Functional Electrical Stimulation Therapy: Recovery of Function Following Spinal Cord Injury and Stroke

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Abstract

 Functional electrical stimulation (FES) is a technology one can use to artificially generate body movements in individuals who have paralyzed muscles due to injury to the central nervous system. More specifically, FES can be used to generate functions such as grasping and walking in individuals with spinal cord injury (SCI), stroke, traumatic brain injury and other neurological disorders that do not affect lower motor neurons. This technology was originally used to develop neuroprostheses that were implemented to permanently substitute impaired functions such as bladder voiding, grasping, and walking. In other words, a consumer would use the device each time he/she wanted to generate a desired function. In recent years, FES technology has been used to deliver, therapies to retrain voluntary motor functions such as grasping, reaching and walking. In this application, FES is used as a short-term therapy, the objective of which is restoration of voluntary function and not lifelong dependence on the FES device, hence the name FES therapy or FET. The FET is used as a shortterm intervention to help the central nervous system of the consumer to relearn how to execute impaired functions. In this chapter, we introduce recent findings and advances in the field of FET.

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The findings to date clearly show that FET for reaching and grasping is a therapeutic modality that should be implemented in every rehabilitation institution that is treating patients with stroke and SCI. The results obtained in a number of randomized control trials to date clearly demonstrate that FET for upper limb should not be ignored any longer. There is also considerable evidence to support the use of FET as a therapeutic modality to treat drop foot problem in both stroke and incomplete SCI populations. Several commercial FES systems are available that can be used to deliver FET for drop foot and grasping, and physiotherapists and occupational therapists should take advantage of this technology.

 Presently, few teams in the world are investigating the use of more complex FES systems (6–16 channels FES systems that stimulate muscles in one or both legs in a physiologically appropriate manner) for retraining voluntary walking function in stroke and incomplete SCI populations. Although comprehensive randomized control trials have not been completed yet with either patient population, preliminary findings are very encouraging.

 As surface FES technology is continuously improving and delivery methods for FET are evolving due to system miniaturization, better stimulation electrodes, and better stimulation protocols, it is foreseeable that, in the next 10–15 years, FET will become one of the dominant interventions for upper and lower limb rehabilitation. Many neuroprostheses are already commercialized and many more are near in the process of being developed and/or commercialized. Thus, we feel very confident that FET field is only beginning to evolve, and that, in the future, it may become one of the key therapeutic interventions not only for patients with stroke and SCI but also for patients with other neuromuscular disorders.

Keywords

 Functional electrical stimulation (FES) • FES therapy • Spinal cord injury • Stroke • Neuroprosthesis

7.1 Introduction

 Individuals with neurological disorders such as spinal cord injury (SCI), traumatic brain injury, and stroke are frequently unable to voluntarily move different body parts and perform functional movements. However, as long as the nerves innervating the muscles and the joints are intact, the electrical stimulation can be used to generate joint movements by contracting muscles that actuate the joints. If the muscle contractions produced using electrical stimulation are coordinated and generate functional movements such as standing, walking, or grasping this form of electrical stimulation is called functional electrical stimulation (FES). This technology was originally develop with an idea to create neuroprostheses. The neuroporstheses are devices that artificially generate functional movements discussed above in the limbs and body parts of paralyzed individuals, by artificially contracting muscles of that individual. In other words, for a consumer to perform a grasping task he/she would need to use the neuroprosthesis for grasping each and every time he/ she wants to grasp an object. In the last decade it has been demonstrated by few research groups

that if the FES is applied as a short-term therapeutic intervention in stroke and incomplete SCI individuals, these individuals are able to partially or completely restore voluntary function that has been trained, namely reaching, grasping and walking. Therefore, FET can be used as a shortterm intervention to help the central nervous system of the consumer re-learn how to voluntarily execute impaired functions, instead of making the consumer dependent on a neuroprosthesis for the rest of his/her life. In this chapter, we introduce recent findings and advances in the field of FET.

7.2 Functional Electrical Stimulation (FES)

7.2.1 Defi nitions

 Individuals with SCI and stroke have injuries that prevent the central nervous system from generating a desired motor command and/or transmitting the desired motor command to the parts of the peripheral nervous system that innervate muscles. As a result, these individuals are frequently unable to voluntarily move different body parts and perform functions such as sitting, standing, reaching, grasping, and bladder voiding. However, as long as the nerves innervating the muscles, the muscles themselves, and the joints and soft tissues supporting the musclejoint structures are intact, the electrical stimulation can be used to generate joint movements by contracting the muscles that actuate them. The electrical stimulation used for this purpose is called neuromuscular electrical stimulation (NMES). An organized and patterned NMES that aims to generate coordinated limb or body movements, instead of isolated muscle contractions, is called functional electrical stimulation (FES). One of the possible applications of FES technology is to artificially generate body movements such as grasping, standing, and walking. In such a context, the FES technology is used as a prosthetic device; in literature, this use of FES technology is referred to as *neuroprosthesis* or *neuroprosthetics* .

Fig. 7.1 A schematic representation of the surface FES system. The FES system causes a muscle contraction by electrically stimulating the motor axons that are connected to the muscles. The electrical stimulation generates action potentials in the motor neurons, which propagate along the motor neurons toward the muscle. When the action potentials reach the muscle, they cause the muscle to contract

7.2.2 Physiology

 In nerve cells, information is coded and transmitted as a series of electrical impulses called action potentials, which represent a brief change in cell electric potential of approximately 80–90 mV. Nerve signals are frequency modulated; that is, the number of action potentials that occur in a unit of time is proportional to the intensity of the transmitted signal. Typical action potential frequency is between 4 and 12 Hz. An electrical stimulation can artificially elicit this action potential by changing the electric potential across a nerve cell membrane (this also includes the nerve axon) by inducing electrical charge in the immediate vicinity of the outer membrane of the cell (Fig. 7.1).

 The stimulated nerve bundle includes motor nerves (efferent nerves – descending nerves from the central nervous system to muscles) and sensory nerves (afferent nerves – ascending nerves from sensory organs to the central nervous system). In some applications, FES can be used to directly stimulate muscles, if their peripheral

nerves have been severed or damaged (i.e., denervated muscles) $[1]$. However, the majority of the FES systems used today stimulate the nerves or the points where the junction occurs between the nerve and the muscle. The main reason is the fact that direct muscle stimulation requires considerably more energy to generate contractions (at least three orders of magnitude more $[2]$), which makes these systems more challenging to implement at home and in clinical settings.

 The electrical charge can stimulate both motor and sensory nerves. In some applications, the nerves are stimulated to generate localized muscle activity, i.e., the stimulation is aimed at generating direct muscle contraction. In other applications, stimulation is used to activate simple or complex reflexes. In other words, the afferent nerves are stimulated to evoke a reflex, which is typically expressed as a coordinated contraction of one or more muscles in response to the sensory nerve stimulation.

When a nerve is stimulated, *i.e.*, when sufficient electrical charge is provided to a nerve cell, a localized depolarization of the cell wall occurs resulting in an action potential that propagates toward both ends of the axon. Typically, one "wave" of action potentials will propagate along the axon toward the muscle (orthodromic propagation), and concurrently, the other "wave" of action potentials will propagate toward the cell body in the central nervous system (antidromic propagation). While the direction of propagation in case of the antidromic stimulation and the sensory nerve stimulation is the same, i.e., toward the central nervous system, their end effects are very different. The antidromic stimulus has been considered an irrelevant side effect of FES. However, in recent years, a hypothesis has been presented suggesting the potential role of the antidromic stimulation in neurorehabilitation $[3]$. Typically, FES is concerned with orthodromic stimulation and uses it to generate coordinated muscle contractions.

 In the case where sensory nerves are stimulated, the reflex arcs are triggered by the stimulation of sensory nerve axons at specific peripheral sites. One example of such a reflex is the flexor withdrawal reflex. The flexor withdrawal reflex occurs naturally when a sudden, painful sensation is applied to the sole of the foot. It results in flexion of the hip, knee, and ankle of the affected leg, and extension of the contralateral leg in order to get the foot away from the painful stimulus as quickly as possible. The sensory nerve stimulation can be used to generate desired motor tasks, such as evoking flexor withdrawal reflex to facilitate walking in individuals following stroke, or they can be used to alter reflexes or the function of the central nervous system. In the later case, the electrical stimulation is commonly described by the term *neuromodulation* .

7.2.3 Technology

 Nerves can be stimulated using either surface (transcutaneous) or subcutaneous (percutaneous or implanted) electrodes. Surface electrodes are placed on the skin surface above the nerve or muscle that needs to be "activated." They are noninvasive, easy to apply, and generally inexpensive. Due to the electrode-skin contact impedance, skin and tissue impedance, and current dispersion during stimulation, much higher-intensity pulses are required to stimulate nerves using surface stimulation electrodes as compared to the subcutaneous electrodes. A major limitation of the transcutaneous electrical stimulation is that some nerves, for example those innervating the hip flexors, are too profound to be stimulated using surface electrodes. This limitation can be partly addressed by using arrays of electrodes which can use several electrical contacts to increase selectivity [4–6].

 Subcutaneous electrodes can be divided into percutaneous and implanted electrodes. The percutaneous electrodes consist of thin wires inserted through the skin and into muscular tissue close to the targeted nerve. These electrodes remain in place for a short period of time and are only considered for short-term FES interventions. One of the drawbacks of using the percutaneous electrodes is they are prone to infection and special care has to be taken to prevent such events. The other class of subcutaneous electrodes is implanted electrodes. These are permanently implanted in the consumer's body and remain in the body for the remainder of the consumer's life. Compared to surface stimulation electrodes,

implanted and percutaneous electrodes potentially have higher stimulation selectivity with much less electrical charge applied, both of which are desired characteristics of FES systems. To achieve higher selectivity while applying lower stimulation amplitudes, it is recommended that both cathode and anode are in the vicinity of the nerve that is stimulated. The drawbacks of the implanted electrodes are they require an invasive surgical procedure to install, and, as is the case with every surgical intervention, there exists a possibility of infection following implantation.

7.3 FES Therapy (FET)

7.3.1 Defi nition

 FES can be used for neuroprosthetic and therapeutic purposes. If FES is used as a neuroprosthesis, the purpose of this device is to generate a body function that the consumer is unable to perform alone, such as walking, biking, bladder voiding, grasping, etc. In this application, the FES system needs to be worn or used each and every time the consumer needs to perform the desired function. In essence, the consumer uses the FES device as a permanent orthotic system.

 The use of neuroprostheses as a means of providing short-term therapeutic intervention for improving and restoring voluntary function has been termed FES therapy or FET [7]. When the FES technology is used to deliver FET, the purpose of that intervention is to restore voluntary function. In other words, FET is used only temporarily as a short-term intervention with the objective of helping the neuromuscular system relearn to execute a function impaired due to neurological injury or disorder. In this application, the ultimate goal of the FES intervention is for the consumer to recover voluntary function, as much as possible, so the consumer does not need to use the FES system for the rest of his/her life. In this application, the central nervous system essentially relearns how to control the impaired muscles and how to contract them in a temporarily appropriate manner to generate the desired body function.

 Some neuroprosthetic systems are also used for cardiovascular conditioning and muscle strengthening. Although the ultimate goal of this type of application is therapeutic, this is not FET. Good examples of these FES systems are neuroprostheses for rowing and biking. Each time the consumer wants to row or bike, he/she needs to use the neuroprosthetic system, without which he/ she would not be able to perform this task at all.

 The implanted FES systems are primarily used as permanent neuroprostheses, and some attempts have been made to use the BION implantable FES system for FET. On the other hand, the surface FES systems have been used equally well as neuroprostheses and platforms to deliver FET. In the past, the main focus of the FES field was on developing neuroprosthetic systems, in particular those that consumers had to use daily. In recent years, the advances made in the field of FET and the use of neuroprostheses for muscle strengthening and cardiovascular exercises have shifted the focus of the FES field, at least partially, toward the use of surface FES systems. As a result, a number of commercially available surface FES systems have been developed in the last decade.

7.3.2 Carryover Effect

 Since the 1970s, some researchers and practitioners in the field of FES have observed that many consumers who use FES on a regular basis experience significant carryover in function that persists even when the device is not in use. This "enigma" of "carryover effect" has interested researchers [8], even though most of these reports were anecdotal in nature at the beginning.

One of the first papers that specifically discussed this phenomenon was an article authored by Merletti et al. in 1975 $[9]$. They investigated the carryover effect of FES on hand opening and elbow extension functions for stroke patients. Three of five patients showed the carryover effect after a 2 months training period, i.e., after the FES intervention session, functional tasks such as the shifting of an object between two specified areas on a desk were improved even without wearing the FES device. The observed carryover effect supported the potential role of neuroprostheses as therapeutic interventions in clinical practice. Despite the fact that FES-related carryover results **Fig. 7.2** NESS L300 foot drop system (Photo courtesy Bioness Inc., Valencia, CA, USA)

were observed as early as the 1970s, a rigorous investigation of FES carryover effect started only recently.

7.4 Current Evidences of FET

 It took almost two decades before the carryover effect started being examined seriously. First, it was examined with the drop foot FES systems, where scientists explored the ability of the system to restore voluntary walking function in individuals with stroke. These studies were then followed by studies examining the use of a neuroprosthesis for grasping, and later, neuroprostheses for reaching and grasping for restoring voluntary arm and hand functions in individuals with stroke and SCI. Finally, the neuroprosthesis for walking was used to investigate restoration of voluntary walking function in individuals with incomplete SCI.

7.4.1 FET for Restoration of Lower Limb Function Following Stroke

 Among stroke patients, the drop foot is a common symptom characterized by a lack of dorsiflexion during the swing phase of gait, resulting in short, shuffling strides. It has been shown that the drop foot stimulator effectively compensates for the drop foot during the swing phase of the gait. At the moment just before a heel-off phase of the gait occurs, the drop foot stimulator induces a stimulus at the common peroneal nerve which results in contraction of the muscles responsible for dorsiflexion (Fig. 7.2). There are number of drop foot stimulators, which use surface FES technology and have been FDA (US Food and Drug Administration) approved, that have been developed to date: the Odstock dropped foot stimulator $[10]$, the WalkAide $[11]$, and the NESS L300 (formally known as NESS drop foot system) $[12]$. The ActiGait $[13]$ and the STIMuSTEP $[14]$ are implantable drop foot stimulators that are also commercially available and have the CE mark in Europe. Drop foot stimulators are one of the most successful neuroprostheses to date. Overall, consumer perception of the drop foot stimulators is they are superior to the ankle-foot orthosis [15].

 There has been a great deal of evidence showing the benefits of FES for the lower limbs of stroke patients. In most of the studies, the effect of the drop foot stimulator has been studied (only few studies have studied FET in gait with stroke patients, e.g., $[16]$). In the early phase, some studies showed a negative result with respect to the carryover effect $[17, 18]$, while other studies showed positive effect on the carryover effect [10]. For example, Granat et al. $[18]$ investigated the effect of a drop foot stimulator on hemiplegic patients $(n=19)$ in a two-period crossover study design (4 weeks control period followed by

4 weeks FES treatment period). The results demonstrated that there was a significant orthotic effect (positive effect when the subject was using the FES system) in inversion of ankle, while the same study did not show a therapeutic effect (positive effect when the subjects were not using the FES system, i.e., carryover effect). In a randomized controlled trial, Burridge et al. [17] investigated the effect of a drop foot stimulator on individuals with stroke. The test group $(n = 16)$ received conventional physiotherapy and FES treatment, while the control group $(n=16)$ received conventional physiotherapy alone. They demonstrated that the mean increase in walking speed was 20.5% in the treatment group when the subjects in that group used the drop foot stimulator as an orthosis. The control group showed only a 5.2% increase in mean walking speed. The physiological cost index (PCI) was reduced 24.9% in the treatment group when they were using the drop foot stimulator as an orthosis, and was reduced 1% in the control group. However, the same study did not show any improvements in the treatment group when the drop foot stimulator was removed. In other words, they were not able to demonstrate the drop foot stimulator's carryover effect. Taylor et al. $[10]$ investigated the effect of a drop foot stimulator in stroke $(n=9)$ and multiple sclerosis (MS) $(n=2)$ patients. Stroke patients showed a mean increase in walking speed of 27% and a reduction in PCI of 31% when the system was used as an orthosis. However, the same study showed a 14% increase in walking speed and a 19% reduction in PCI when the stimulator was removed from the patients, i.e., carryover effect. The MS patients showed similar benefits when they used the drop foot stimulator as an orthosis, with no noticeable carryover effects.

 Recently, in a relatively larger population study, Stein et al. $[11]$ investigated the effect of a drop foot stimulator in stroke $(n=41)$ and MS $(n=32)$ patients. They demonstrated that both stroke and MS patients showed increased walking speed when the system is used as therapeutic and orthotic devices. After 3 months of drop foot stimulator training, both groups had a similar and significant orthotic (increments of 5.0% and 5.7%

for stroke and MS patients, respectively) and therapeutic (17.8% and 9.1% for stroke and MS patients, respectively) effects on walking speed during on ground figure-8 walking. After 11 months of following the baseline, the therapeutic effect on figure-8 speed diverged between the two groups to 28.0% and 7.9% for stroke and MS patients, respectively. Overall, PCI showed a decreasing trend. They concluded that both subject groups had an orthotic benefit from FES up to 11 months. The therapeutic effect increased up to 11 months in stroke patients, which is a nonprogressive neurologic disorder, while in the MS patients, as expected, the therapeutic effect increased only in the first 3 months following the baseline.

 In summary, there is considerable evidence that the drop foot stimulators, if they are used to deliver FET, produce lasting positive changes in gait in individuals with hemiplegic stroke.

7.4.2 FET for Restoration of Lower Limb Function Following SCI

 Impairment in lower limb function is a common symptom following SCI. Various FES systems have been developed to help individuals with SCI to improve walking function. In individuals with SCI, the scope of impairment is not limited to the ankle joint, as is the case with many stroke individuals, but rather affects many muscles in the legs, pelvis, and trunk. Thus, the FES technology for walking for individuals with SCI is more diverse and targets the muscles of the entire lower limb. However, it is not uncommon that in some individuals with SCI, the above-discussed drop foot stimulators have been also used as a means to assist with gait.

 As early as the 1960s, Kantrowitz demonstrated paraplegic standing by applying continuous electrical stimulation to the quadriceps and gluteus maximus muscles of a patient with complete SCI, using surface FES technology [19]. This earliest neuroprosthesis for paraplegic "gait" provided continuous stimulation to the quadriceps to produce a mode of gait similar to long leg-brace walking, by inducing stiffened legs.

 Fig. 7.3 Parastep electrical stimulation system (Photo courtesy Sigmedics, Inc., Fairborn, OH, USA)

Later systems used alternating bilateral quad/glut stimulation (during stance phase) out of phase with peroneal nerve stimulation to induce the flexor withdrawal reflex (during swing phase) $[20]$. Following that, Kralj et al. described a technique for paraplegic gait using surface electrical stimulation, which remains the most popular method in use today $[21]$. Electrodes are placed over the quadriceps muscles and peroneal nerves bilaterally. The user controls the neuroprosthesis with two pushbuttons attached to the left and right handles of a walking frame, or on canes, or crutches. When the neuroprosthesis is turned on, both quadriceps muscles are stimulated to provide a standing posture. The left button initiates the swing phase in the left leg by briefly stopping stimulation of the left quadriceps and stimulating the peroneal nerve. This stimulation is applied suddenly, so as to trigger the flexor withdrawal reflex, resulting in simultaneous hip and knee flexion, as well as dorsiflexion. After a fixed period of time, peroneal nerve stimulation is stopped, and quadriceps stimulation is initiated while the reflex is still active to complete the stride. Similarly, the right button initiates swing phase in the right leg. Many current FES systems for walking have employed this technique as the

basic concept. As microprocessor technology developed, neuroprostheses for walking became more portable and flexible. Examples of this type of neuroprosthesis are Parastep $[22, 23]$, HAS [24], and RGO [25], and the Case Western Reserve University (CWRU)/VA neuroprosthesis [26–29]. The Parastep system is one of most popular products and uses Kralj's technique $[22, 23]$ (Fig. 7.3). The HAS and the RGO walking neuroprostheses are devices that, in addition to FES, also apply active and passive braces, respectively. The braces were introduced to provide additional stability during standing and walking and to conserve the user's energy. CWRU/VA neuroprosthesis is an implant system $[26-29]$. Parastep, HAS, and RGO systems were designed for orthotic use; however, they could be potentially implemented as FET devices as well.

 The above neuroprostheses for walking apply the flexor withdrawal reflex to generate sapping movement during the walking cycle. There is a disadvantage in using this approach as the flexor withdrawal reflex is highly variable and is subject to rapid habituation. However, there are systems that do not use the flexor withdrawal reflex; instead they stimulate muscles in a manner that is as close as possible to the physiologically correct

muscle activation pattern that generates the bipedal walking cycle. Good examples of such systems are the Case Western Reserve University (CWRU)/VA neuroprosthesis [26–29], Praxis [30], and Compex Motion neuroprosthesis for walking $[31, 32]$. The Praxis and CWRU/VA neuroprosthesis are implantable FES device that have 22 and 8–16 stimulation channels, respectively. They are able to generate sit-to-stand, walking, and stand-to-sit functions, and are suitable for orthotic applications. However, recently the Cleveland team tested the therapeutic effects of their implantable system in a single-subject study [26]. Compex Motion neuroprosthesis for walking is an eight to sixteen channel surface FES system used to restore walking in stroke and SCI individuals $[31]$. The system uses a push button control strategy, similar to the one used in the Parastep system, and a gate phase detection sensor $[33]$ to trigger the FES sequences. What is unique about this FES system is that it was specifi cally developed for FET applications. The benefits of FES for lower limbs of individuals with incomplete SCI were discussed in a review by Bajd et al. $[34]$. The review concluded that there are various benefits including therapeutic effect of FES for individuals with SCI, of strength training, drop foot stimulator, and plantar flexor stimulation during gait phase.

In addition to those studies, Wieler et al. [35] investigated, in a multicenter study, the effect of a drop foot stimulator and a withdrawal reflex stimulator on individuals with SCI $(n=31)$ and with cerebral impairment $(n=9)$. The results showed that the walking speed increased by approximately 40% when the drop foot stimulator was used as an orthotic device and 20% as when it was used as FET device.

Thrasher et al. $[32]$ hypothesized that direct muscle stimulation would have greater rehabilitative potential than the stimulation of flexor withdrawal reflexes. They investigated the effect of a gait-patterned multichannel FES in five individuals with chronic, incomplete SCI. These subjects were trained for 12–18 weeks using Compex Motion multichannel neuroprosthesis for walking. All subjects demonstrated considerable improvements in walking function over the training period. Four of the subjects achieved significantly increased walking speeds, which were due to increases in both stride length and step frequency. The fifth subject experienced a significant reduction in preferred assistive devices. The results suggest that the proposed FES-based gait training regimen was effective for improving voluntary walking function in a population for whom significant functional changes are not expected, and that this application of FET is viable for restoration of voluntary gait in incomplete SCI.

 In summary, there is mounting evidence that, in individuals with incomplete SCI, neuroprostheses for walking can be used as FET devices to improve voluntarily walking function. Most of the work has been done using drop foot stimulators. However, more complex FES systems have been recently tested as FET systems and have shown encouraging results with respect to improving voluntary walking function in more severely disable individuals with SCI.

7.4.3 FET for Restoration of Upper Limb Function Following Stroke

 Impaired reaching and grasping functions are common symptoms among individuals with stroke. Numerous neuroprostheses have been designed to compensate for lost grasping $[36-47]$ $[36-47]$ $[36-47]$, and grasping and reaching $[7, 31, 48-50]$ $[7, 31, 48-50]$ $[7, 31, 48-50]$ functions in stroke patients.

 Some notable grasping and/or reaching neuroprostheses (not necessarily developed for individuals with stroke) are the Freehand system $[51]$, the NESS H200 (formally known as NESS Handmaster) $[40]$ (Fig. [7.4](#page-9-0)), the Bionic Glove [41, 44, 52], the ETHZ-ParaCare neuroprosthesis for grasping $[31, 53]$, the systems developed by Rebersek and Vodovnik [45], the Belgrade Grasping-Reaching System [49], Compex Motion neuroprosthesis for reaching and grasping $[31]$, and the percutaneous systems by Chae et al. [36, 37. These neuroprostheses for grasping were shown to restore the power grasp and the precision grip. The power grasp is used to hold larger and heavier objects between the palm of the hand and the four fingers. During a power grasp, the object is held in a clamp formed by partly flexed fingers and the palm counter pressure being

applied by the thumb lying more or less in the plane of the palm. Precision grip is used to hold smaller and thinner objects, such as keys and paper, between the thumb and forefinger. The precision grip is generated by flexing the fingers followed by opposition of the thumb. The Freehand system is an implantable FES system designed for individuals with SCI, while the remaining devices are surface FES systems that can be used to deliver FET to both stroke and SCI individuals.

 Use of FES as means of improving hand function following stroke has been intensively studied for a long time. A meta-analysis in 1996 already proved that FES is effective in recovery of muscle strength after stroke in terms of muscle strength $[54]$. Recent studies that have specifically examined FET have suggested positive outcomes in acute $[7, 41, 42, 48]$ $[7, 41, 42, 48]$ $[7, 41, 42, 48]$ and chronic $[37, 41, 42, 48]$ [46, 47, 52](#page-15-0)] stroke individuals. These were then followed by randomized control trials that confirmed the positive outcomes of FET in acute $[38, 50, 55]$ $[38, 50, 55]$ $[38, 50, 55]$ and chronic $[36, 50]$ stroke individuals. In most of discussed studies, surface FES technology has been used to deliver FET, while a percutaneous FES system has been used in studies published by Chae et al. $[36, 37]$ $[36, 37]$ $[36, 37]$. In most studies, the upper limb FET has been delivered in a clinical setting with the assistance of therapists. However, a self-administered FET intervention, i.e., those that were conducted at home, has been recently explored using the NESS system $[53]$ and a new version of the Bionic Glove $[41, 52, 56]$.

 It is important to mention that, to date, most of the clinical trials conducted using FET for grasping in the stroke population targeted individuals who had partially preserved reaching and/or grasping functions. Namely, the targeted patients typically had Chedoke McMaster Stages of Motor Recovery scores 4 and 5, which means that they were able to place the hand voluntarily within at least 20–30% of the hand/arm workspace and were able to initiate some or many wrist, hand, and finger movements. However, recently in randomized controlled trials, Popovic and colleagues [48, 50] investigated the use of FET for reaching and grasping in severe stroke patients, i.e., stroke patients who had Chedoke McMaster Stages of Motor Recovery scores 1 and 2. These individuals were unable to initiate or execute voluntarily any component of reaching or grasping function. Popovic et al. have shown that the FET is able to improve both reaching and grasping functions in severe stroke patients (Fig. 7.5). What these studies have shown is that in severe stroke patients, the FET is able to improve gross motor function, but was unable to improve fine motor tasks of the hand.

7.4.4 FET for Restoration of Upper Limb Function Following SCI

 An SCI at T1 level or above frequently results in a partial or complete loss of grasping and reaching functions. Various therapies, surgical interventions, and/or devices have been proposed to

rehabilitation system (Photo courtesy Bioness Inc., Valencia, CA, USA)

 Fig. 7.5 Use of two Compex Motion systems for grasping for restoring bilateral voluntary hand function

help improve those functions in individuals with SCI. Among these interventions, FES devices have shown the most promise $[57]$. The same neuroprostheses for grasping and reaching as discussed above have been used with the SCI population. However, almost all these devices, except for Bionic Glove, ETHZ-ParaCare neuroprosthesis, and Compex Motion system, have been used with SCI subjects as orthotic systems and were all efficacious as orthoses.

While the benefit of FET has been intensively investigated with stroke patients, it has not been investigated with individuals who have SCI. From the above-listed FES systems that were used to deliver FET in individuals with SCI, ETHZ-ParaCare and Compex Motion systems were able to deliver both palmar and lateral grasps using the same electrode configuration. The ETHZ-ParaCare grasping neuroprosthesis was primarily used as an orthotic system. However, Mangold et al. [58] provided some evidence that a few of the SCI patients who used the device experienced a weak carryover effect. A clinical trial using Bionic Glove showed that the Bionic Glove can considerably improve upper limb function in individuals with C5–C7 SCI. This study was conducted by Popovic et al. (not the author of this article) and presents the first concrete evidence that FET for grasping could be effective in SCI population $[36]$.

In 2006, the first randomized controlled trial was carried out carefully examining the impact of FET on grasping function in individuals with traumatic C4–C7 SCI $[59]$. In this study, the individuals received 40 one-hour FET treatments (treatment group) or 40 one-hour conventional occupational therapy treatments. The therapy was tested on individuals with complete and incomplete SCI. Although this particular study was underpowered, it provided clear evidence that both individuals with complete and incomplete SCI greatly benefited from the FET for grasping. This study was then followed by another randomized controlled trial; FET for grasping was evaluated in individuals with incomplete, traumatic C3–C7 SCI $[60]$. What is

relevant to mention is that this was a very conservative study with respect to FET. In this study, both control and treatment groups received 1 h of conventional occupational therapy daily, as described in $[59]$. Then both groups were given at least a 2 h break followed by another dose of therapy where the control group got 1 h of conventional occupational therapy and treatment group received 1 h of FET for grasping. Both groups received therapy 5 days a week (working days) for 8 weeks (40 session days in total). At the end of the study, there were 9 subjects in the treatment group and 12 in the control group. The results obtained were statistically significant and have revealed that FET dramatically improves hand function in this patient population. Also, the long-term follow-up in this study has shown that 6 months after the baseline assessment, both control and treatment groups maintained or further improved their hand function as compared to the assessments performed at discharge from the study $[61]$. In other words, this study suggests that the changes in the hand function produced by FET are dramatic and they persist over time.

7.4.5 Hybrid FET with Orthoses or Robotic Devices

 In the past, it has been shown that FES-assisted walking has several limitations such as muscle fatigue, reduced joint torques generated using FES alone as compared to volitionally activated torques in healthy subjects, modified reflex activities, and spasticity $[62]$. To overcome these limitations, a combined use of FES and a mechanical brace or an orthosis has been suggested. These systems are better known as hybrid assistive systems (HAS) or hybrid orthotic systems (HOS) $[24, 63, 64]$. Such mechanical supports have been used mainly for safety and prevention of adverse events during standing and gait $[62]$.

 In recent years, the rehabilitation robotics field has experienced rapid growth. Instead of being passive orthotic systems or braces, rehabilitation robots now have active joints and are used to help move upper and lower limbs in a physiologically correct manner, mimicking

proper walking and reaching functions, respectively. Similarly, FET has been used to allow patients to execute various repetitive upper and lower limb tasks. Since both technologies have advantages and disadvantages, it was only natural to consider merging these technologies as means to overcome the disadvantages and benefit from the advantages that these two technologies offer. For example, FES systems are currently unable to generate very accurate limb movements but are able to engage muscles in task execution and generate much more significant proprioceptive and sensory feedback, which is critical for retraining the neuromuscular system. On the other hand, robotic systems are very good in executing accurate limb movements, but, in general, these systems do not have to generate muscle activations and significant proprioceptive and sensory feedback. Hence, it is expected that the combination of FES with robotic devices will enhance the therapeutic effects of both interventions. A recent study by Freeman et al. $[65]$ has proposed a robotic device for reaching movement with upper limbs that can be combined with FES. The study tested and confirmed the accuracy of the trajectory that the robotic system executed with 18 healthy subjects using FES applied to the triceps muscle. The results confirmed the efficacy of a combined robotic device and FES system and showed the feasibility of the proposed device. The same authors started to test the system with 5 stroke patients in treatment sessions comprised of up to 25 one-hour visits. For walking, Stauffer et al. [66] developed a hybrid robotic and FES system (WalkTrainer). The robotic device consisted of leg and pelvic orthoses, active bodyweight support, and a mobile frame that allowed the user to perform walking therapy during overground walking. The system also had a closed loop–controlled FES system. This system was tested with six paraplegic patients, and its feasibility as a rehabilitation tool was confirmed.

 Hybrid rehabilitation systems, consisting of a robotic device and an FES system, are not a new idea. However, this idea has become a more attractive and realistic solution in recent years. It is very likely that in the near future we will see

more devices that are combining FES and robotic technologies to develop advanced neurorehabilitation tools and interventions.

7.5 Potential Mechanisms of FET

 At the present time, the exact mechanisms responsible for the observed FET carryover effect are not known. However, a few hypotheses have been proposed that may provide at least a partial explanation of the FETs carryover effect.

 Three possible "peripheral" mechanisms might be considered. At first, FET may improve the muscle functions in the remaining motor units through simple muscle training and strengthening. However, this does not necessarily happen only during FET; other training mechanisms can be used to improve muscle strength and endurance. Second, FET may improve the flexibility and range of motion of the affected limbs/joints, and as a consequence, the voluntary function may be improved. However, stretching during physiotherapy should be able to generate similar results. Third, FES might reduce the amount of spasticity in the affected limb, and by doing so, it may improve the motor function. Although it has been shown in the past that FES does improve the spasticity $[67]$, the FET carryover effect has been observed even in the affected limbs that did not have spasticity. Thus, although all three above carryover mechanisms may be possible, they alone could not account for the observed carryover effect.

 It has been reported that cortical reorganization can occur following stroke recovery $[68]$. As FES activates both motor and sensory nerve fibers, high-frequency sensory stimulation may be capable of modifying cortical connectivity [69]. Thus, through forced repetitive movements, FET may promote the neuroplasticity in the central nervous system through sensory nerve stimulation $[70]$.

 In addition to the cortical reorganization mechanism, Rushton $[3]$ suggested a hypothesis that accounts for the carryover effect as uniquely due to FES. Electrical stimulation of a motor nerve fiber generates both an orthodromic (centrifugal) and an antidromic (centripetal) impulse. When the voluntary, descending command comes down from the brain to the spinal motor neuron, it can meet the antidromic impulse at the motor neuron during FES. This coincidence of two impulses at the spinal motor neuron can strengthen the synaptic connection via Hebb's rule. This enhancement of the synaptic connection would increase the efficacy of the voluntary, descending command to activate impaired muscle in individuals with stroke and SCI. Recent results that showed a facilitation of motor evoked potential using TMS after FES support this hypothesis $[71, 72]$.

 The last hypothesis that could also explain the mechanisms behind FET is the one proposed by Popovic et al. [31, 32, [48, 50, 59–61](#page-15-0)]. If a subject, who attempts to execute a motor task, is assisted with the FET to carry out that task, he/ she is effectively voluntarily generating the motor command (desire to move the arm, leg, etc., i.e., command input). In this situation, FET is providing afferent feedback (system's output), indicating that the command was executed successfully. By providing both the command input and system's output to the central nervous system (CNS) repetitively for prolonged periods of time, this type of treatment facilitates functional reorganization and retraining of intact parts of the CNS and allows them to take over the function of the damaged part of the CNS. It is important to add that during the FET, the subjects perform motor tasks repetitively. The combination of performing diverse and meaningful tasks with high repetition and with a subject's persistent active engagement (i.e., the subject has to devote 100% of his/her attention to the tasks performed) may play a critical role in retraining voluntary motor function. This hypothesis and use of FET is fully in tune with recent findings in the field of neuroplasticity and suggests that FET is potentially another effective method that can be used to retrain the neuromuscular system.

 In any event, the carryover effect is probably multifactorial and needs to be fully examined. However, what is certain is that the FET is an effective method for restoring voluntary upper and lower limb functions in individuals following stroke and SCI. It is our impression that the FET is a very promising intervention that is only now being seriously examined and has the potential to revolutionize the way we rehabilitate individuals with diverse neuromuscular disorders.

7.6 Conclusions, Limitations, and Perspectives

This chapter summarizes the research findings regarding the effects of FET in individuals with stroke and SCI. The findings to date clearly show that FET for reaching and grasping is a therapeutic modality that should be implemented in every rehabilitation institution that is treating patients with stroke and SCI. The results obtained in a number of randomized control trials to date clearly point out that FET for upper limb should not be ignored any longer. There is also considerable evidence to support the use of FET as a therapeutic modality to treat drop foot problem in both stroke and incomplete SCI populations. There are a couple of FES systems on the market that can be used to deliver FET for drop foot and grasping, and physiotherapists and occupational therapists should take advantage of this technology. Presently, few teams in the world are investigating use of more complex FES systems (6–16 channels FES systems that stimulate muscles in one of both legs in a physiologically appropriate manner) for retraining voluntary walking function in stroke and incomplete SCI populations. Although comprehensive randomized control trials have not been completed yet with either patient population, preliminary findings are very encouraging.

 The results obtained to date suggest that FET can be used effectively with both chronic and subacute stroke and SCI patients. However, the results published to date suggest that FET produces better results if it is applied during early rehabilitation, i.e., during subacute phase following injury. Further, the effect of FET has shown good results in individuals with complete and incomplete SCI, and stroke subjects. However, to date, statistically significant results have only been obtained with stroke and incomplete SCI patients. It should be noted that FET therapy does

not require any voluntary movement in the affected limb as an indication for the therapy. In other words, FET can be applied to individuals who are profoundly paralyzed (i.e., cannot move the limb at all), and one can expect to see partial or full recovery of the limb function at the end of the FET.

 As the surface FES technology is continuously improving and delivery methods for FET are evolving due to system's miniaturization, better stimulation electrodes, and better stimulation protocols, it is foreseeable that in the next 10–15 years, FET will become one of the dominant interventions for upper and lower limb rehabilitation. Many neuroprostheses are already commercialized and many more are in the process of being developed and/or commercialized. Thus, we feel very confident that FET field is only beginning to evolve, and that, in the future, it may become one of the key therapeutic interventions not only for patients with stroke and SCI but also for patients with other neuromuscular disorders.

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