treatment period, this subject received three 2-hour EMG training sessions (horizontal bar labeled "EMG" in Figure 4B) outside of the AMES device over a 2-week period, after which extension torque developed in the correct direction with continued treatment with the AMES device. One other subject who received EMG training responded in the manner described in Figure 4.

Joint Positioning Test

All subjects' performances on the joint positioning test improved during the 6-month treatment period. As with the strength test, a negative exponential was the most common trajectory for joint positioning test scores. Table 3 illustrates that of 18 subjects performing this test all showed clear improvement. For subjects with a negative exponential trajectory (15/18), the average time to 90% of the projected asymptotic value was 120 days for subjects treated for lower extremity impairment and 111 days for subjects treated for upper extremity impairment (Table 4). Comparing the difference between the first and last 3 joint positioning tests, the subjects treated for lower extremity paresis improved on average by 109%, and those treated for upper extremity paresis improved by 73%. The 3 subjects who were provided EMG training showed a comparable improvement in the joint positioning test score (77%).

Gains in strength and in joint position control were not significantly correlated. The Pearson correlation coefficient for flexion strength versus joint position control was $R = .08$, and the coefficient for extension strength versus joint position control was $R = .19$.

Gait and Weight Distribution Tests

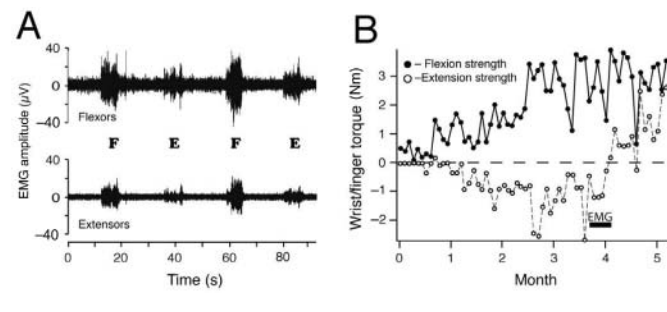
The gait and weight distribution of subjects treated for lower extremity paresis improved over the 6-month treatment period, and these gains were sustained for at least 6 months after the end of AMES treatment (Figure 5). Gait was quantified by ground velocity, cadence, and stride length and compared pretreatment and post-treatment when using the same assistive devices. On average (Figure 5A), ground velocity increased from 0.27 to 0.37 m/s, a 37% change ($P \leq .05$) and then again to 0.42 m/s during the 6 months posttreatment. Cadence increased from 0.44 to 0.50 strides/s, a 14% increase ($P \leq .05$) and then stabilized at that rate (ie, 0.51 strides/s). Stride length increased from

Table 4
Days to 90% Recovery (Exponential)

Ankle (Mean Days \pm SD)			Wrist and Hand (Mean Days \pm SD)		
Flexion Strength	Extension Strength	Joint Position	Flexion Strength	Extension Strength	Joint Position
73 (52)	83 (56)	120 (49)	101 (56)	NA	111 (26)

Abbreviations: SD, standard deviation; NA, not applicable.

Figure 4
Co-contraction in a Subject

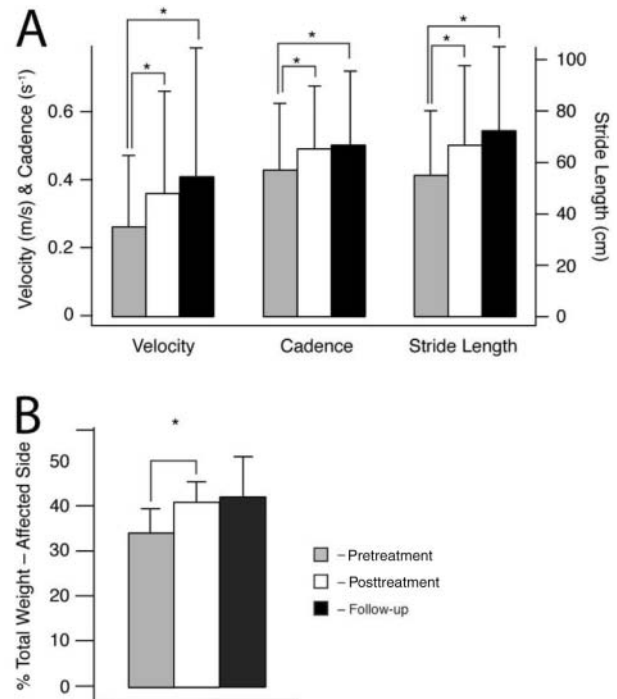


Note: (A) Finger flexor and extensor EMG activity shows co-contraction during both attempted flexion (“F”) and extension (“E”). (B) Time course of strength recovery shows a negative exponential recovery of flexor strength, but with increased flexion torque during attempted extension, presumably due to the combination of co-contraction and increased flexor strength. Three 2-hour sessions of EMG biofeedback at the 3 1/2 month point of treatment (black horizontal bar “EMG” in B) led to a reversal from negative to positive extensor strength.

55.1 to 66.8 cm, a 21% increase ($P \leq .05$) and then again to 72.3 cm during the 6 months posttreatment. Thus, for each parameter, the gains achieved during treatment were statistically significant, and these gains were at least sustained, if not improved, during the 6-month period following treatment. In several subjects, gait tests conducted posttreatment and at 6-month follow-up also included trials in which the subjects walked without one or more assistive devices used during the pretreatment evaluation. Five of the 12 subjects tested were able to walk securely with fewer assistive devices than originally used, 2 subjects eliminating a cane and 3 subjects eliminating an ankle-foot orthosis. In all 5 of these subjects, the gait parameter scores measured posttreatment while eschewing assistive devices were equal to or better than those obtained in the original gait evaluation with the assistive devices.

Similarly, average body weight distribution changed during AMES treatment (Figure 5B), shifting from a relatively asymmetric stance to one more closely approximating normal (ie, equal weight support by both legs). For the 7 subjects participating in the weight distribution test, the average percentage of weight supported by the paretic leg increased from 33.9% to 40.6% during the treatment period ($P \leq .05$) and stabilized thereafter.

Figure 5
Improvement in Gait and Weight Distribution

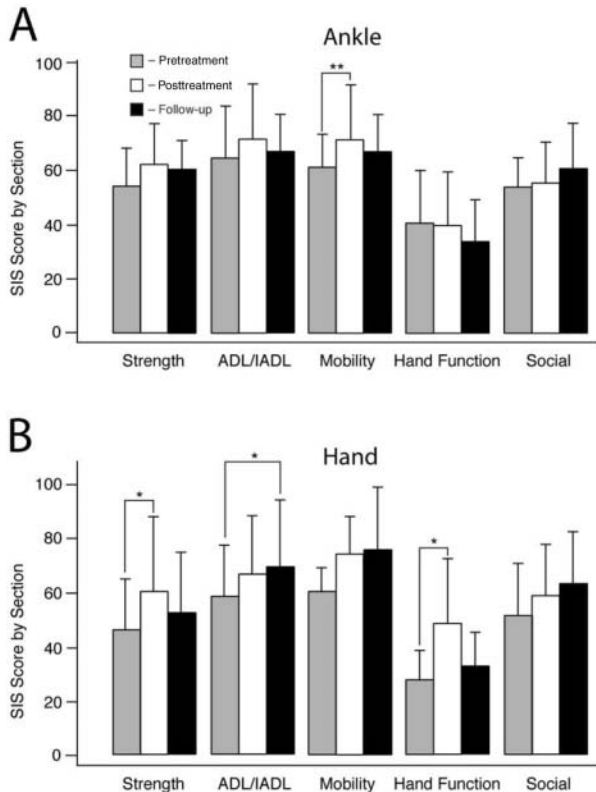


Note: (A) Average gait velocity, cadence, and stride length are compared at the entry point to the study (“pretreatment”), after 6 months of treatment (“posttreatment”), and 6 months after the end of treatment (“follow-up”). Asterisk indicates $P \leq .05$ ($n = 10$). (B) Average percentage of total weight supported by affected leg in subjects treated for lower extremity disability. Asterisk indicates $P \leq .05$ ($n = 6$).

Stroke Impact Scale

Figure 6 illustrates the results of the SIS questionnaire grouped by category (ie, Strength, ADL, Mobility, Hand Function, and Social). Subjects ($n = 8$) treated for lower extremity impairment (Figure 6A) improved significantly during the treatment period for Mobility ($P \leq .01$), and they showed a trend toward improvement in the Strength ($P = .07$) and ADL ($P = .07$) categories. Gains were sustained 6 months posttreatment in the Strength category, but not for the ADL and Mobility categories. No gains were observed in Hand Function. Subjects ($n = 5$) treated for upper extremity (Figure 6B) impairment improved

Figure 6
Stroke Impact Scale



Note: Average scores on the SIS are shown for categories of Strength, Adaptation, ADL, Mobility, and Hand Function for lower extremity treatment in (A) and upper extremity treatment in (B) * $P \leq .05$ and ** $P \leq .0005$ ($n = 7$, ankle; $n = 5$, hand).

significantly during the treatment period in the Strength ($P \leq .05$), Mobility ($P \leq .05$), and Hand Function ($P \leq .05$) categories, and they showed a trend toward improvement in the ADL ($P = .10$) category. Gains were sustained 6 months posttreatment in the Strength category; gain increased to the level of significance in the ADL category ($P \leq .05$), but Strength ($P = .08$) and Hand Function ($P = .15$) went from significant to not significant.

Discussion

Rationale for the Methodology

AMES is a new treatment approach for stroke rehabilitation and is based on the hypothesis that strengthening sensory-to-motor connectivity within the central nervous system, possibly through a Hebbian-type learning, is an effective means of restoring motor function. The goal of AMES methodology is to activate—both simultaneously and repetitively—antagonistically related motor-output neurons and sensory-receiving neurons in the sensorimotor cortices to strengthen the connections between these brain areas.^{18,19}

The methodology for AMES was designed to provide the stroke victim with several advantages over conventional and other newer approaches to stroke rehabilitation. The AMES device is noninvasive, and the relatively small amplitudes of tendon vibration and movement make the device relatively safe to use. Because AMES assists with movement, it can be used to treat individuals who are relatively low functioning, including those with significant hypertonicity, dyssynergia, and with minimal voluntary movement.

As demonstrated, the AMES procedure and the device are sufficiently straightforward that stroke patients can self-apply the treatment at home. However, treatment in the clinic under the supervision of a clinician might be equally, or more, effective. AMES was designed to match the treatment to each subject's capacity at the entry point and then to adjust the treatment upwards as the subject's motor function improved. Finally, by making the treatment device capable of testing strength and voluntary joint positioning each time the patient used the device, that patient's progress could be followed to project a rational endpoint for the treatment.

Among the most recently developed stroke therapies, AMES falls within a subgroup that employs robotic manipulation of the limb,^{20,23} and within the robotic group, it is distinguished by the inclusion of tendon (muscle) vibrators that amplify the sensation of motion and displacement, motion relating to the sensation of continuing joint rotation and velocity, and displacement relating to a quasi-independent sensation of position.^{24,25} The sensations of both motion and displacement are "distorted" by tendon vibration due to the relatively selective effect of vibration on muscle spindle Ia afferent firing.⁶ The relationship between vibratory pulse and afferent action potential can be 1:1 with a properly tuned vibrator,^{26,27} up to 70 pps,⁷ even though the typical firing rate of muscle spindle afferents is likely to be much lower during natural movements.^{28,29} Therefore, the choice of 60 to 70 pps vibration with the AMES device was to amplify maximally the sensation of motion and displacement without exceeding a ≈ 70 pps ceiling, at which point the 1:1 entrainment drops to subharmonics of the vibration rate.⁷

Safety and Efficacy

Based on more than 2000 hours of 20 stroke subjects self-administering the treatment, the risk to subjects using AMES appears to be very low. No injuries or other adverse events associated with the instructed use of the device were reported.

Based on the data acquired from the strength test, joint positioning test, gait test, weight distribution test, and SIS, the motor capabilities of most of our subjects in this report not only improved but also these improvements were sustained for at least 6 months following treatment. Increases in the strength and range of motion of subjects during treatment included joints proximal to those specifically treated, suggesting a distal-to-proximal radiation of the effects of treatment. For example, knee and hip range of motion during gait increased significantly, even though these joints were not directly treated (data not shown).

The causes of weakness, as tested, were not distinguished by the study. However, the combination of ranging the joint(s), assisting this motion robotically, and sensory input timed to the movement contributed to gains in motor function. Although functional gains following stroke can result from neural plasticity, our results do not provide any direct evidence that AMES treatment alters the connectivity of cortical neuronal ensembles.

Improvements in strength due to therapy could result from a remediation of any one or more of the multiple factors that may contribute to motor impairment. Conversely, treatment of just one of these factors may increase strength at a joint insufficiently to result in functional gains. Accordingly, in some subjects incapable of generating active torque in finger/wrist extension, but with co-contraction at those joints, we applied supplementary EMG training, which helped those subjects restore finger and wrist extension.

The strength and joint positioning tests proved to be useful in predicting objectively the endpoint for maximal gains using AMES therapy. In most subjects, this endpoint occurred well before the end of the 6-month treatment period, but in others, additional improvement continued up to the endpoint of treatment. The subjects' scores on the joint positioning test showed consistent improvement, with all subjects tested in this manner generating a clear upward trend in scores over the 6-month treatment period (Tables 3 and 4). The joint positioning test is also a composite measure that focuses on both active range of motion and static and dynamic joint-position control. Although neither active range of motion nor joint position control is completely independent of strength, there was no clear correlation between the results of the strength test and the joint positioning test, indicating that these tests likely quantify somewhat different aspects of motor control. Although neither the strength test nor the joint positioning test is a direct measure of functional motor skill, both are simple enough to track recovery during the rehabilitation period. In the joint positioning test, the presentation of a numerical score to the subjects was useful, providing each subject with an ongoing measure of progress and the motivation to compete with the previous best score.

Functional motor performance improved in most subjects using an ankle device, with gait speed, stride length, and weight distribution all showing significant improvement in the subjects (Figure 5). The SIS scores for both upper and lower extremities (Figure 6) indicated that these subjects thought they had improved in areas in which they should have benefited (eg, the treated limb), but not in those in which they should not have (eg, the nontreated limb).

Conclusions

The treatment device employed in this study appears to present minimal risk and may improve motor function in low-functioning chronic stroke patients. A future study will determine whether AMES is effective in treating subacute stroke

patients; however, a challenge of this subacute study will be to redesign the AMES device so that it can be used in the clinic, where it will need to be adjusted quickly and easily to a wide range of arm and leg sizes.

Preliminary measures of efficacy in chronic stroke subjects seem promising, but the study needs to be repeated with a broader assessment of motor function in a larger controlled study. If further studies show that AMES can restore some functional motor activities to lower functioning stroke victims, these same individuals may be able to benefit subsequently from other interventions that have been shown to benefit stroke victims with higher levels of function.

Acknowledgments

PC and LC have a significant financial interest in a medical equipment company that could potentially benefit from the results of this study.

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