

# Neuroprosthesis for Retraining Reaching and Grasping Functions in Severe Hemiplegic Patients

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## ■ ABSTRACT

During the course of rehabilitation hemiplegic patients who have Chedoke McMaster Stages of Motor Recovery scores 4 and 5 measured three weeks after onset of stroke often improve their arm and hand function to the point that they can later use it in the activities of daily living (ADL) (1). These patients can be considered to have mild arm and hand paralysis since they can grasp objects and manipulate them with minor restrictions in the range of movement and force. On the other hand, hemiplegic patients who have Chedoke McMaster Stages of Motor Recovery scores 1 and 2 measured three weeks after onset of stroke, during the course of rehabilitation seldom improve their arm and hand function, and when they do, the improvements are not sufficient to allow these patients to use the arm and hand in ADL (1). These patients can be also described as patients who have severe arm and hand paralysis. Patients with severe arm and hand paralysis cannot move their arm and hand voluntarily at all or have very limited voluntary movements that cannot be used to carry out ADL. In recent years a variety of treatments such as constraint induced therapy, functional electrical therapy, bio-feedback therapy, and robotics assisted therapies,

were proposed which main objective is to improve reaching and grasping functions in subjects with unilateral arm paralysis. These therapies have shown encouraging results in patients with mild arm and hand paralysis. However, the efficacy of these therapies was limited when they were applied to patients with severe arm and hand paralysis. This article describes a new rehabilitation technique that can improve both reaching and grasping functions in hemiplegic patients with severe unilateral arm paralysis. A neuroprosthesis that applies surface electrical stimulation technology was used to retrain hemiplegic patients who had severe arm and hand paralysis to reach and grasp. The neuroprosthesis was applied both to acute and long-term hemiplegic patients. Patients who were treated with the neuroprosthesis were compared to those patients who were administered only standard physiotherapy and occupational therapy appropriate for hemiplegic patients with unilateral upper extremity paralysis (controls). The treated and control patients had approximately the same time allocated for arm and hand therapy. After the treatment program was completed, the patients treated with the neuroprosthesis significantly improved their reaching and grasping functions and were able to use them in ADL. However, the majority of the control patients did not improve their arm and hand functions significantly and were not able to use them in ADL. ■

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**KEY WORDS:** arm and hand, functional electrical stimulation, functional electrical therapy, hemiplegia, neurorehabilitation, neuroprosthesis, stroke

## INTRODUCTION

According to the Heart and Stroke Foundation of Canada, there were between 1300 and 1600 strokes per million inhabitants in Canada in 2002. Stroke often leads to hemiplegia, a unilateral arm and/or leg paralysis. Patients who start improving their arm and leg functions immediately during the first three weeks after stroke may fully recover. However, a significant number of hemiplegic patients with unilateral arm and leg paralysis do not recover completely. Typically, patients improve their walking function to the point that they can walk slowly on their own using a cane or a walker, while the reaching and grasping functions frequently remain impaired. Comprehensive information regarding stroke and its epidemiology can be found in References 1-7.

Rand et al. (1) reported that stroke survivors who participated in standard physiotherapy and occupational therapy (2,3), which lasted approximately two months, at the completion of the therapy were discharged with the following outcomes pertaining to their arm and hand function: 55% were classified as patients with nonfunctional arm and hand, these patients were unable to use their arm and hand at all in ADL; 30% were classified as patients with intermediate recovery, these patients have shown some improvement in arm and hand function, in particular range of motion or strength, however, the improvement did not precipitate into substantial or more frequent use of arm and hand in ADL; and 15% were classified as patients with good recovery: these patients were able to use both arm and hand to carry out ADL. This statistics suggests that approximately 85% of all stroke survivors who are discharged home are unable to use their arm and hand in ADL.

The first two categories of patients, nonfunctional and those with intermediate recovery, can also be classified as patients with severe arm paralysis. These patients cannot move their arm and hand voluntarily at all, or have very limited voluntary movements that cannot be used to carry out ADL. If these patients are assessed with Chedoke McMaster Stages of Motor Recovery (CMSMR) the scores they would typically receive are either 1 or 2 (1,8). On the other hand the patients with good recovery (last group of patients) can also be classified as patients with mild arm and hand paralysis.

These patients can grasp objects and manipulate them with difficulty, restricted range of motion, and restricted grasping force. Patients with mild arm and hand paralysis typically have CMSMR scores 4 and 5 (1). These findings, reported by Rand et al. (1), can be rephrased in the following way:

85% of stroke survivors at discharge, after two months of standard occupational therapy and physiotherapy, have CMSMR scores 1 and 2 and are unable to use their arm and hand in ADL

15% of stroke survivors at discharge, after two months of standard occupational therapy and physiotherapy, have CMSMR scores 4 and 5 and are able to use their arm and hand in ADL

In the last 10-15 years a number of therapies such as constraint induced therapy (9,10), functional electrical therapy (11,12), biofeedback therapy (13-15), and robotic assisted therapy (16) were proposed, which have shown potential to improve arm and hand function in stroke survivors with unilateral arm paralysis. Although these therapies have distinctive ways of engaging the patient and promoting arm and hand recovery, they have one thing in common. These therapies were only effective if they were applied to hemiplegic subjects who had mild arm and hand paralysis, that is, CMSMR scores 4 and 5. If they were applied to patients with severe arm and hand paralysis, or CMSMR scores 1 and 2, the efficacy of these therapies was difficult to prove. In this article, a new intervention is presented which has resulted in improvements in arm and hand functions in hemiplegic patients with severe arm and hand paralysis.

The purpose of this study was to compare two types of therapies for upper extremity hemiparesis: conventional physiotherapy and occupational therapy (2,3) vs. FES therapy. These two therapies were applied to hemiplegic patients with severe arm and hand paralysis (CMSMR scores 1 and 2) using a randomized treatment-vs.-control design.

We hypothesized that the FES therapy would give rise to a greater improvement in arm and hand function as measured by (1): parts of the Chedoke McMaster Stages of Motor Recovery (CMSMR) test, pertaining to arm and hand functions of the hemiparetic arm (8); (2) parts of the Fugl-Meyer Assessment (FMA) pertaining to shoulder, elbow, forearm, wrist, and hand functions of

the hemiparetic arm (17); and (3) Rehabilitation Engineering Laboratory Hand Function Test for Functional Electrical Stimulation Assisted Grasping (REL Test) (18).

## MATERIALS AND METHODS

The study presented in this manuscript describes a randomized clinical trial with the following main characteristics: (1) the method for analyzing data was specified in the protocol before the study began; (2) the study received ethics approvals from the University of Toronto and the Toronto Rehabilitation Institute ethics boards; (3) the patients were invited to participate in the study and they gave consent before the inclusion/exclusion criteria were applied; and (4) after the patients were admitted to the program they were randomly assigned to control or intervention group. The flow chart of the recruitment, therapies, and assessments that were applied to all participants, both controls, and those who participated in the FES therapy, is shown in Fig. 1.

### Participants

The study was conducted with stroke patients with severe unilateral upper extremity paralysis (CMSMR scores 1 or 2). When they joined the program, the participants either could not generate the following movements voluntarily at all, or were able to generate a twitch or a very weak contraction in some of the muscles responsible for the following movements: (1) flex, extend,

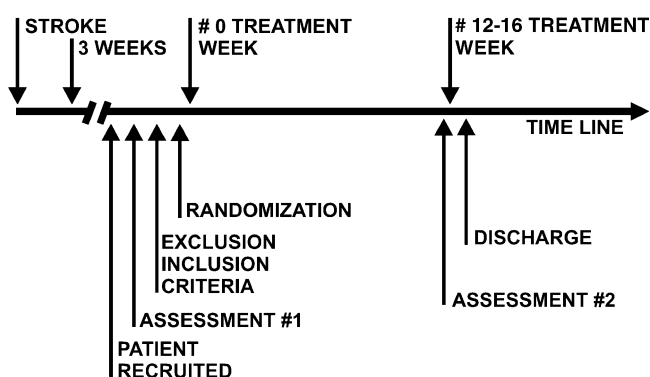
abduct, adduct, and rotate the shoulder; (2) flex and extend the elbow; (3) pronate and supinate the forearm; (4) flex, extend, abduct, and adduct the wrist; and (5) move fingers. Acute patients were recruited to the study at the rehabilitation unit at the Toronto Rehabilitation Institute at least three weeks after the onset of stroke (see Fig. 1). Long-term patients were recruited to the study through an outpatient follow-up clinic at the Toronto Rehabilitation Institute at least 12 months after the onset of stroke. From our experience, patients who do not show any signs of spontaneous recovery during the first three weeks after stroke typically do not have significant spontaneous recovery of the arm and hand in the following months and years. That is why the participants for our study were recruited only after the third week following stroke and only if they did not show any signs of spontaneous recovery. A medical doctor, or another member of the patients' core care team, identified potential candidates. The same team member approached the candidates, and made the initial contact. The patients' names were then passed on to our research team.

The inclusion criteria for this study were:

- Patient was eligible to provide informed consent as determined by a social worker.
- Patient had hemiplegia and the level of hemiplegia was confirmed by an attending physiatrist.
- Stroke was confirmed with a computed tomography or magnetic resonance imaging scan in an acute care facility.

The exclusion criteria were:

- Patient had global aphasia or had significant language barrier as determined by an attending speech language pathologist.
- Patient had skin rash, allergy or wounds at the locations where stimulation electrodes were expected to be placed.
- Patient had seizure episodes.
- Patient had edema in the paralyzed arm or had Shoulder Hand Syndrome.
- Patient had early signs of spontaneous recovery of the hemiplegic arm and hand functions (within first three weeks postonset of stroke) and had a score of motor recovery greater than 2 according to the Chedoke McMaster Stages of Motor Recovery (8).



**Figure 1.** The flow chart of the recruitment, therapies and assessments that were applied to both controls and patients who participated in the neuroprosthesis (FES) therapy.

After they were admitted to the program the subjects were randomly assigned to two groups: Group A: the control group who were administered only standard physiotherapy and occupational therapy; and Group B: the treatment group who were trained with the neuroprosthesis in addition to standard physiotherapy and occupational therapy (this training will be referred to further in the text as neuroprosthesis treatment). The treated and control patients had approximately the same time allocated for arm and hand therapy, as discussed later in this section.

### Randomization

Participants were randomized using two sets of sealed envelopes. An unmarked set of 40 envelopes were presented to a patient to select one. The unmarked envelopes contained a single sheet of paper with a printed number in the range from 1 to 40. In the second set of envelopes, which were marked with numbers from 1 to 40, control and intervention sheets were sealed. Twenty randomly selected numbers in the range from 1 to 40 were assigned to control group and the remaining 20 numbers were assigned to intervention group. Randomization was done using *randperm m*. function seeded with an arbitrary clock value in Matlab (The MathWorks, Inc., Natick, MA). This ensured that the relationship between numbers 1–40, and control and intervention options were properly randomized. Since the subjects chose a random envelope from the unmarked set, and since the relationship between the unmarked and marked sets of envelopes was randomized, the participants were randomly assigned to control and intervention groups. This was later confirmed in our statistical analysis presented in the Results section. Once an unmarked envelope was drawn, the unmarked envelope and its matching marked partner were destroyed. This ensured that the randomization process could not be contaminated.

### Outcome Measures

The following tests were administered both before and after the intervention to measure change in motor functions following the neuroprosthetic and conventional interventions. The tests also served to characterize the intervention and control par-

ticipants. All but one of the following tests were standard clinical tests with previously demonstrated reliability and validity. The Rehabilitation Engineering Laboratory Hand Function Test (REL test) was the only nonstandard test applied in this study. It was designed by our team to assess a gross motor function of grasping. In the scientific literature, a test that can properly perform such assessment does not exist yet (18). Since FES therapy primarily promotes improvement in gross motor function of grasping, a test that can provide increased sensitivity to the presence of subtle changes in gross motor function of the grasp as well as to provide enhanced ecologic validity, was needed. That is why our team had to develop the REL test, to which preliminary validity and reliability data are provided (18).

The following tests were administered to all participants in the study (both Group A and Group B).

Neurological test:

Canadian Neurological Scale (19) was used to assess neurological profile of the subjects.

Functional tests:

Functional Independence Measure (FIM)—total score (20)

Barthel Index (BI)\*—total score (21)

Chedoke McMaster Stages of Motor Recovery (CMSMR)—only a part of the total score pertaining to arm and hand functions of the hemiparetic arm (8)

Fugl-Meyer Assessment (FMA)—complete upper limb section score; that is, only a part of the total score pertaining to shoulder, elbow, forearm, wrist, and hand functions of the hemiparetic arm (17)

Rehabilitation Engineering Laboratory Hand Function Test (REL test) of the hemiparetic arm—total score (18) (See the following subsection for details).

The FIM and BI tests were used to determine the level of disability with respect to ADL. The CMSMR test was used to assess the functional state of the hemiplegic upper extremity since this test can capture the neuromuscular recovery of

\*FIM and BI are routinely collected with all stroke patients at the Toronto Rehabilitation Institute.

the patient's arm/hand. The FMA was used to assess development of the upper limb motor function in post-stroke patients. The REL test was used to assess a patient's unilateral hand function and its improvements. After signing a letter of consent, participants were administered the FIM, BI, CMSMR, FMA, and REL tests. FIM and BI were routinely collected with all stroke patients at the Toronto Rehabilitation Institute. Following the tests, the final admissibility of the subject to the program was approved and the subject was randomly assigned to one of the two groups (see Fig. 1).

The FIM, BI, CMSMR, FMA, and REL test results were used as a baseline against which patients' subsequent test scores were compared. After the treatment was completed, the same functional tests were performed again to measure the level of improvement as a result of the neuroprosthesis treatment compared to subjects who received standard physiotherapy and occupational therapy alone. The tests were always performed in the same, chronologic order: (1) FIM, (2) BI, (3) CMSMR, (4) FMA, and (5) REL. The measured scores for all five tests were scaled with respect to the maximum score and were presented as percentages of the maximum score. The scaling of the scores into percentages allowed us to present different tests in a uniform manner, which was later found useful when the data was statistically analyzed and presented.

Due to the nature of the treatment used in the study, it was impossible to blind the therapists and participants from the knowledge of which of the two groups individual participants were assigned to. An attempt was made to blind the assessor from the knowledge of which of the two groups individual patients were assigned to. However, substantial differences in the final outcomes in patients in Group B compared to Group A was clear indication to the assessor as to which of the two groups the participant was assigned to. After we realized our failure to blind the assessor, a statistician who was not a member of the core research team was asked to process the data.

### Rehabilitation Engineering Laboratory Hand Function Test for Functional Electrical Stimulation Assisted Grasping

The REL test was developed to evaluate improvement of the gross motor function of the unilateral



**Figure 2.** The REL Hand Function Test: Itemized objects used in the test.

grasp due to neuroprosthesis for reaching and grasping treatment. Hand functions that were tested with the REL test were: lateral or pulp pinch, and palmar grasps. The REL test consisted of three tests. The first test evaluated the palmar grasp, the second evaluated the pulp or lateral pinch grasp, and the third evaluated the strength of both palmar and pulp/lateral pinch grasps. To test the palmar grasp, the subject was presented with the following five items: mug, book, soda can, isosceles triangular sponge, and mobile telephone. (Fig. 2, items 1, 3, 5, 7, and 9, respectively). To test lateral or pulp pinch grasp, the subject was presented with the following five items: paper sheet, ziplock bag filed with five golf balls, die, credit card, and pencil (Fig. 2, items 2, 4, 6, 8, and 10). To test the strength of the grasps, the subject was presented with the following items: nine rectangular blocks, instrumented cylinder, credit card attached to a dynamometer, and wooden bar (Fig. 2, items 11, 12, 13, and 14).

With exception to the instrumented cylinder, credit card attached to a dynamometer and wooden bar, all test objects in Fig. 2 were placed on a desk 20–30 cm in front of the subject, one after another. The subject was expected to pick up the objects, lift them in front of his/her chest and move the objects from supination, to neutral and then to pronation position. In each position, the subject was expected to hold the object for 20–30 s. If in any of these three positions, the subject was unable to hold the object, he/she received 0 points for that position. If the subject could hold

the object for a short period of time (2–10 s) and eventually dropped the object, the subject was awarded 1 point. Finally, if the subject was able to hold the object for 20–30 s, he/she received 2 points for that hand position. Since holding the mug and the zip-lock-bag in supination position has no practical value, the subject was not asked to perform these two tasks.

The *instrumented* cylinder, credit card attached to a dynamometer, and wooden bar were used to measure torque generated by the palmar grasp, force produced by the pinch grasp, and exocentric load that the palmar grasp can sustain, respectively. For more details about the REL test, please consult Reference 18.

For the purpose of this study, scores for the mug, book, pop can, isosceles triangular sponge, mobile phone, paper sheet, ziplock bag filled with five golf balls, die, credit card, and pencil were all summed together to produce the REL Test—object manipulation score. Scores from the nine rectangular blocks tests were summed together to produce the REL Test—wooden blocks score. Scores for the instrumented cylinder were presented as REL Test—torques score, and scores obtained with the credit card attached to a dynamometer produced the REL Test—forces score. Scores for the wooden bar tests were presented as the REL Test—eccentric load score. The rationale for arranging the scores in this way was to group them according to the skills that were tested and the type of measures applied to obtain the score. Please note that the maximum scores for the REL Tests object manipulation, wooden blocks, forces, torques, and eccentric load score were 56, 18, 5 Nm, 50 N, and 60 cm, respectively.

### **Conventional Physiotherapy and Occupational Therapy**

Conventional physiotherapy and occupational therapy included: muscle facilitation exercises emphasizing the neurodevelopmental treatment approach; task-specific, repetitive functional training; strengthening and motor control training using resistance to available arm motion to increase strength; stretching exercises; electrical stimulation applied primarily for muscle strengthening (this is not FES therapy); activities of daily living including self-care where the upper limb was used as an assist

if appropriate; and caregiver training (4). Therapy sessions were 45 min daily, 3–5 days per week, for 12–16 weeks.

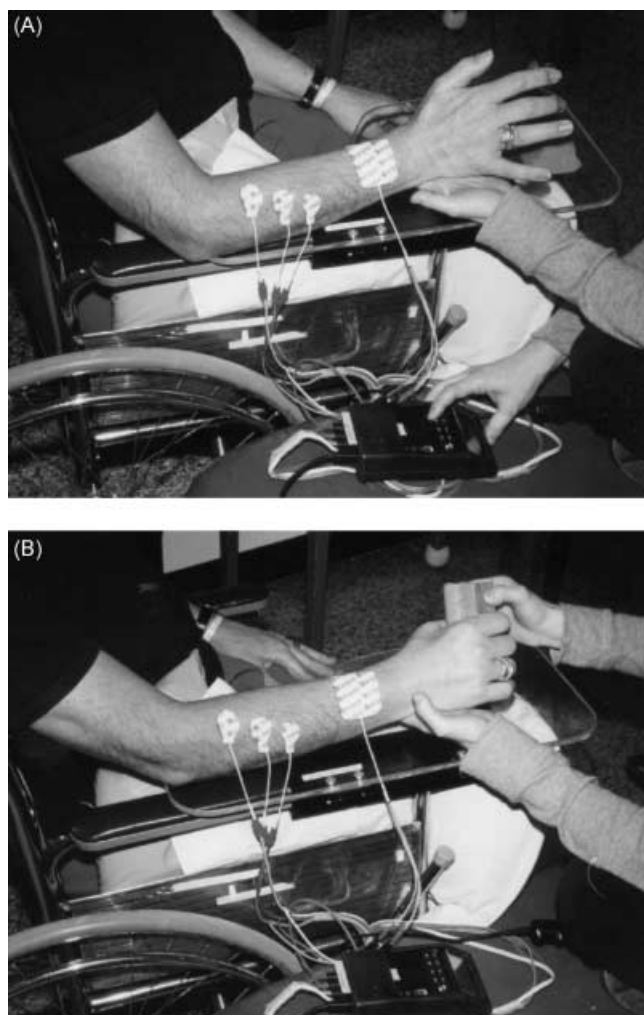
### **FES Therapy**

#### ***Neuroprosthesis Hardware***

The Complex Motion electric stimulator was used as a hardware platform for the neuroprosthesis for reaching and grasping (22). This is a fully programmable FES system with standard self-adhesive surface stimulation electrodes that can be used to develop sophisticated, custom-made neuroprostheses. During the course of the treatments, the patients' arm functions improved in different ways, requiring individualized stimulation protocols and custom-made neuroprostheses “fine-tuned” to meet particular patients' needs. Individualized and evolving stimulation protocols allowed us to maximize the training results with respect to the patients' disabilities and latest impairment status/condition.

#### ***FES Protocols Used in the Study***

The neuroprosthesis treatment consisted of a functional training program carried out in the following way. The subject was asked to execute a task with the impaired arm (for example, reaching and grasping a pen). The subject would then try to execute the task unassisted. The components/sequences of the task the subject was unable to carry out him/her self were assisted with the neuroprosthesis (see Fig. 3). During the treatment, a therapist controlled/triggered the reaching and grasping functions using a pushbutton. In the early stages of the treatment, the arm/hand tasks were performed by the neuroprosthesis alone. As the patient improved, the neuroprosthesis assistance was reduced to the necessary minimum and eventually was removed from the treatment protocol. Typically, the stimulation protocols were adjusted weekly or biweekly. The participant was asked to repeat the same arm/hand task 20–30 times during a single treatment session. The treatment sessions lasted up to 45 min, 25–30 min of which were used for active treatment alone. The remaining 15–20 min were used for donning and doffing of the neuroprosthesis. During the arm/hand movements, the physiotherapist guided the arm and assisted the patient with the neuroprosthesis in performing the desired task. This assistance



**Figure 3.** (A) Finger extension generated with the neuroprosthesis (FES) and (B) voluntary finger flexion.

ensured that all movements were carried out in a physiologic way, that is, neuroprosthesis induced movements did not oppose natural joint movements and respected the anatomy of bone and soft tissue composition. The exact therapy dose is discussed in the Results section.

In stroke patients, the neuromuscular recovery typically starts proximally followed by the recovery of distal neuromuscular compartments. Therefore, the neuroprosthesis treatment began by training shoulder and upper arm muscles first. *Anterior deltoid m.* and *biceps m.* were stimulated simultaneously to produce the arm movement that resembled a feeding movement. Once the hand reached the mouth, *posterior deltoid m.* and *triceps m.* were stimulated simultaneously to produce an arm extension movement and place the arm in a

relaxed position next to the body. Typically, the shoulder flexion function recovered first (*anterior deltoid m.*) in all our participants, followed by the recovery of the *biceps m.*, *posterior deltoid m.*, and *triceps m.*, respectively.

As soon as the patient showed signs of recovery of both the voluntary extension and flexion of the shoulder, the *extensor digitorum m.* was stimulated together with the *triceps m.* In this way, the patient was trained to extend the fingers when the elbow was fully extended. Since a large number of hemiplegic patients with unilateral upper extremity paralysis have spastic finger flexors, this stimulation protocol promoted finger extension in the arm configuration that is the most challenging from the biomechanical point of view to perform finger extension. This stimulation protocol helped reduce spasticity and tone in the fingers allowing patients to better control finger flexion and extension. The most difficult and time-consuming task was to train patients to voluntarily extend the fingers or to relax them. This function is essential to allow patients to voluntarily grasp and release objects.

Once the patient was able to voluntarily extend or relax the fingers, the *flexor digitorum superficialis m.*, *flexor digitorum profundus m.*, *median nerve* (or *thenar m.*), and *flexor pollicis longus m.* were stimulated to generate palmar and/or pinch grasp. This phase of the treatment was terminated when the patient was able to perform voluntarily palmar and/or pinch grasp combined with the reaching function.

In the study the following muscles and nerves were stimulated with surface stimulation electrodes:

- flexor digitorum superficialis m.* and the *flexor digitorum profundus m.* (finger flexion)
- median nerve or *thenar m.* and *flexor pollicis longus m.* (thumb opposition and flexion)
- extensor digitorum m.* (finger extension)
- flexor carpi radialis m.* and *flexor carpi ulnaris m.* (wrist flexion)
- extensor carpi radialis longus* and *brevis m.*, and *extensor carpi ulnaris m.* (wrist extension)
- biceps m.* (elbow flexion)
- triceps m.* (elbow extension)
- anterior* and *posterior deltoid m.* (shoulder flexion and extension, respectively)

Proper placements for the surface stimulation electrodes for the muscles and nerves listed above

can be found in Reference 23. Stimulation parameters used to stimulate the muscles and nerves were: balanced, biphasic, current regulated electrical pulses pulse amplitude from 8 to 50 mA (typical values 17–30 mA); pulse width from 100 to 250  $\mu$ s (typical value 250  $\mu$ s); and pulse frequency from 20 to 40 Hz (typical value 40 Hz).

### Statistical Analysis

The following hypotheses were tested

Hypothesis 1: On admission, Group A and Group B had the following scores equal:

- 1.1 REL Test—object manipulation
- 1.2 REL Test—wooden blocks
- 1.3 REL Test—forces
- 1.4 REL Test—torques
- 1.5 REL Test—eccentric load
- 1.6 FIM
- 1.7 BI
- 1.8 FMA
- 1.9 CMSMR

Hypothesis 2: On discharge, Group A and Group B had the differences of the following scores, measured on discharge and admission, equal:

- 2.1 REL Test—object manipulation
- 2.2 REL Test—wooden blocks
- 2.3 REL Test—forces
- 2.4 REL Test—torques
- 2.5 REL Test—eccentric load
- 2.6 FIM

- 2.7 BI
- 2.8 FMA
- 2.9 CMSMR

Hypothesis 3: Group A had the following scores equal, on admission and discharge:

- 3.1 REL Test—object manipulation
- 3.2 REL Test—wooden blocks
- 3.3 REL Test—forces
- 3.4 REL Test—torques
- 3.5 REL Test—eccentric load
- 3.6 FIM
- 3.7 BI
- 3.8 FMA
- 3.9 CMSMR

The hypotheses were tested using a Wilcoxon rank-sum test, which is nonparametric and robust to non-normal distributions of data. Since the outcome measures were expected to produce highly skewed data distributions, the hypotheses could not be tested using the standard Student's *t*-test

## RESULTS

### Participants

The study was conducted with 13 stroke patients who were randomly assigned to the control group, (Group A) and the treatment group (Group B).

#### *Group A: Standard Therapy—Control Group*

Eight subjects were assigned to Group A (Table 1).

**Table 1** Demographic Data and Stroke Diagnosis for Subjects

Subject	Sex	Age	Diagnosis	Affected arm	Treatment start date (days after stroke)
Group A: Standard Therapy—Control Group					
1	F	48	Right cerebral infarct	Left	21
2	F	78	Right middle cerebral artery internal capsule stroke	Left	21
3	F	73	Right parietal bleed with mass effect	Left	19
4	M	69	Right thalamic stroke	Left	47
5	M	79	Right internal capsule stroke	Left	33
6	M	81	Left middle cerebral artery territory infarct	Right	46
7	F	39	Intracerebral hemorrhage in the left basal ganglia	Right	40
8	F	29	Right intracerebral hemorrhage	Right	33
Group B: Neuroprosthesis Intervention Group					
1	M	73	Corona radiate, ischemic stroke	Right	338
2	M	32	Hemorrhage in the left lentiform nucleus	Left	19
3	F	50	Right introcranial hemorrhage	Left	57
4	M	59	Ischemic stroke in the left pons	Right	31
5	M	74	Cerebral vascular accident in the left hemisphere	Right	16



Five patients had had strokes affecting the right hemisphere and three patients had had strokes affecting the left hemisphere. Five patients were females and three were males. Their average age was  $62 \pm 20.3$  years and they joined the program 26 days post-stroke. At admission, the patients had the following average functional test scores: (1) FIM was 59.5; (2) BI was 38.1; (3) CMSMR pertaining to arm and hand functions was 3.6; (4) FMA upper limb score was 3.1; and (5) REL scores were 0, 0, 0.5 Nm, 0.63 N, and 0 cm.

### Group B: Neuroprosthesis Intervention Group

Five subjects were assigned to Group B (Table 1). Three patients had had strokes affecting the left hemisphere and two patients had had strokes affecting the right hemisphere. One patient was female and four were males. Their average age was  $57.6 \pm 17.5$  years. In this particular case, we had a bimodal distribution of the time post-stroke: one patient was recruited 338 days post-stroke and four patients were recruited at a mean of 30.8 days post-stroke. Overall mean was 92 days. At admission, the patients had the following average functional test scores: (1) FIM was 70.6; (2) BI was 48; (3) CMSMR pertaining to arm and hand functions was 4.6; (4) FMA upper limb score was 3.6; and (5) REL scores were 0.8, 2, 0.11 Nm, 7 N, and 0 cm.

Subjects in Group B received FES therapy 45 minutes daily, 3 to 5 times per week, for 12 to 16 weeks. It is important to mention that some of the FES therapies were combined with additional conventional physiotherapy and occupational therapy. In particular, 36.3% of the total FES therapies delivered to Group B were carried out in combination with additional conventional physiotherapy and occupational therapy sessions. These additional therapies were primarily delivered during first six to eight treatment weeks. The exact number of hours of FES therapies and FES therapies combined with physiotherapy and occupational therapy is presented in Table 2. Please note that subject No. 4 received 19 weeks of therapy instead of 16 (maximum originally prescribed dose) and that subject 5 received 9 weeks of therapy instead of 12 (minimum originally prescribed dose).

**Table 2.** Exact Number of Therapy Sessions Delivered to Group B

Subject	Number of delivered FES therapies combined with physiotherapy and occupational therapy	Number of delivered FES therapies that were not combined with physiotherapy and occupational therapy
1	0	77
2	36	0
3	18	59
4	31	62
5	28	0

### Raw Data

Tables 3 and 4 summarize the raw data obtained from both Groups A and B at admission and discharge. The raw data was then scaled and presented as percentages of the maximum scores that can be achieved with individual tests (Fig. 4). The data was scaled because the individual tests had very different ranges of scores and some tests had physical units such as REL Test—forces & torques. Scaled data were then statistically processed to obtain minimum, mean, maximum, and standard deviation values, which are presented in Tables 2 and 3. The difference between mean scores obtained on discharge and admission for both Groups A and B are shown in Fig. 5. “Box and Whisker” plot of the same data is provided in Fig. 4. From Figs 4 and 5 and Tables 3 and 4, the following conclusions can be drawn:

Group A subjects (control group) who were administered standard physiotherapy and occupational therapy appropriate for severe hemiplegic patients did not improve their arm and hand functions substantially according to mean values of the REL, FMA, and CMSMR tests. However, these subjects showed substantial improvement in the FIM and BI scores.

Group B subjects (intervention group) who were administered the neuroprosthesis treatment improved their arm and hand function considerably according to mean values of the REL, FMA, and CMSMR tests. These subjects also showed substantial improvement in the FIM and BI scores, similar to the Group A subjects.

Mean and standard deviation values obtained for both Groups A and B for all tests before the

**Table 3.** Group A (Control Group) Raw Data Collected at Admission and Discharge and Statistics

Subject	REL Test					FIM	BI	FMA	CMSMR
	objects	blocks	torques (Nm)	forces (N)	eccentric load				
Tests at admissions (before)									
1	0	0	0	0	0	66	35	0	3
2	0	0	0	0	0	80	50	8	3
3	0	0	0	0	0	56	50	13	4
4	0	0	0.2	2.5	0	45	25	4	2
5	0	0	0	0	0	44	40	0	4
6	0	0	0	0	0	61	30	4	3
7	0	0	0	0	0	59	45	0	4
8	0	0	0	0	0	65	30	0	2
Upper limit	56	18	5	50	60	126	100	66	14
Statistically processed data presented in percentage of the maximum scores that can be achieved with the individual tests									
Min.	0	0	0	0	0	34.9	25	0	14.3
Mean	0	0	0.5	0.63	0	47.2	38.1	5.49	22.3
Max.	0	0	4	5	0	63.5	50	19.7	28.6
S.D.	0	0	1.41	1.76	0	9.28	9.61	7.24	5.96
Tests at discharge (after)									
1	0	0	0	0	0	111	75	0	4
2	0	0	0	0	0	103	80	8	4
3	8	4	0.1	2	0	97	80	16	6
4	11	9	0.5	5	0	92	40	14	5
5	0	0	0	0	0	67	50	0	4
6	0	0	0	0	0	74	45	4	4
7	0	0	0	0	0	110	90	0	4
8	0	0	0	0	0	106	75	4	4
Upper limit	56	18	5	50	60	126	100	66	14
Statistically processed data presented in percentage of the maximum scores that can be achieved with the individual tests									
Min.	0	0	0	0	0	53.17	40	0	28.57
Mean	4.24	9.03	1.5	1.75	0	75.40	66.88	8.712	31.25
Max.	19.6	50	10	10	0	88.10	90	24.24	42.86
S.D.	7.982	18.29	3.505	3.615	0	13.09	18.89	9.642	5.314

treatment was initiated were similar, suggesting that the subjects were randomly assigned to groups. This is discussed in more detail later in this section.

Mean values for Groups A and B subjects for the REL, FMA, and CMSMR tests after the treatment was performed show significant differences. The Group B subjects have substantially higher mean scores for the REL, FMA, and CMSMR tests compared to the Group A subjects. The standard deviations for the REL test are similar for both subject groups.

Mean values for Groups A and B subjects for the FIM and BI tests after the treatments were performed show very little difference, despite the fact that the REL, FMA, and CMSMR tests showed substantial difference.

The above results suggested that differences between the scores obtained for Group A (control group) and Group B (neuroprosthesis treatment group) were considerable and that the statistical significance of these findings needed to be tested.

### Results of the Statistical Analysis

The results of the statistical analysis are presented in Table 5. In Table 5, items with bold *p* values indicate that the hypothesis can be accepted, and the items with italic *p* values indicate that the hypothesis should be rejected. In summary, the results of the analysis suggest the following:

Subjects in Groups A and B were selected in random fashion, that is, Hypothesis 1 could not

**Table 4.** Group B (Intervention Group) Raw Data Collected at Admission and Discharge and Statistics

Subject	REL Test					FIM	BI	FMA	CMSMR
	objects	blocks	torques (Nm)	Forces (N)	eccentric load				
Tests at admissions (before)									
1	4	10	0.55	35	0	112	55	16	4
2	0	0	0	0	0	57	45	0	2
3	0	0	0	0	0	75	40	0	4
4	0	0	0	0	0	54	55	0	4
5	0	0	0	0	0	55	45	7	4
Upper limit	56	18	5	50	60	126	100	66	14
Statistically processed data presented in percentage of the maximum scores that can be achieved with the individual tests									
Min.	0	0	0	0	0	42.86	40	0	14.29
Mean	1.429	11.11	2.2	14	0	56.03	48	6.970	25.71
Max.	7.143	55.56	11	70	0	88.89	55	24.24	28.57
S.D.	3.194	24.85	4.919	31.31	0	19.59	6.708	10.69	6.389
Tests at discharge (after)									
1	32	18	2.5	45	50	112	95	42	8
2	39	15	1.5	12	3	108	95	41	8
3	14	11	0.4	16	0	106	90	22	7
4	40	16	1.5	45	30	105	90	41	6
5	56	18	0.1	15	20	97	90	55	6
Upper limit	56	18	5	50	60	126	100	66	14
Statistically processed data presented in percentage of the maximum scores that can be achieved with the individual tests									
Min.	25	61.11	2	24	0	76.98	90	33.33	42.86
Mean	64.64	86.67	24	53.2	34.33	83.81	92	60.919	50
Max.	100	100	50	90	83.33	88.89	95	83.33	57.14
S.D.	27.15	16.01	19.29	33.72	34.23	4.369	2.739	17.84	7.143

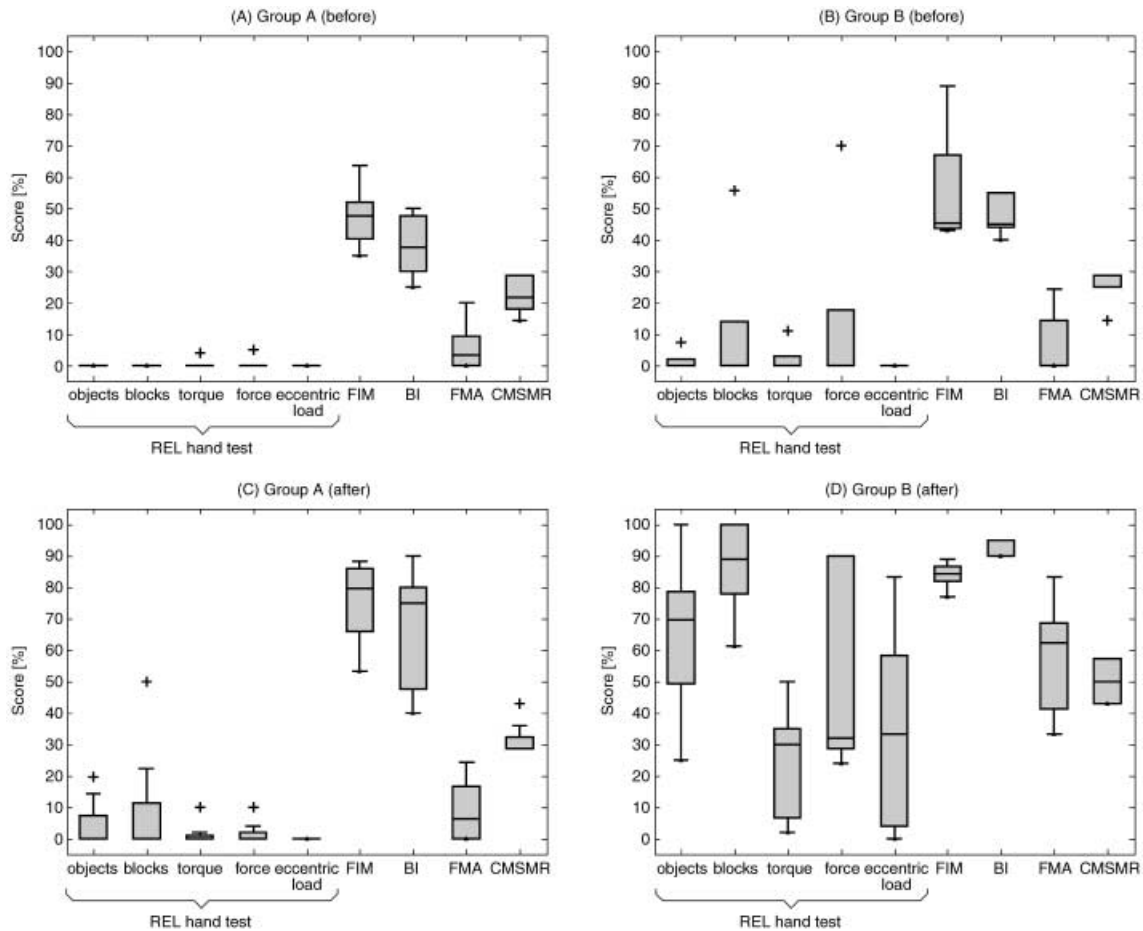
be rejected. Subjects in both groups had similar arm and hand functions, and had similar abilities to perform ADL when they were assigned to the groups.

Subjects in Group A, after the treatment was completed, only improved the FIM and BI scores; the arm and hand function scores (REL, FMA and CMSMR scores) did not improve

**Table 5.** Results of the Wilcoxon Rank-Sum Analysis Conducted to Test Hypotheses: 1.1–1.9, 2.1–2.9 and 3.1–3.9

Statistics	REL Test					FIM	BI	FMA	CMSMR
	objects	blocks	torques	forces	eccentric load				
Hypothesis	1.1	1.2	1.3	1.4	1.5	1.6	1.7	1.8	1.9
Group A vs. Group B before									
T-stat	39	39	37	37	35	37	46.5	34	39
<i>p</i> -value <sup>a</sup>	<b>0.769</b>	<b>0.769</b>	<b>0.769</b>	<b>0.769</b>	<b>1.000</b>	<b>0.833</b>	<b>0.099</b>	<b>0.957</b>	<b>0.769</b>
Hypothesis	2.1	2.2	2.3	2.4	2.5	2.6	2.7	2.8	2.9
Group A delta vs. Group B delta									
T-stat	55	48	52.5	55	47	38	48.5	55	50.05
<i>p</i> -value <sup>a</sup>	<i>0.002</i>	<b>0.053</b>	<i>0.008</i>	<i>0.002</i>	<b>0.070</b>	<b>0.681</b>	<i>0.048</i>	<i>0.002</i>	<i>0.025</i>
Hypothesis	3.1	3.2	3.3	3.4	3.5	3.6	3.7	3.8	3.9
Group A before vs. Group A after									
T-stat	60	60	64	64	68	38	43	64.5	60
<i>p</i> -value <sup>a</sup>	<b>0.467</b>	<b>0.467</b>	<b>0.733</b>	<b>0.733</b>	<b>1</b>	<i>0.001</i>	<i>0.007</i>	<b>0.761</b>	<b>0.467</b>

<sup>a</sup>Items in italics indicate that the hypothesis can be rejected ( $p < 0.05$ ). Items in boldface indicate that the hypothesis could not be rejected ( $p > 0.05$ ).



**Figure 4.** “Box and Whisker” plots of the scaled data for REL Tests: object manipulation, wooden blocks, torques, forces, and eccentric load; FIM; BI; FMA; and CMSMR tests: (A) Group A scores before the treatment; (B) Group B scores before the treatment; (C) Group A scores after the treatment; and (D) Group B scores after the treatment.

significantly. In other words, Hypotheses 3.6 and 3.7 were rejected with alphas 0.005 ( $p = 0.001$ ) and 0.01 ( $p = 0.007$ ), respectively, while Hypotheses 3.1, 3.2, 3.3, 3.4, 3.5, 3.8 and 3.9 could not be rejected.

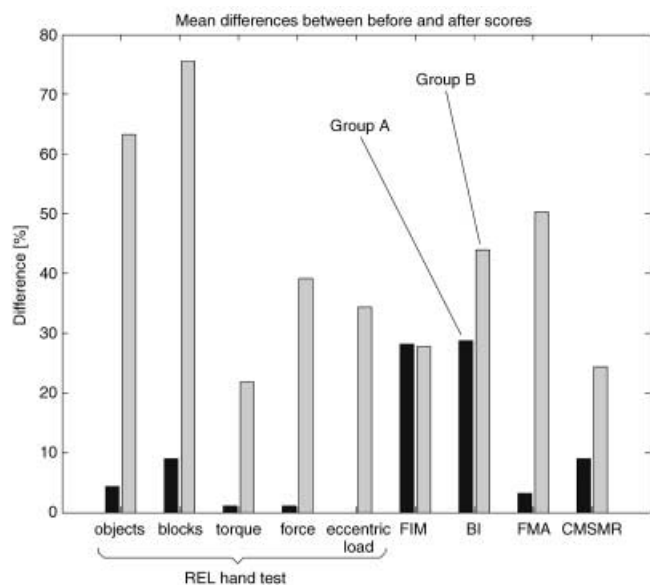
When Group A and Group B subjects were compared on discharge, subjects in Group B showed significant improvement in the arm and hand functions compared to Group A subjects, as shown with the REL Test—object manipulation, REL Test—forces, REL Test—torques, FMA, BI, and CMSMR scores. Also, the FIM, REL Test—blocks, and REL Test—eccentric load showed improvements in function; however, the significance of the changes could not be demonstrated with the given number of subjects. In other words, Hypotheses 2.1, 2.3, 2.4, 2.7, 2.8, and 2.9 were rejected with alphas 0.005 ( $p = 0.002$ ), 0.01 ( $p = 0.008$ ), 0.005 ( $p = 0.002$ ),

0.05 ( $p = 0.048$ ), 0.005 ( $p = 0.002$ ), and 0.05 ( $p = 0.025$ ), respectively, while Hypotheses 2.2, 2.5, and 2.6 could not be rejected.

In summary, the statistical analysis confirmed our hypothesis that the neuroprosthesis therapy gives rise to greater improvement in arm and hand functions, compared to traditional physiotherapy and occupational therapy alone.

### Observations Pertaining to Group B Subjects

During the treatment, all patients reached a functional plateau after 12–16 weeks of neuroprosthesis treatment. In addition to arm/hand function improvement, the subjects also improved the way they controlled their upper body during sitting, standing, and walking. All subjects reported that they felt more natural with respect to their arm,



**Figure 5.** Differences between the after and before mean scores for: (1) REL Test—object manipulation; (2) REL Test—wooden blocks; (3) REL Test—torques; (4) REL Test—forces; (5) REL Test—eccentric load; (6) FIM; (7) BI; (8) FMA; and (9) CMSMR tests. The black bars represent the differences for Group A and the light gray bars represent the differences for Group B.

and that the arm “followed” the natural movements of the body after the FES treatment was completed. In addition, subjects who had shoulder subluxation and had to take pain medication because of it (Group B, subjects 3 and 4), did not have shoulder subluxation after the neuroprosthesis treatment and stopped taking the pain medication.

We have observed that the initial improvements in reaching and grasping functions due to the neuroprosthesis training have strongly motivated patients to continue participating in the program. Furthermore, the reinforced motivation and the regained function encouraged patients to increase active use of the paralyzed arm and hand in ADL, which further promoted recovery and gradually eliminated the “learned nonuse pattern” typical for these patients.

## DISCUSSION

We compared the outcomes of two groups of hemiplegic stroke subjects with severe unilateral upper extremity paralysis. One group of subjects was administered conventional occupational therapy and physiotherapy, commonly applied to rehabilitate

these patients. The other group was administered neuroprosthesis therapy. The results of this study have shown that the subjects who were treated with the neuroprosthesis for reaching and grasping improved significantly compared to control subjects.

Our study differs from previously published results in the following ways. First, our patients were unable to move the paralyzed arm at all or were able to perform very limited movements with the arm, and as such, were not candidates for constraint induced therapy (9,10), FES therapy proposed by Popovic et al. (11) and Cauraugh et al. (12), or biofeedback therapy (13–15). As the patients regained some components of the voluntary active movement of the arm and hand, the FES support for those recovered components of the movement were phased out. Second, the recovery achieved with our treatment produced radical improvements in arm and hand functions, instead of incremental improvements observed with constraint induced therapy and FES therapy proposed by Popovic et al. and Cauraugh et al. (11,12).

We believe that our results provide more compelling evidence that FES therapy can be successfully used, not only to treat mild and moderate arm paralysis in hemiplegic patients, but also to treat patients with severe paralysis. Second, our treatment protocol stresses the importance of applying surface FES treatment that can be tailored/adjusted to patients’ needs on a daily basis and can evolve as the patients improve their function. Third, our findings suggest that if a hemiplegic patient who strains to execute a reaching or grasping task is assisted with the FES to carry out that task, he/she is effectively voluntarily generating the motor command (desire to move the arm, i.e., *command input*) and FES is providing the afferent feedbacks (*system output*), indicating that the command was executed successfully. We hypothesize that, by providing both the command input and system output to the central nervous system repetitively for prolonged periods of time, this type of treatment facilitates functional reorganization and retraining of intact parts of the of central nervous system and allows them to take over the function of the damaged part of the central nervous system. It is important to add that during the treatment, the subjects were performing reaching and grasping tasks repetitively. However, the exact

reaching and grasping tasks differed from day to day to encompass as many different reaching and grasping strategies and arm kinematic configurations as possible. We believe that diversity of meaningful tasks combined with high repetition may play an important role in retraining reaching and grasping functions. Similar findings were also reported by Hesse et al. (16).

The results presented in this article clearly indicate that in severe hemiplegic patients, improvement of the unilateral arm function when the other arm is fully functional have little or no effect on the improvement in FIM scores. Second, the results also indicate that a hemiplegic subject can achieve high FIM and BI scores in spite of having one arm completely paralyzed. Third, the results also suggest that established physiotherapy and occupational therapy commonly administered to severe hemiplegic subjects have a positive effect on the improvement of the unilateral arm and hand functions. However, these positive changes have very limited impact on object manipulation tasks; that is, in spite of improvement, subjects still have very limited ability to grasp and manipulate objects in ADL, as shown by the REL Test scores, CMSMR, and FMA. On the other hand, subjects that were administered the neuroprosthesis treatment achieved substantially greater improvements in the arm and hand functions compared to the control subjects, and were able to apply them effectively in ADL, as shown by the REL Test scores, CMSMR, and FMA.

Although this is an ongoing study, and thus far only 13 subjects have participated (five who were administered the neuroprosthesis therapy and eight control subjects), the obtained results are statistically significant. This clearly indicates that the neuroprosthesis treatment provides significant and radical improvement in reaching and grasping function in severe hemiplegic patients with unilateral arm deficit, compared to established rehabilitation techniques. Since the number of subjects used to produce these results was very low, we feel confident that additional subjects will further reinforce these findings and would help reject hypotheses 2.2 and 2.5 (the differences for the REL Test—blocks and REL Test—eccentric load tests for Group A and Group B, before and after the therapy are the same). Our future work is aimed at better understanding the mechanisms

responsible for the success of the proposed neuroprosthesis therapy.

### Weaknesses of the Study

The nature of the neuroprosthesis therapy did not allow us to blind the therapists and participants from the knowledge of which participant received the neuroprosthesis therapy and which participants were controls. Furthermore, despite our efforts to blind the assessor from the knowledge of which of the two groups individual patients were assigned to, the assessor was able to realize which subjects received the neuroprosthesis therapy. The reason for this was substantial difference in final outcomes in patients that participated in the neuroprosthesis therapy compared to controls.

### CONCLUSIONS

A neuroprosthesis that applies surface FES technology can be successfully used to improve reaching and grasping functions in both acute and long-term hemiplegic patients with severe arm paralysis. The key to the success of this therapy is a repetitive and intensive neuroprosthesis treatment that can be tailored to a patient's needs on a daily basis and can evolve as the patient improves his/her arm and hand functions.

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