

Functional Electrical Stimulation in Spinal Cord Injury: From Theory to Practice

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This article outlines steps to practical application of functional electrical stimulation (FES) within activity-based restorative therapy (ABRT). Drawing from current evidence, specific applications of FES intended to help restore function lost to spinal cord injury and associated neurologic disease are discussed. The medical and therapeutic indications, precautions, and contraindications are reviewed to help participants with appropriate patient selection, treatment planning, and assessment. Also included are the physiological implications of FES and alterable parameters, including dosing and timing, for a desired response. Finally, approaches to improve cortical representation and motor learning and to transition emerging movement into functional tasks are reviewed. **Key words:** activity-based restorative therapy, functional electrical stimulation, spinal cord injury

Functional electrical stimulation (FES) has long been used in orthopedic and neurological rehabilitation. Its efficacy and application are well-documented in diagnoses from knee osteoarthritis to stroke. Its use in spinal cord injury (SCI), however, is only supported by studies of small sample size, leading to what amounts to insufficient evidence to determine whether its use is clinically indicated and necessary. Emerging research indicates that neural restoration is possible; there is now a significant amount of literature demonstrating the role of activity-dependent neural plasticity in recovery of function after SCI. Systematic application of FES in patients with SCI provides a mechanism for optimizing the neural activity amount below injury level, while reducing secondary complications and improving overall health.

Neuroplasticity

The nervous system is capable of change in response to stimulation. Permanent changes are possible with long-term, repeated exposure. The amount and type of activity plays a critical role in both development and plasticity within the nervous system, including gene expression,¹⁻⁵ modification of synaptic strength (eg, LTP),^{6,7} synapse elimination,⁶ myelination and maintenance of myelination,⁸⁻¹¹ and axonal

growth.¹²⁻¹⁴ The widespread dependence of development and plasticity in the central nervous system (CNS) on neural activity suggests that optimized neural activity might also be important for regeneration, given the common cellular mechanisms participating in development and regeneration.^{8,15} There is further evidence supporting this concept demonstrated by the fact that increased and decreased neural activity enhances and inhibits multiple components of spontaneous regeneration, respectively.¹⁶⁻²¹

Clinically, a significant number of individuals with so-called complete SCI retain some connectivity across injury site; this could be represented by nonfunctioning myelin or denuded axons that could potentially provide conductivity across injury site given optimal activation. In patients with complete or incomplete SCI, there is now proof of FES-induced activation of the central pattern generator mechanism, and increased stepping responses have been observed in response to FES.²²⁻²⁴ Some patients who were regularly treated with FES demonstrated improved lower limb ASIA motor and sensory scores²⁵ and

decreased spasticity,²⁶ indicating some degree of neuromodulation and remediation of paralysis in response to stimulation.

Medical Benefits

In addition to the incremental changes observed in nervous system activity, overall health measures demonstrate significant response to FES. If not more important than the nervous system changes, these benefits are more immediate and contribute to significant quality of life improvements.

Cardiovascular conditioning can be achieved and maintained in individuals with SCI following FES training. FES exercise produced a 2-fold increase in the oxygen uptake, a 3-fold increase in ventilation rate, and a 5 beats per minute increase in heart rate from the resting value in 7 volunteers with C5 to T12 SCI.²⁷ In another study, peak oxygen uptake increased by 103% and maximum power output increased by 113% after one year of 3 times per week home-based FES ergometry training in an individual with C6 motor complete SCI.²⁸ Similar results were found when training 2 to 3 times per week for 6 months at 30 or 50 rpm.²⁹ Daily FES cycling for 4 weeks reversed the femoral artery size reduction and decreased wall compliance associated with SCI paralysis.³⁰

Metabolic benefits have also been outlined, including increases in lean muscle mass²⁵ and capillary number³¹ and decreases in adipose tissue,³² in response to FES training. Beyond body composition, FES has been demonstrated to decrease blood glucose and insulin levels in patients with SCI.^{25,33,34}

The most well-studied aspect of FES training may be the muscle and bone response. Muscles improve in size, strength,³⁵⁻³⁷ and composition. Conversion from type IIB to type IIA and type I muscle fibers has been demonstrated,³⁸ indicating improved fatigue resistance and oxidative capacities. Finally, FES leg cycle ergometer training results in proportional increases in fiber area and capillary number.³⁹

Recovery of lost bone mass, demonstrated especially in the lower extremities,⁴⁰ is also associated with FES. Improvements in muscle mass and bone density may lead to fewer life-

threatening complications, including fractures, pressure ulcers, and infections.

Therapeutic Applications

There are a wide variety of therapeutic applications of FES. FES has been used to maintain or increase range of motion, reduce edema, promote healing of fracture or tissue, reduce muscle spasm and the effects of spasticity, improve circulation, prevent or reverse disuse atrophy, and facilitate movement. It has also been used for neuromuscular re-education and orthotic substitution. Before moving too far into the pragmatics of application, however, it is important to note that there are 3 distinct types of electrical stimulation commonly utilized in activity-based restorative therapy:

1. Neuromuscular electrical stimulation (NMES) is electricity applied across the surface of the skin over an intact peripheral nerve, which evokes an action potential in the nerve fiber, causing an exchange of ions to drive the muscle to contract. It includes FES.
2. Functional electrical stimulation (FES) is the application of electrical stimulus to a paralyzed nerve or muscle to restore or achieve function. FES is most often used in neurorehabilitation and is routinely paired with task-specific practice. A common example is orthotic substitution, also known as a neuroprosthesis.
3. Transcutaneous electrical nerve stimulation (TENS) is used for pain modulation by exciting peripheral nerves using sensory, motor, or noxious settings. Clinically, TENS has been used for lower back pain, neurogenic pain, arthritic pain, and various other forms of pain. In activity-based restorative therapy, TENS sensory settings are also used to achieve sensory input to the nervous system and for tone and spasticity management techniques.

When applying any form of electrical stimulation, it is important to keep in mind that an electrically driven contraction differs from a physiological contraction in 2 main ways. First, the action potential (AP) generated in an electrically

drive contraction travels both anterograde, to the neuromuscular junction, and retrograde, to the anterior horn cell. Second, the recruitment of motor units differs in both type and number. Recruitment of motor units by electrical stimulation progresses from large to small, the reverse order of voluntary contractions, because axons of the largest diameter are the easiest to activate. Voluntary contractions preferentially recruit force-producing, slow-contracting, fatigue-resistant (type I) fibers, before the more forceful, faster, fatigable (type II) units. This allows for asynchronous activation of varied motor units, which enables smooth switching between active and inactive motor units to maintain muscle activity, while allowing recovery time for individual motor units and for smooth and graded movement. Electrically elicited contractions lack smooth, gradual onset, reflecting biased and synchronous motor unit recruitment. The contractions recruit motor units based on size and proximity to the stimulation electrode. This produces multiple combinations of motor units that are activated, preventing graded and isolated movement. This all or nothing recruitment is also a factor in fatigue. Fatigue occurs more rapidly in an electrically generated contraction, as a greater portion of fatigable motor units is necessary for a given contraction. Combining voluntary contractions with ES produces the best and strongest contraction, as ES recruits different motor units that are not activated at a given moment by a voluntary contraction.

It is important to critically evaluate a patient's medical history when determining whether he or she is a candidate for treatment with FES. A history of implanted electrical device, cancer, osteomyelitis, thrombosis/hemorrhage, or epilepsy may exclude a patient from treatment. Active metastases and pregnancy may exclude a patient for a limited time. In any case, it is incumbent on the treatment team to evaluate the risks and benefits prior to beginning treatment. More significant, when deciding a course of treatment, it is important to determine if the desired peripheral nerve is intact. Lower motor neuron (LMN) syndrome results from damage to axon or cell body in peripheral nervous system. In SCI, this can occur with damage to anterior horn cells, stretching of nerve

roots, foraminal stenosis or compression, cauda equina/conus medularis injury, or associated peripheral nerve injury (eg, brachial plexus). It is characterized by the loss of voluntary movement, low to no muscle tone, and absent reflexes. It is commonly found at the level of injury or with chronic injuries and comorbidities, like impingement, stenosis, and traction neuropathies. Upper motor neuron (UMN) syndrome results from damage to the neural pathway above the anterior horn (or the motor nuclei of cranial nerves). It is characterized by decreased voluntary movement, impaired or absent sensation, and pathological reflexes. The easiest way to determine LMN or UMN presentation is via reflexes. Intact reflexes signal intact peripheral nerves or UMN presentation, which would clear the way for FES usage. However, due to long-term atrophy and spotty innervations, these once intact reflexes may be diminished. Therefore nerve and muscle response to FES needs to be examined. Mulcahey, Smith, and Betz showed that a muscle with intact peripheral innervation should produce a grade 3 muscle contraction when stimulated at 10-20 Hz and 200-400 μ s.⁴¹ Their work specifically looked at patterns of innervation in high tetraplegia, as an indicator of FES application alone versus the use of FES prior to the following muscle transfer. It is still worth considering FES with an LMN patient, as the results are unclear. Kern et al found that home-based FES of denervated muscle resulted in rescue of muscle mass and tetanic contractility in a 2-year longitudinal prospective study of 25 patients with complete conus/cauda equina lesions. They also found important immediate benefits for the patients, including improved cosmetic appearance of lower extremities and the enhanced cushioning effect for seating.⁴²

Once it has been decided that a patient is a suitable candidate for FES, the therapist should determine appropriate parameters to yield the desired response. Basic parameters for any form of NMES are waveforms, intensity or amplitude, frequency, pulse width, reciprocation, ramp, and duration. These combine to create electrical current. The goal, when selecting parameters, is to generate the lowest possible current, while maintaining the desired response. This

Table 1. Considerations for appropriate parameter selection

Goal	Frequency	Pulse width	Intensity	Notes
Increase comfort	Increase	Decrease	Decrease	Can also try using larger electrodes
Decrease electrical bleed	Increase or decrease	Decrease	Decrease	Can also try using smaller electrodes
Minimize fatigue	Decrease	Decrease	Decrease	Overall, aim to minimize current, consider variable waveform
To improve quality of tetany	Increase	Increase or decrease	Decrease	Look for smooth fused contraction

will protect against fatigue. Parameters can be manipulated to produce a desired response or in response to patient's reaction. For example, if a patient complains of an uncomfortable pulsing, the frequency can be increased to smooth the contraction. Additional considerations while selecting parameters are outlined in **Table 1**.

After appropriate parameters have been defined, the range of FES applications is limited only by the therapist's creativity. Using careful electrode placement and a trigger to time stimulation, a therapist can generate a reach and grasp pattern, stepping pattern, or sequence muscles to help a patient transition from supine to sitting. A

stimulated reach and grasp pattern may be used to compliment a self-feeding goal. A therapist may choose to use the stimulation to augment a patient's own emerging function; where timing or strength is lacking, the FES can assist. The therapist may choose to use FES as a method to provide high-repetition practice for a patient with no active movement. FES can be applied in isolation or to multiple muscle groups. It can be used within the movement of a piece of equipment, like the Biodex or ergometer, or to move freely through space. FES intervention is intended to complement treatment goals, which should be functional and patient-centered, as with any intervention.

REFERENCES

1. Ono T, Inokuchi K, Ogura A, Ikawa Y, Kudo Y, Kawashima S. Activity-dependent expression of parathyroid hormone-related protein (PTHrP) in rat cerebellar granule neurons. Requirement of PTHrP for the activity-dependent survival of granule neurons. *J Biol Chem.* 1997;272:14404-14411.
2. Muslimov I, Banker G, Brosius J, Tiedge H. Activity-dependent regulation of dendritic BC1 RNA in hippocampal neurons in culture. *J Cell Biol.* 1998;141:1601-1611.
3. Sgambato V, Abo V, Rogard M, Besson M, Deniau J. Effect of electrical stimulation of the cerebral cortex on the expression of the Fos protein in the basal ganglia. *Neuroscience.* 1997;81: 93-112.
4. Karlsson M, Hallbook F. Kainic acid, tetrodotoxin and light modulate expression of brain-derived neurotrophic factor in developing avian retinal ganglion cells and their tectal target. *Neuroscience.* 1998;83:137-150.
5. Mingo N, Cottrell G, Zhang L, Wallace M, Burnham W, Eubanks J. Kainic acid-induced generalized seizures alter the regional hippocampal expression of the rat m1 and m3 muscarinic acetylcholine receptor genes. *Epilepsy Res.* 1997;29:71-79.
6. Zhou Q, Poo M. Reversal and consolidation of activity-induced synaptic modifications. *Trends Neurosci.* 2004;7:378-383.
7. Daoudal G, Debanne D. Long-term plasticity of intrinsic excitability: learning rules and mechanisms. *Learn Mem.* 2003;10:456-465.
8. McDonald J, Becker D, Sadowsky C, Jane J, Conturo T, Schultz L. Late recovery following spinal cord injury. Case report and review of the literature. *J Neurosurg.* 2002;97:252-265.
9. McDonald J. Repairing the damaged spinal cord: from stem cells to activity-based restoration therapies. *Clin Neurosurg.* 2004;51:207-227.
10. Becker D, Sadowsky C, McDonald J. Restoring function after spinal cord injury. *Neurologist.* 2003;9:1-15.

11. Wilson G, Chiu S. Potassium channel regulation in Schwann cells during early developmental myelinogenesis. *J Neurosci*. 1990;10:1615-1625.
12. Howe C. Depolarization of PC12 cells induces neurite outgrowth and enhances nerve growth factor-induced neurite outgrowth in rats. *Neurosci Lett*. 2003;351:41-45.
13. Cantallops I, Routtenberg A. Activity-dependent regulation of axonal growth: posttranscriptional control of the GAP-43 gene by the NMDA receptor in developing hippocampus. *J Neurobiol*. 1999;41:208-220.
14. van Oyen A, van Pelt J. Activity-dependent neurite outgrowth and neural network development. *Prog Brain Res*. 1994;102:245-259.
15. Grill W, McDonald J, Peckham P, Heetderks W, Kocsis J, Weinrich M. At the interface: convergence of neural regeneration and neural prostheses for restoration of function. *J Rehabil Res Dev*. 2001;38:633-639.
16. Perreau V, Adlard P, Anderson A, Cotman C. Exercise-induced gene expression changes in the rat spinal cord. *Gene Expr*. 2005;12:107-121.
17. Engesser-Cesar C, Anderson A, Basso D, Edgerton V, Cotman C. Voluntary wheel running improves recovery from a moderate spinal cord injury. *J Neurotrauma*. 2005;22:157-171.
18. Cotman C, Engesser-Cesar C. Exercise enhances and protects brain function. *Exerc Sport Sci Rev*. 2002;30:75-79.
19. van Praag H, Shubert T, Zhao C, Gage F. Exercise enhances learning and hippocampal neurogenesis in aged mice. *J Neurosci*. 2005;25:8680-8685.
20. Rhodes J, van Praag H, Jeffrey S, et al. Exercise increases hippocampal neurogenesis to high levels but does not improve spatial learning in mice bred for increased voluntary wheel running. *Behav Neurosci*. 2003;117:1006-1016.
21. Kempermann G, van Praag H, Gage F. Activity-dependent regulation of neuronal plasticity and self repair. *Prog Brain Res*. 2000;127:35-48.
22. Querry R, Pacheco F, Annaswamy T, Goetz L, Winchester P, Tansey K. Synchronous stimulation and monitoring of soleus H reflex during robotic body weight-supported ambulation in subjects with spinal cord injury. *J Rehabil Res Dev*. 2008;45(1):175-186.
23. Behrman AL, Lawless-Dixon AR, Davis SB, et al. Locomotor training progression and outcomes after incomplete spinal cord injury. *Phys Ther*. 2005;85:1356-1371.
24. Harkema S, Gerasimenko Y, Hodes J, et al. Effect of epidural stimulation of the lumbosacral spinal cord on voluntary movement, standing, and assisted stepping after motor complete paraplegia: a case study. *Lancet*. www.thelancet.com. Published May 20, 2011. doi:10.1016/S0140-6736(11)60547-3
25. Griffin L, Decker M, Hwang J, et al. Functional electrical stimulation cycling improves body composition, metabolic and neural factors in persons with spinal cord injury. *J Electromyogr Kinesiol*. 2009;19:614-622.
26. van der Salm A, Veltink PH, IZerman MJ, Groothuis-Oudshoorn KC, Nene AV, Hermens HJ. Comparison of electric stimulation methods for reduction of triceps surae spasticity in spinal cord injury. *Arch Phys Med Rehabil*. 2006;87:222-228.
27. Bhambhani Y, Tuchak C, Burnham R, Jeon J, Maikala R. Quadriceps muscle deoxygenation during functional electrical stimulation in adults with spinal cord injury. *Spinal Cord*. 2000;38: 630-638.
28. Kakebeeke T, Hofer P, Frotzler A, Lechner H, Hunt K, Perret C. Training and detraining of a tetraplegic subject: high-volume FES cycle training. *Am J Phys Med Rehabil*. 2008;87:56-64.
29. Fornusek C, Davis GM. Cardiovascular and metabolic responses during functional electric stimulation cycling at different cadences. *Arch Phys Med Rehabil*. 2008;89:719-725.
30. De Groot P, Crozier J, Rakobowchuk M, Hopman M, Macdonald M. Electrical stimulation alters FMD and arterial compliance in extremely inactive legs. *Med Sci Sports Exerc*. 2005;37(8):1356-1364.
31. Nash MS, Montalvo BM, Applegate B. Lower extremity blood flow and responses to occlusion ischemia differ in exercise-trained and sedentary tetraplegic persons. *Arch Phys Med Rehabil*. 1996;77:1260-1265.
32. Scremin A, Kurta L, Gentili A, et al. Increasing muscle mass in spinal cord injured persons with a functional electrical stimulation exercise program. *Arch Phys Med Rehabil*. 1999;80:1531-1536.
33. Jeon J, Weiss C, Steadward R, et al. Improved glucose tolerance and insulin sensitivity after electrical stimulation-assisted cycling in people with spinal cord injury. *Spinal Cord*. 2002;40:110-117.
34. Jeon J, Hettinga D, Steadward R, Wheeler G, Bell G, Harber V. Reduced plasma glucose and leptin after 12 weeks of functional electrical stimulation-rowing exercise training in spinal cord injury patients. *Arch Phys Med Rehabil*. 2010;91:1957-1959.
35. Johnston T, Betz R, Smith B, et al. Implantable FES system for upright mobility and bladder and bowel function for individuals with spinal cord injury. *Spinal Cord*. 2005;43:713-723.
36. Field-Fote EC, Lindley SD, Sherman AL. Locomotor training approaches for individuals with spinal cord injury: a preliminary report of walking-related outcomes. *J Neurol Phys Ther*. 2005;29(3):127-137.
37. Postans NJ, Hasler JP, Granat MH, Maxwell DJ. Functional electric stimulation to augment partial weightbearing supported treadmill training for patients with acute incomplete spinal cord injury: a pilot study. *Arch Phys Med Rehabil*. 2004;85:604-610.
38. Davis G, Hamzaid N, Fornusek C. Cardiorespiratory, metabolic, and biomechanical responses during functional electrical stimulation leg exercise: health and fitness benefits. *Artificial Organs*. 2008;32(8):625-629.
39. Chilibeck P, Jeon J, Weiss C, Bell G, Burnham R. Histochemical changes in muscle of individuals with spinal cord injury following functional electrical stimulated exercise training. *Spinal Cord*. 1999;37(4):264-268.
40. Frotzler A, Coupaud S, Perret C, Kakebeeke T, Hunt K, Eser P. Effect of detraining on bone and muscle tissue in subjects with chronic spinal cord injury after

- a period of electrically-stimulated cycling: a small cohort study. *J Rehabil Med.* 2009;41:282-285.
41. Mulcahey M, Smith B, Betz R. Evaluation of the lower motor neuron integrity of upper extremity muscles in high level spinal cord injury. *Spinal Cord.* 1999;37:585-591.
 42. Kern H, Carraro U, Adami N, et al. Home-based functional electrical stimulation rescues permanently denervated muscles in paraplegic patients with complete lower motor neuron lesion. *Neurorehabil Neural Repair.* 2010;24:709.

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