Neurorehabilitation of Upper Extremities in Humans with Sensory-Motor Impairment

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■ ABSTRACT

Today most clinical investigators agree that the common denominator for successful therapy in subjects after central nervous system (CNS) lesions is to induce concentrated, repetitive practice of the more affected limb as soon as possible after the onset of impairment. This paper reviews representative methods of neurorehabilitation such as constraining the less affected arm and using a robot to facilitate movement of the affected arm, and focuses on functional electrotherapy promoting the movement recovery. The functional electrical therapy (FET) encompasses three elements: 1) control of movements that are compromised because of the impairment, 2) enhanced exercise of paralyzed extremities, and 3) augmented activity of afferent neural pathway. Liberson *et al.* (1) first reported an important result of the FET; they applied a peroneal stimulator to enhance functionally essential ankle dorsiflexion during the swing phase of walking. Merletti *et al.* (2) described a similar electrotherapeutic effect for upper extremities; they applied a two-channel electronic stimulator and surface electrodes to augment elbow extension and finger extension during different reach and grasp activities. Both electrotherapies resulted in immediate and carry-over effects caused by systematic application of FET. In studies with subjects after a spinal cord lesion at the cervical level (chronic tetraplegia) (3–5) or stroke (6), it was shown that FET improves grasping and reaching by using the following outcome measures: the Upper Extremity Function Test (UEFT), coordination between elbow and shoulder movement, and the Functional Independence Measure (FIM). Externally applied electrical stimuli provided a strong central sensory input which could be responsible for the changes in the organization of impaired sensory-motor mechanisms. FET resulted in stronger muscles that were stimulated directly, as well as exercising other muscles. The ability to move paralyzed extremities also provided awareness (proprioception and visual feedback) of enhanced functional ability as being very beneficial for the recovery. FET contributed to the increased range of movement in the affected joints, increased speed of joint rotations, reduced spasticity, and improved functioning measured by the UEFT, the FIM and the Quadriplegia Index of Function (QIF). ■

KEY WORDS: functional electrical therapy, neurorehabilitation, spinal cord injury, stroke.

INTRODUCTION

Most persons develop a so-called ''no-use'' pattern of the affected extremity after a central nervous system (CNS) lesion (7). Some subjects with a given extent and locus of lesion recover

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more movement than others with similar lesions suggesting that additional factors may be involved; one of these might be the operation of a no-use mechanism (8). The comprehensive conventional therapies could improve the motor functioning of paralyzed extremities; thus, reducing the disability caused by the CNS lesion and the no-use pattern. These therapies (9) include: pharmacologic means (10), enhanced physical therapy (11,12), and integrated behavioral and physical therapy (13–15).

Neurorehabilitation is a term that relates to methods and technologies for maximizing the functioning of impaired sensory-motor mechanisms in human after CNS lesion. Maximizing function relates to developing new sensory motor pathways and CNS strategies that could benefit from the available yet unused sensory-motor mechanism (16). The CNS provides the basis for structuring neurorehabilitation activities to promote and enhance recovery of function following injury or disease. Spontaneous recovery occurs through the process of compensation, substitution, and dynamic reorganization through externally elicited exercise. The actions in the actual application of the neurorehabilitation to the subjects with CNS lesions include the following: providing constant and systematic augmented feedback, insisting on a prolonged and intensive training directed to tasks that require integration of functional structures, progressively increasing the difficulty of the training task, and ensuring successful endeavors.

MOTOR RECOVERY ENHANCED BY MOVEMENT INDUCED THERAPY

A family of rehabilitation techniques, called Constraint-Induced (CI) movement therapy, has been developed (8). Experiments have shown that CI therapy in stroke subjects is effective in improving limb use in the real-world environment. The therapy involves constraining movements of the less affected arm with a sling for 90% of waking hours for two weeks, while intensively training the use of the more affected arm. The common therapeutic factor in all CI therapy would appear to be inducing concentrated, repetitive use of the more affected limb. A number of neuroimaging and transcranial magnetic stimulation studies have shown that the massed practice of CI therapy produces a massive use-dependent cortical reorganization that increases the area of cortex involved in the innervation of movement of the more affected limb (8). The CI therapy approach has been used successfully to date for the upper limb in subjects with chronic and subacute stroke and subjects with chronic traumatic brain injury and for the lower limb in subjects with stroke, incomplete spinal cord lesion, and fractured hip. Assessment of the effectiveness of CI therapy showed a substantial improvement in the performance times of the laboratory tests and in the quality of movement, although some of the findings have been questioned and contradicted (17–20). The focal transcranial magnetic stimulation (TMS), EEG, and magnetic source imaging (MEG) studies with humans, carried out by several groups of investigators suggest that cortical reorganization is associated with the therapy.

Sunderland and colleagues (21) followed the recovery of arm function after acute stroke, and compared conventional physiotherapy with an enhanced therapy regime, which increased the amount of treatment. They also introduced behavioral methods to encourage motor learning. In a single-blind randomized trial, 132 consecutive stroke subjects were assigned to two groups. Six months after stroke the enhanced therapy group showed a small, but statistically significant advantage in the recovery of strength, range, and speed of movement. This effect seemed concentrated among those who had a mild initial impairment. The study does not provide answers why this improved recovery occurred and whether further development of this therapeutic approach might offer clinically significant gains for stroke subjects.

The use of robots to enhance therapy provides further proof that the extensive exercise is beneficial. The MIT-Manus robot (MIT, Cambridge, MA) provided interactive, goal-directed motor activity. It was used for clinical neurologic applications to test whether the externally driven impaired limb influences motor recovery of subjects after stroke. Twenty subjects with a history of a single stroke were enrolled in a standard rehabilitation program supplemented by either robot-aided therapy or sham robot-aided

therapy (22). These two groups were comparable in age, initial physical impairment, and the time between onset of the stroke and enrollment in the trial. Impairment and disability declined in both groups between hospital admission and discharge. The robot-treated group showed a greater degree of improvement in all measures of motor recovery, and the change in motor status measured in the proximal upper limb musculature was significant.

In a continuation study 56 subjects with stroke received standard poststroke rehabilitation and were randomly assigned either to receive robotic training for at least 25 h during three weeks of exposure or placebo (23). Outcomes were assessed by the same masked raters, before treatment began and at the end of treatment, with the upper extremity component of the Fugl-Meyer (FM) Motor Assessment, the Motor Status score, the Motor Power score, and the Functional Independence Measure (FIM). The robot treatment and control groups had comparable clinical characteristics, lesion size, and pretreatment impairment scores. By the end of treatment, the robot-trained group demonstrated improvement in motor outcome for the trained shoulder and elbow that did not generalize to the untrained wrist and hand. The robot-treated group also demonstrated significantly improved functional outcome.

THERAPEUTIC ELECTRICAL STIMULATION (TES)

Electrical stimulation of peripheral sensory-motor systems contributes to the facilitation of voluntary movement, strengthening of atrophied muscles, change of the muscle length and bulk, change of muscle type and function, interactions between agonist and antagonist muscles, increasing the range of movement, and moderation of spasticity. Electrical therapy has been applied as a therapy in humans with CNS lesions although there are no conclusive results about which technique works the best for a given indication.

Kraft and colleagues (24) investigated the improvement in the upper limb of chronic stroke subjects who received one of two electrical stimulation treatments, conventional treatment, or no treatment. Twenty-two right-handed subjects were assigned to one of four groups and studied for 12 months post-treatment. Subjects received: 1) EMG-initiated electrical stimulation of wrist extensors (movement generated); 2) subthreshold (no direct motor response) electrical stimulation of wrist extensors combined with voluntary contractions; 3) intensive therapist-assisted exercises of the wrist, or 4) only conventional treatment for three months. Before, upon completion, and three and nine months after the treatment subjects were evaluated by the FM motor recovery test and by grip strength. During the course of treatment, FM scores of subjects receiving only exercise (group 3) improved 18%, low-intensity electrical stimulation (group 2) improved 25%, and EMG-initiated stimulation (group 1) improved 42%. The aggregate FM improvement of the treated groups was significant from pretreatment to post-treatment, and the improvement was maintained at three-month and nine-month follow-ups. The treated subjects' improvement in grip strength was also maintained at both follow-ups ($p < 0.01$). In contrast, the control group showed no significant change in FM scores or grip strength at three and nine months. Glanz et al. (25) presented a meta-analysis from the reported randomized controlled trials of FES in stroke published between 1978 and 1992. The intervention in all these studies was therapeutic electrical stimulation applied to the paretic extremity, and the results were always compared with the appropriate controls. The overall finding is that the improvement in daily functioning is statistically significant.

The influence of suprathreshold electrical stimulation of the extensor and flexor carpi radialis muscles on biomechanical and functional movement parameters is compared with the effect of a standardized active repetitive training of hand and fingers (26). In a single-blinded, randomized, controlled multicenter trial, 100 consecutive stroke subjects were allocated to either an experimental group that received an additional treatment of sensory-motor stimulation below the motor threshold or to a control group (27). The intervention was applied for six weeks. Subjects were evaluated for level of impairment (FM test), and disability (Action

Research Arm–ARA test, Barthel Index–BI) before, midway, and after the intervention period and at follow-up six and 12 months after stroke. The subjects in the experimental group performed better in the FM test than those in the control group throughout the study period, but differences were significant only at follow-up. The results in the ARA test and BI revealed no effect at the level of disability. The effect of the therapy was attributed to the repetitive stimulation of muscle activity. The treatment was most effective in subjects with a severe motor deficit and hemianopia or hemi-inattention. The main conclusion is that an intervention during the acute phase after stroke augments motor recovery.

Forty-six stroke subjects, admitted to the inpatient rehabilitation unit, were randomly assigned to receive either neuromuscular stimulation or placebo (28). Twenty-eight subjects completed the study. The treatment group received surface neuromuscular stimulation to produce wrist and finger extension exercises at least six months after the stroke. The control group received placebo stimulation over the paretic forearm. All subjects were treated one hour per day, for a total of 15 sessions. Outcomes were assessed in a blinded manner with the upper extremity component of the FM test and the self-care component of the FIM at pretreatment, post-treatment, and at four and 12 weeks after treatment. Parametric analyses revealed significantly greater gains in FM scores for the treatment group immediately and four and 12 weeks after treatment. The FIM scores were not different between groups at any of the time periods.

Francisco and colleagues (29) assessed the efficacy of EMG-triggered neuromuscular stimulation above motor threshold in enhancing upper extremity motor and functional recovery of acute stroke subjects. Voluntarily controlled contraction of synergistic muscles (EMG) was used to trigger stimulation; significantly greater gains in FM and FIM scores were measured in the treated subjects than in the controls. Cauraugh and colleagues (30–32) reported on the effect of EMG-triggered neuromuscular electrical stimulation on the wrist and finger extensors when applied to stable stroke individuals (more than one year after the onset). Subjects first completed 12 sessions attempting wrist and finger extension without any external assistance, and then they had 12 sessions of the electrical stimulation. The Box and Block test and the force-generation task (sustained muscular contraction) revealed significant improvement due to electrical therapy. The experimental group moved significantly more blocks and displayed a higher isometric force after the electric therapy. The results of the study suggest that the use of the EMG-triggered neuromuscular electric stimulation is effective for rehabilitating wrist and finger extension of hemiparetic individuals.

Electrical therapy can also be applied at levels where only the afferent pathways are activated (33). Activating sensory mechanisms could in principle play a role in the modification of the neural circuits after the CNS lesion. The effects of whole-hand electrical stimulation via a wired mesh-glove upon the residual motor control of the upper extremity have been investigated (34). To study the effect of mesh-glove afferent stimulation on motor control of voluntary wrist movement in stroke subjects who have chronic neurologic deficits, the surface EMG of the arm muscles, and kinematics of voluntary wrist movements on three occasions were assessed: before and immediately after the initial session of mesh-glove stimulation, and then after a daily mesh-glove stimulation program conducted over several months (34). The inclusion criteria for the mesh-glove study were: a history of stroke lasting longer than 6 months; completion of a rehabilitation program during early recovery; and preserved cognitive and communicative ability. A single initial and then daily mesh-glove electrical afferent stimulation was applied to the hand of the involved upper limb for 20–30 min in 14 subjects. Surface EMGs from the affected biceps brachii and wrist extensor muscles and amplitudes of wrist movements showed that the single, initial mesh-glove application had no effect. Following a daily mesh-glove stimulation program, however, both the amplitude of wrist extension movement and wrist extensor integrated EMG were significantly increased while coactivation of biceps brachii decreased. These findings were most prominent in subjects with partially preserved voluntary wrist movements. Sonde et al. (35,36) reported similar findings

when applying low intensity, low frequency stimulation to stroke survivors.

Table 1 summarizes the results of the described studies. The common denominator is that both the electrical therapy and the extensive physical exercise with enhanced feedback contribute and that the contribution is more expressed if the treatment is applied in a timely manner, ie, shortly after the stroke. Most of the studies were limited to outcome measures (FM test, BI, Ashworth scale, FIM), which do not provide realistic information on the actual effect size to the quality of human life after stroke. The results summarized in Table 1 suggest that the electrically-induced functional movements could consolidate the benefits from both the electrical therapy and extensive functional exercise.

These conclusions provoked us to revisit our clinical evaluations of assistive systems for restoring grasping in chronic tetraplegic subjects in order to analyze therapeutic effects caused by the daily usage of a neuroprosthesis. The conclusions motivated us also to start the clinical tests of the functional electrical therapy in stroke subjects by means of a neuroprosthesis.

NEUROREHABILITATION PROMOTED BY FUNCTIONAL ELECTRICAL THERAPY

Functional Electrical Therapy (FET) is a new phrase describing a combination of functional electrical stimulation that generates life-like movement and intensive exercise in humans with impaired sensory-motor mechanisms after stroke or spinal cord injury (SCI). Conventional electrical therapy stimulates sensory-motor mechanisms, but in most cases it does not generate functional movement. Intensive externally induced physical therapies and constraint-induced therapy intensify movement, but they do not activate all the afferent and efferent pathways although they provide a strong sensory input generated by proprioceptive sensory mechanisms. The FET simultaneously provides both effects: 1) external augmentation or generation of movement, and 2) activation of afferent and efferent neuroneal pathways.

One of the earliest studies on the efficacy of FET to improve functioning of the upper extremities after stroke (2) applied a two-channel electrical stimulator to augment elbow extension and fingers/wrist extension. The device used proportional control, and it allowed independent control of each of the stimulation channels. The protocol required at least three weekly sessions lasting for 30 min. The study included eight subjects, and the measure of the abilities was to grasp a basket and transfer it between two arbitrary points. The conclusions were that FES allowed the improvement of both hand and elbow control in all study subjects after two months. The improvement was substantial in five subjects, yet in the remaining three, the improvement was significant at the elbow extension. Simple functional tasks that could not be done without electrical stimulation became possible.

During the development of a new controller to enhance reaching and grasping in humans with spinal cord injuries at cervical level (C5-C7; References 37–39), the outcome measures for efficacy were: the UEFT, the FIM, and coordination between the neighboring joints compared with able-bodied subjects. The outcomes have been followed for at least six months in blinded clinical studies. In all cases, the control applied within the assistive system was based on cloning life-like control of self-paced movement in able-bodied subjects. The devices used for the clinical trials were the Bionic Glove (4,40), and the Belgrade Grasping/Reaching System (3,39,41,42).

The Bionic Glove (40) is a Functional Electrical Stimulation (FES) device designed to improve the function of the paralyzed hand after SCI or stroke. Signals from a sensor in the glove detecting voluntary wrist movement are used to control FES of muscles either to produce hand-grasp or to open the hand. When the glove is donned, the conductive area on its inside surface automatically makes contact with self-adhesive electrodes on the skin. The Bionic Glove system has been evaluated in clinical and home use (4); the results from this study (12 subjects, blinded, randomized study) suggest two major benefits: the externally activated grasping increased the activity of the arm and the hand while accomplishing daily activities and there were carry-over effects from using the Bionic Glove.

The outcome measures in the study were the Quadriplegia Index of Function (QIF), the FIM,

Table 1. An Overview of the Representative Results of the Efficacy of Neurorehabilitation in Stroke Subjects

Treatment	Number of subjects	Time after the onset	Duration of treatment	Outcome measures	Improvement
Constraint-Induced (CI) Movement Therapy (8)	>200	chronic subacute	2 weeks	Quality of movement (laboratory tests)	Significant
				TMS, Neuro-imaging	Increased and modified cortical regions
Constraint-Induced (CI) Movement Therapy (20)	15	subacute	12 days during 2 weeks	Range of movement	Large, significant
Intensive physiotherapy regime & enhanced feedback (21)	132	chronic (6 months)	6 months	Range and speed of movement, strength	Small, significant
Robot enhanced therapy (22)	20	chronic	25 hours during 3 weeks	Motor recovery	Status of proximal muscles, little change in hand functions
Robot enhanced therapy (23)	56	chronic	25 hours during 3 weeks	Fugl-Meyer test, FIM	Status of proximal muscles, FIM increased
EMG initiated electrical therapy (24)	6	chronic	3 months	Fugl-Meyer test, motor recovery test, grip strength	Significant
EMG-triggered stimulation (29)	24	3 months	30 minutes, during 8 weeks	Fugl-Meyer, FIM	Significant
TES below motor threshold (24)	6	chronic	3 months	Fugl-Meyer test, motor recovery test, grip strength	Modest, smaller than TES above motor threshold (EMG-initiated therapy)
Electrical stimulation of wrist extensors in stroke (31)	60	2–4 weeks	30 minutes for 3 days during 8 weeks	Strength and movement range	Modest
FES with surface electrodes of wrist and finger extension (28)	28(46)	6 months	1 hour per day, 15 sessions	Fugl-Meyer test, FIM	Significant FM test very small change in FIM
FES of wrist extensors (32)	60	30–240 days	40 sessions during 8 weeks	Barthel index Ashworth scale	Significant for both FES and control groups, better for FES group
EMG-triggered FES of wrist and finger extension muscles (30)	24	1 year	12 sessions	Box and Block test and the force-generation task	Significant
Mesh-glove stimulation (33,34)	>50	Range and speed of movement, Ashworth scale, Barthel index	Modest to significant improvement of the range and speed, decreased spasticity		
Electrical therapy below the motor threshold (27)	100	6 months	6 weeks	Fugl-Meyer test, Action Research Arm test, Barthel index	Significant differences only at follow-ups, small differences during the treatment

FIM, Functional Independence Measure; TMS, Transcranial Magnetic Stimulation.

the UEFT, and Weekly Usage Log forms (WUL) (4). All tests were done at the beginning of the test, after one, three, and six months of usage. Here (Figure 1) we show the results of the UEFT that included the following tasks: 1) combing hair; 2) using a fork; 3) picking up a VHS tape; 4) picking up a full juice can; 5) picking up a full pop/soda can; 6) writing with a pen;7) answering the telephone; 8) brushing teeth; 9) pouring from a one liter juice box; 10) drinking from a mug; and 11) handling finger food.

Twelve young (25.4 ± 6.7 years of age), male subjects with a SCI between C5 and C7 were included in the evaluation. Ten subjects had a neurologically complete lesion, one a central syndrome, and one a Brown–Sequards syndrome. The subjects were also classified using a four-category Frankel classification: FA–10 subjects (one with a C5 lesion, eight with a C6 lesion, and one with a C7 lesion), FC – one subject (C6), and FD – one subject (C6). Six subjects had received only conservative treatment after their injury, and six had undergone spinal surgery and received conservative treatment. At the beginning of the evaluation, all subjects were over 24 months postinjury. All the subjects signed an informed consent approved by the local ethics committee before they were tested and included in the study.

The *Belgrade grasping/reaching system (BGS)* comprises a four-channel electronic stimulator, electrodes, and a set of sensors. The BGS was designed to enhance the grasping and reaching of humans after SCI and raise their level of independence (3,5). The control is described in

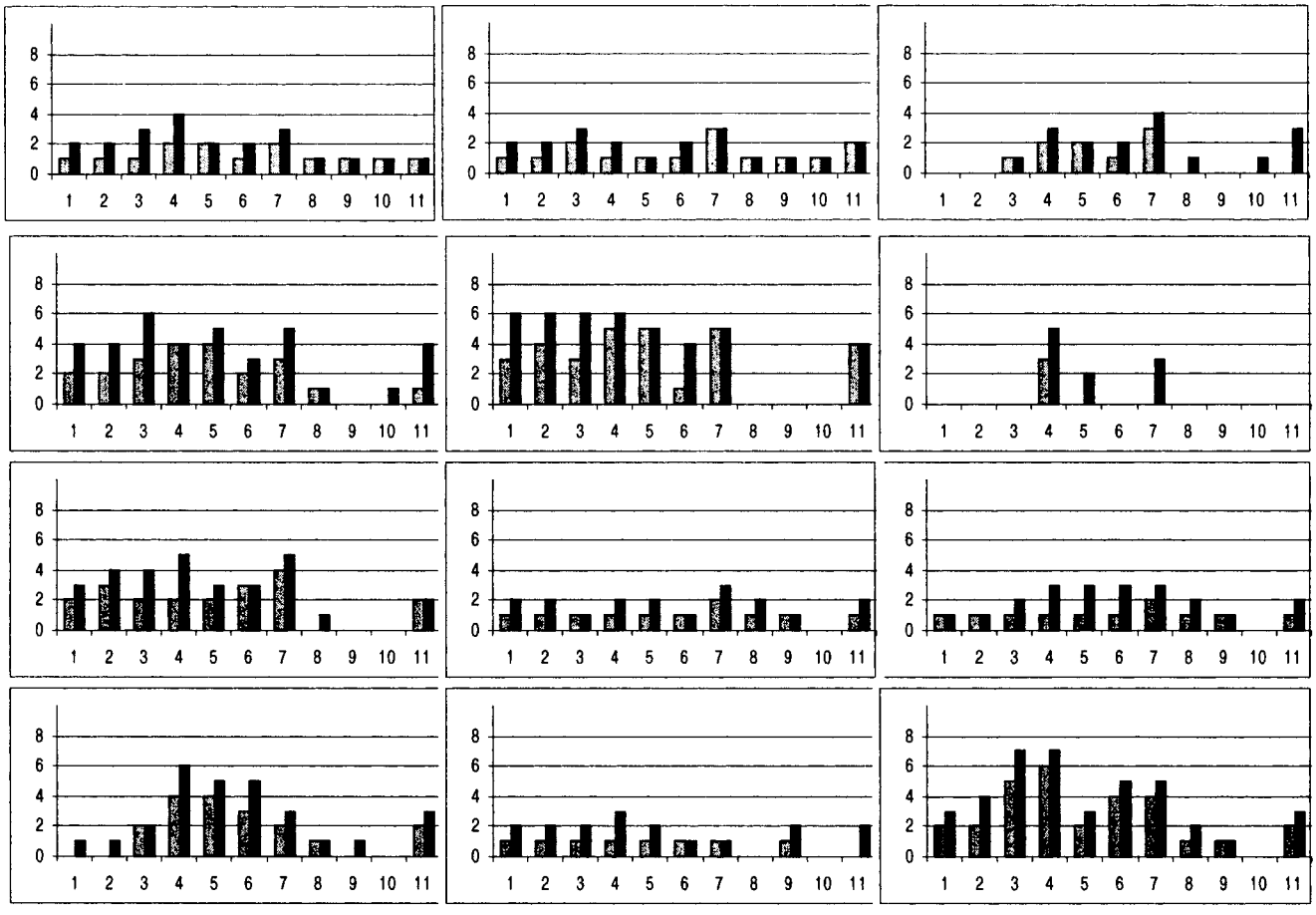

Figure 1. Results of the Upper Extremity Function Test (UEFT) for 12 tetraplegics who used the Bionic Glove to restore grasping (4) for six months. Eleven tasks (horizontal axes) have been evaluated (see text for details). The right (dark) bars are the numbers of successful grasping without the Bionic Glove after six months, the left (light) bars shows the numbers at the beginning of the study with the assistive system.

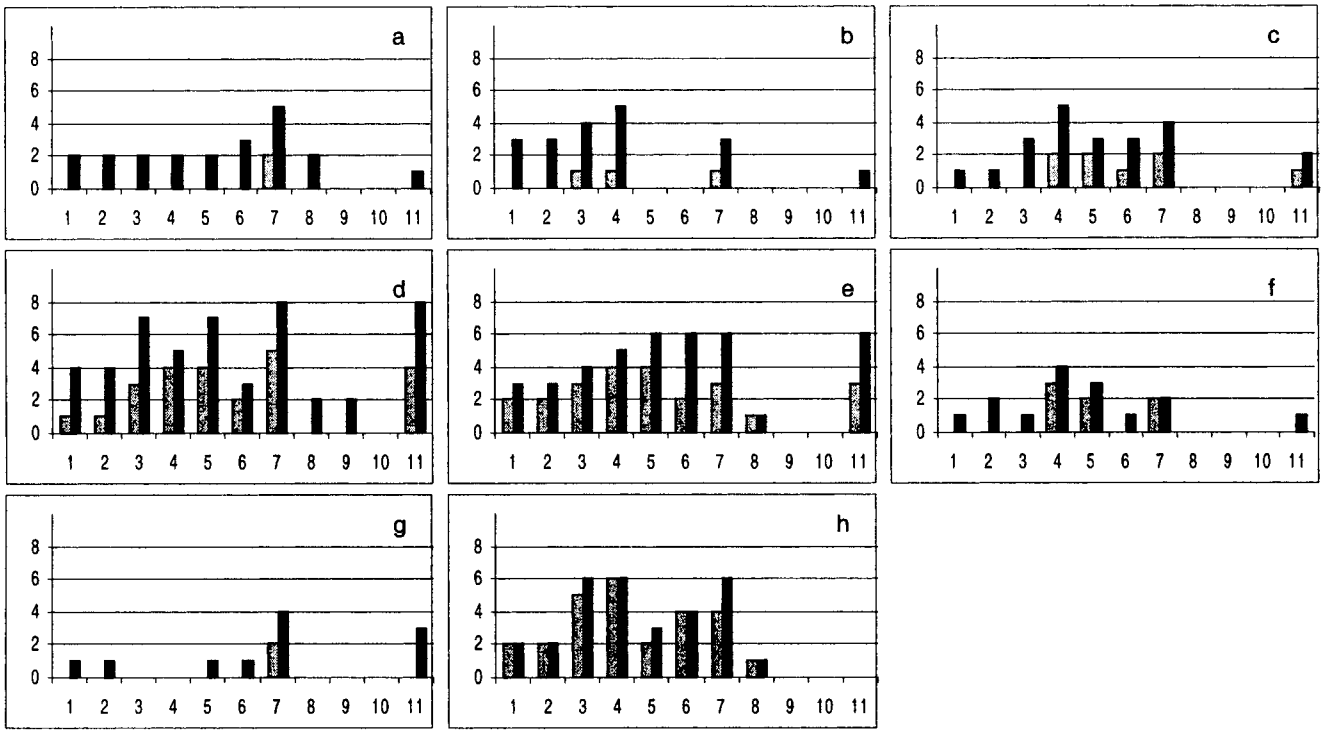

Figure 2. Results of the UEFT for eight tetraplegics who used the Belgrade Grasping System (BGS) (3) for six months. Eleven tasks (horizontal axes) have been evaluated (see text for details). The right (dark) bars are the numbers of successful grasping without the BGS after six months of using the assistive system; the left (light) bars are the measures at the beginning of the study with the assistive system.

details elsewhere (37,39,41,42). This controller implements a sensory-triggered preprogrammed control. BGS provides palmar and lateral grasping and control of elbow joint flexion/extension. The BGS was tested in eight subjects with chronic tetraplegia. Here we show only the results of the UEFT (Figure 2). The main finding from the study is a replica of the results from the study with the Bionic Glove (4): the externally activated grasping increased the activity of the arm and the hand while accomplishing daily activities, and there were carry-over effects from using the BGS.

Eight young (23.8 ± 5.6 years of age), male subjects with a SCI between C5 and C6 were included in the evaluation. All eight subjects had a neurologically complete lesion diagnosed at the time of inclusion in the study. The subjects were classified using a four-category Frankel classification: FA – six subjects (one subject C5, five subjects C6), FC – one subject with C6 lesion, and FD – one subjects with C6 lesion. Four subjects had received only conservative treatment after injury, and four had undergone spinal surgery and received conservative treatment. All subjects had their injury for more than 24 months. All the subjects signed an informed consent approved by the local ethics committee before they were tested and included in the study.

All eight subjects improved their functioning with and without the BGS to a great extent. Figure 2 shows the number of tasks that the subjects were able to do without the BGS at the beginning and at the end of the 6-month evaluation. The summed results of the UEFT are about 20% better when the BGS is applied, yet seven of eight subjects decided not to continue the daily use. The major reason was the complexity of positioning of the electrodes, and donning and doffing of the system. The subject who continued the use of the BGS maintained the muscle bulk and strength, and claims to have reduced spasticity.

The study on shoulder/elbow coordination (37) with an earlier version of the BGS was an important indication of the therapeutic efficiency

of the FES. The FES was driving the elbow flexion/extension based on the shoulder flexion/extension and the scaling synergy (38). The study included 12 chronic tetraplegics with a complete sensory-motor lesion at C5/C6 level. Subjects were asked to sit in their wheelchair, and move their hand between different pairs of initial (I) and target (T) positions, all in the horizontal plane. Subjects were required to move five times their hand between the initial and a target position and repeat this as many times as possible during a five-minute interval. The treatment lasted six weeks.

The top two panels in Figure 3 show typical recordings of the joint angles recorded in one of the subjects prior to the treatment. This subject was able to move his hand five times between the different points I_j and T_j (j = 1 − 6) in five minutes. The two bottom panels show the unassisted movements recorded in the same subject after he used the assistive system for reaching for six weeks; the subject was able to move his hand five times between the initial and target positions to 18 different pairs: I_j and T_j (j = A-S) during a five-minute session. For comparison, an able-bodied subject can typically manage between 25 and 30 different targets when asked to do self-paced movement, during a five-minute interval (37). Two major findings from this study are that six weeks of FES resulted in 1) a new coordination between the shoulder and elbow, and 2) movements became much faster.

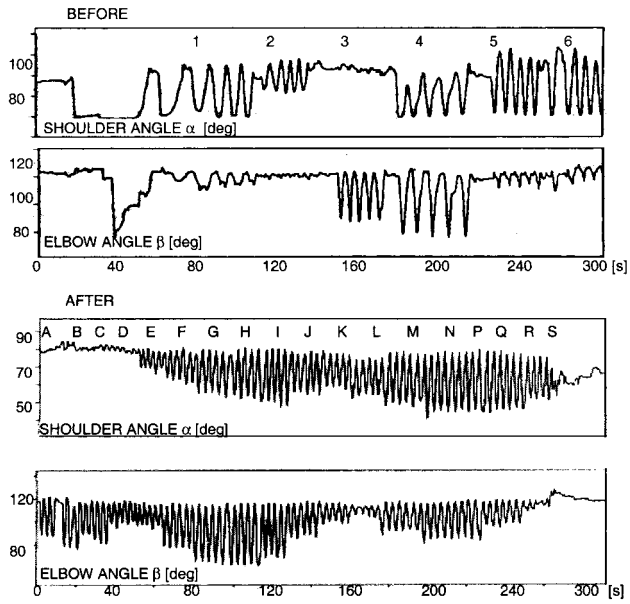

Figure 3. The shoulder and elbow joints (flexion and extension) recorded from a tetraplegic subject before (top two panels) and after the treatment (bottom two panels). The task was to move the hand five times between different initial points and targets as many times as possible during a five-minute interval.

BGS in Stroke Subjects

In a study in progress, eight subjects, less than 2 months after the onset of stroke, participated in a three-week long FET program (6). The subjects were six males and two females, 60.5 ± 2.8 years of age, seven of them with left hemiplegia, and one with right hemiplegia. The spasticity at the beginning of the study was measured by using the Ashworth scale; it ranged from 1 + to 4 (mean 2 +). The subjects were characterized in the so-called Higher Functioning Group (HFG) (8) prior to inclusion in the study based upon their active range of motion capability at the wrist and fingers. The determinations were made with the subject sitting, the forearm resting on a supported surface, and the forearm in pronation. The hand hung over the edge of the supporting surface(eg, the arm of a chair) to allow for maximum wrist flexion with gravity. The subjects were assigned to the HFG if they were able to actively extend the paretic wrist at least 20 degrees, and actively extend the MP and IP joints of the thumb and at least two additional digits 20 degrees.

The FET was applied with the BGS and surface disposable electrodes. Two channels were used to stimulate the finger flexors and finger extensors. The subjects used a switch, which sequentially triggered opening and closing of the hand. The pulse duration and the frequency were set for each subject in such a manner to minimize unpleasant sensation and pain, yet provide active, externally assisted grasp. The FET sessions lasted for 30 min, for at least five days a week, during the three consecutive weeks. An FET session consisted of performing exercise tasks as many times as possible. The exercise tasks were randomly selected among the 11 activities being part of the UEFT, and it consisted of the following: reach an object located within the

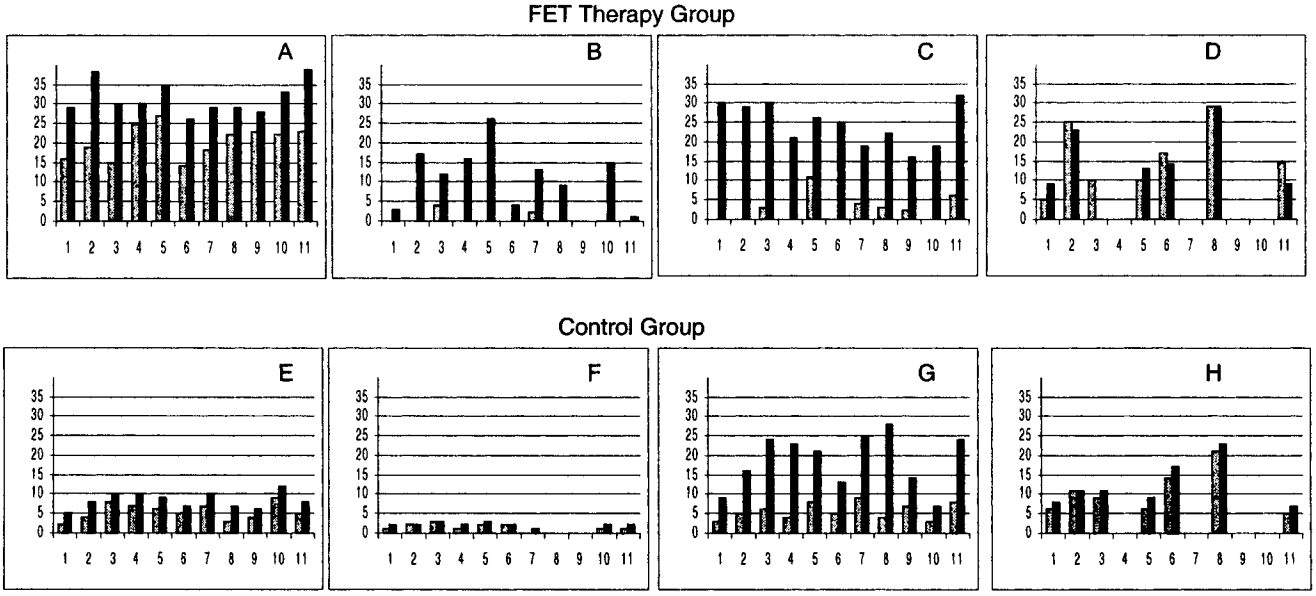

Figure 4. Upper Extremity Function Test in subacute stroke subjects: FET group (A-D) and controls (E-H). Eleven functional tasks (horizontal axes) have been evaluated (see text for details). The right (dark) bars are the results after three weeks (FET or only conventional therapy), and the left (light) bars are at the beginning of the study.

workspace, grasp, and use it functionally (eg, drink from a can, write with a pen, put the tape in the VCR recorder, pick up a telephone receiver and talk to other party), return the object to its original position, and release it. The subjects from the control group were required to exercise the same as the FET group, yet without the electrical stimulation of the muscles.

Here we present two outcome measures: the UEFT, and the drawing of the square on the digitizing board. The purpose of the UEFT was to determine the differences in the performance of certain activities of daily living before and after the FET. The performance was graded as success (YES) if the subject was able to perform the task (reach, grasp, use, return the object to the original post, and release it) with the affected arm/hand, and failure (NO) if opposite. In cases where the performance was "YES", we counted the number of repetitions of the selected task during one-minute interval. Figure 4 shows the UEFT for FET and control group before and at the end of the three weeks of therapy.

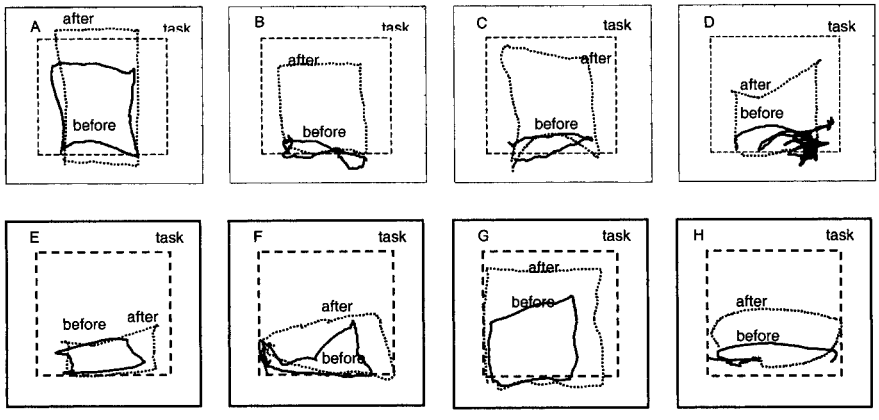

Figure 5. Results of drawing of the FET group (subjects A-D), and the controls (subjects E-H) at the digitizing board (30 cm × 30 cm). Full lines show the recordings before FET, and doted lines after FET. The task was to track the square (20 cm × 20 cm) shown with the dashed line.

Table 2. Average Number of Successful Functional Movements and the Numbers of Accomplished Tasks (Maximum 11) During One Minute

Average number of accomplished trials during one minute			Average number of accomplished tasks during one minute			Number of subjects	Therapeutic device
Before	After	Difference	Before	After	Difference		
Chronic tetraplegic subjects C5-C7 (minimum 2 years post-injury)							
1.43 ± 0.60	2.30 ± 0.75	0.9 ± 0.65	8 ± 2	9 ± 1	1 ± 1	12	Bionic Glove
2.36 ± 0.72	2.7 ± 1.01	0.34 ± 0.32	4 ± 3	8 ± 1	4 ± 2	8	BGS
Sub-acute and acute stroke subjects (two to six weeks after the onset of stroke)							
2.29 ± 0.78	4.57 ± 2.26	2.28 ± 1.12	9 ± 2	10 ± 1	1 ± 1	4 (controls)	none
4.06 ± 3.24	9.63 ± 4.38	5.57 ± 4.01	8 ± 3	10 ± 1	2 ± 1	4 (FET)	BGS

The top portion of the table are the results from the 12 tetraplegics who used the Bionic Glove for six months (4), and 8 tetraplegics who used the Belgrade Grasping System (BGS) for six months (3), The bottom part of the table are the results from stroke subjects who received FET or only conventional therapy shortly after the cerebro-vascular infarction for three weeks (6).

Figure 5 shows the drawings of the square on the digitizing board for the FET and control group. Plots illustrate the difference in coordination of the upper arm/lower arm to external space before and after the FET for the group assigned to the therapy. Two elements are characteristic for all subjects: they were able to draw much faster, and they followed the task template (size and straight-line movement) much better at the end of the therapy.

The functional outcome of the FET in spinal cord injured and stroke subjects described above are summarized in Table 2. These three studies are a strong indicator that the FES systems developed for assisting movement in humans with upper-limb disabilities have two major impacts: 1) they contribute to the immediate functional ability to reach and grasp; and 2) they promote faster long-term restitution of functional movement, that is, they increase independence and provide potentially better quality of life. This statement needs to be supported by larger multicenter trials in which the FET would be compared with other neurorehabilitation techniques.

DISCUSSION

The therapeutic effects of the FET could be associated to the two following components: 1) the electrical stimulation generates very strong central input that is combined with the volitional commands. This sensory input is likely to become integrated into the newly developed sensory-motor scheme being responsible for the improved functioning. Other sensory-motor mechanisms that are part of the motor program are reactivated and thereby contribute to the cortical organization of the movement; and 2) intensive exercise of affected extremities during which the joints are driven close to the normal range of movement contributes to the otherwise unavailable propriceptive input to the CNS. Therapeutic electrical stimulation rebuilds the muscle and increases the muscle fatigue resistance. Once the treatment is over, it is expected that if movements are reinstituted, the exercise will continue through volitional, regular daily activity; that is, the no-use pattern will be eliminated.

In addition, the improved functioning is likely to be a strong motivation for increased activity with the paralyzed/paretic arm and hand. The awareness that the movement is available increases the voluntary employment of the paralyzed/paretic arm and hand; thus, better symmetry between the affected and unaffected sides will be developed. This symmetry is an important asset for normalizing postural control, thereby better usage of the affected extremity.

The focal transcranial magnetic stimulation (TMS), EEG, and magnetic source imaging (MEG) studies with humans, carried out by several groups of investigators suggest that cortical reorganization may be associated with the therapeutic effect of the rehabilitation therapy. Elbert and coworkers (43) found that the cortical somatosensory representation of the digits on the left hand was larger in string players,

who use their left hand for the dexterous task of fingering the strings, than in nonmusician controls. Moreover, the representation of the fingers of blind Braille readers who use several fingers simultaneously to read was both enlarged and disordered; the latter neurophysiologic aberration was associated with a perceptual disturbance in which the subjects could not discriminate which of their fingers was being touched (44). The ''massive'' cortical reorganization could take place after somatosensory deafferentation of an entire forelimb in primates (45). The amount of cortical reorganization is strongly correlated with the following pathologic conditions: phantom limb pain (46), tinnitus (47), and focal hand dystonia in keyboard musicians and guitarists (48). The CNS correlates of these conditions had been long sought; however, it was not possible to identify them until Elbert et al. (49) and Yang et al. (50) showed that massive cortical reorganization takes place in humans after CNS lesion. These results, especially those relating to use-dependent cortical reorganization, suggest that the size of the cortical representation of a body part in an adult human depends on the amount of use of that part.

Liepert and colleagues (51,52) reported the treatment-induced plastic changes in the human brain after a treatment-induced movement in stroke subjects. They used focal transcranial magnetic stimulation to map the cortical motor output area of a hand muscle on both sides in 13 stroke subjects in the chronic stage of their illness before and after a 12-day period of constraint-induced movement therapy. Before treatment, the cortical representation area of the affected hand muscle was significantly smaller than the contralateral side. After treatment, the muscle output area size in the affected hemisphere was significantly enlarged, corresponding to a greatly improved motor performance of the paretic limb. Shifts of the center of the output map in the affected hemisphere suggested the recruitment of adjacent brain areas. In follow-up examinations up to 6 months after treatment, the motor performance remained at a high level, whereas the cortical area sizes in the two hemispheres became almost identical, representing a return of the balance of excitability between the two hemispheres toward a normal condition.

Other questions need to be answered before desired effects of the FET can be achieved. The most important questions relate to when and to whom the therapy should be applied, and what is the optimal duration of the therapy. The more complex questions are: should it be more effective to combine FET with other therapies (eg, constraint-induced therapy), and is it necessary to reapply FET if the redeveloped arm-hand mechanisms start disappearing in the long term?

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