Functional Gains for Stroke Survivors in Response to Functional Electrical Stimulation

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For those with persistent gait and upper limb deficits after stroke, it is difficult to obtain recovery of motor control and functional capability in response to standard care methods. Functional electrical stimulation (FES) is a promising intervention. Surface FES for wrist and hand muscles can result in improved impairment sufficient to produce important gains in functional capability. In addition, an FES gait training system with multiple channels and implanted electrodes has shown a statistically significant additive advantage for the recovery of coordinated gait components versus a comparable comprehensive gait training treatment without FES. Results were sufficiently robust to show important gains in quality of life.

Key words: *stroke, functional electrical stimulation, neuromuscular electrical stimulation, functional neuromuscular stimulation, functional recovery, rehabilitation*

Introduction

For those with persistent gait and upper limb deficits after stroke, it is difficult to obtain recovery of motor control and functional capability in response to standard care methods. The recovery of persistent motor control and functional capability is dependent upon gains in strength and coordination that are sufficient to perform the complex coordinated movements of the upper limb and components of gait that are required for functional activities. Functional electrical stimulation (FES) is a promising intervention in the recovery of gait and upper limb function (Figure 1).

Upper Limb Treatment Response to Intervention with Functional Electrical Stimulation

Functional electrical stimulation has been used clinically and studied for many years.[1] A number of studies have demonstrated the feasibility and promise of using FES in stroke survivors to improve the impairments of weakness, spasticity, and dyscoordination.[2–4] However, only a few studies of FES have reported improvements in impairment measurements that were sufficient to produce meaningful functional gains.

Muscle Strength Improvement

As early as 1996, a meta-analysis of treatment response to surface FES (which involves placing electrodes on the surface of the skin) was conducted for studies published in 1978–1992.[5] Among those studies, only four randomized controlled trials (RCTs) were identified and qualified for the meta-analysis, all having used a common measure, muscle force. Using those four studies, the meta-analysis showed an advantageous good effect size of 0.63 for FES versus other available interventions (such as conventional exercise) with regard to gains in muscle force or strength (95% confidence interval 0.29–0.98, $p < .05$). Each of the four RCTs reported a statistically significant advantage of FES for improving muscle strength versus other available treatments for various muscle groups: wrist extensors,[6] knee extensors,[7] ankle dorsiflexion,[8] and wrist and finger flexors and extensors.[9]

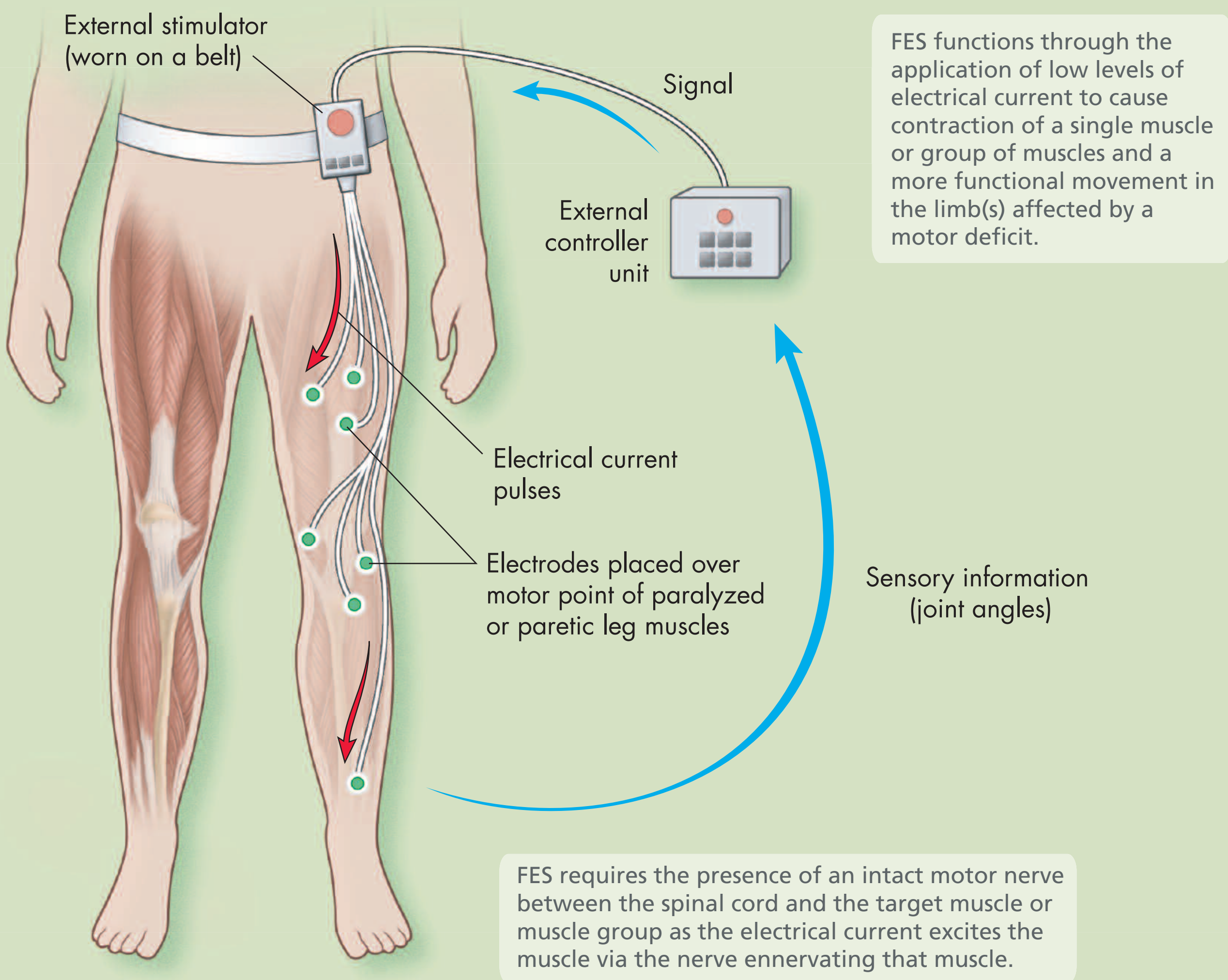
Reduced Spasticity

Though promising, the evidence for FES-induced spasticity reduction is less convincing than that for strength gains. Surface FES treatment response was studied according to a measure of the electromyography (EMG) amplitude of the biceps muscle during an elbow-extension task.[10,11] In other studies, there was either a mean improvement or statistically significant improvement (compared with conventional therapies such as exercise) in the modified Ashworth spasticity scale results for the shoulder, elbow, wrist, and finger muscles.[12,13]

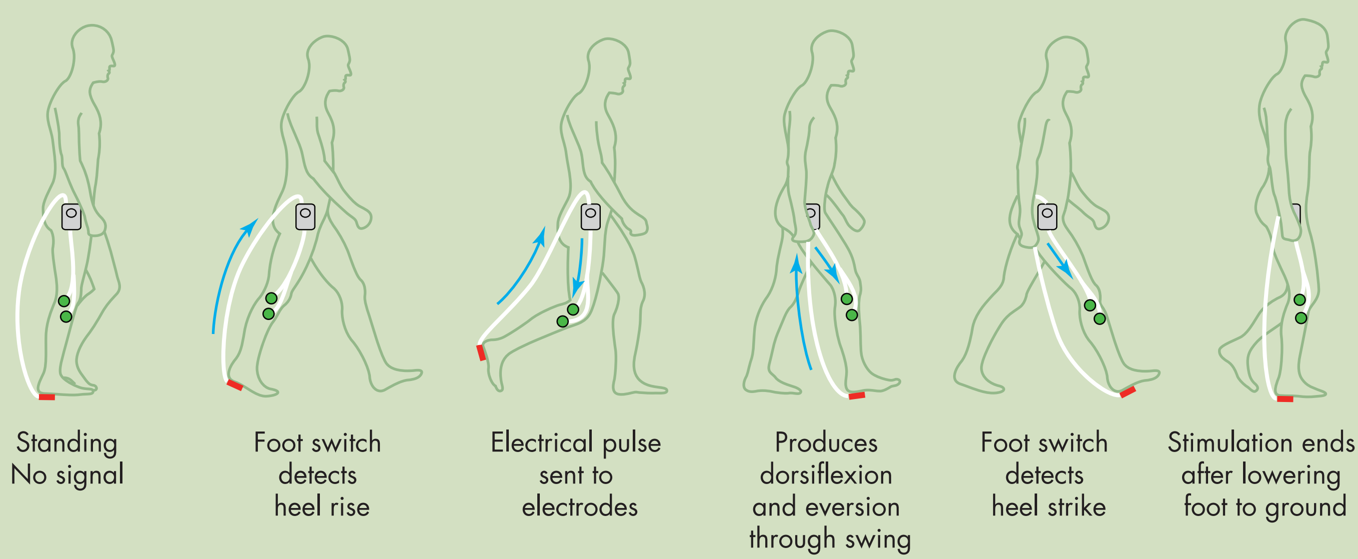
Reduced Shoulder Pain

A multicentre clinical trial focused on the study of a percutaneous FES system (which involves implanted electrodes and an external stimulator) for shoulder pain reduction and functional recovery. Results showed that shoulder pain could be significantly reduced and the benefits maintained for up to 12 months after the end of treatment.[14,15] Those who were within 1.5 years of the stroke were most likely to benefit.[16] Surface FES systems have not been rigorously studied to determine whether the same level of benefit can be obtained, though some studies suggest promise.[3]

Figure 1: Functional Electrical Stimulation (FES)



Surface FES and Gait Assistance



Reduced Dyscoordination

Researchers have shown that surface FES is promising as a means to treat dyscoordination. Some researchers using the Fugl-Meyer coordination measure have found improvement. A randomized controlled trial demonstrated a statistically significant advantage of FES as compared to conventional exercise as demonstrated using the Fugl-Meyer measure of upper limb coordination.[9,17]

Measures of Functional Movement Components and Actual Functional Activity

Though gains in reduced impairment are promising, one critical rehabilitation goal is the recovery of meaningful function. Some clinical scientists have shown promising results when combining surface FES with functional task practice. In a cohort study of subjects with mild to severe upper limb paresis, FES was provided for wrist and hand muscles, along with function movement component practice.[13,18] There was a statistically significant improvement as compared to conventional therapies in results of standardized measures of functional movement components such as grasp and release (Jebsen heavy and light cylinder subscales) and translational shoulder movements in the horizontal plane[13] (Box and Blocks test). In two RCTs, FES combined with functional task practice produced a statistically significant advantage versus the same treatment without FES, according to measures of actual functional tasks. In the study of mildly involved subjects (<6 months post-stroke), there was a gain in results of the Upper Extremity Functional Test.[19] In a study of severely involved subjects, FES for wrist and finger muscles was combined with functional task practice; there was a statistically significant advantage for FES versus the same functional training intervention without FES but with an alternative modality treatment, as shown by the Arm Motor Ability Test—Wrist/Hand, a measure composed of 13 actual functional tasks.[20]

Gait Recovery in Response to Functional Electrical Stimulation Gait-Assist or FES Gait Training Interventions

Impairments and Gait Deficits

Persistent gait deficits can result in falls,[21] an elevated energy cost,[22,23] and poor endurance.[24] The impairments in the lower limb that occur after a stroke include muscle weakness, abnormal muscle tone, dyscoordination, and impaired balance, all of which result in gait deficits.[25,26] The application of FES can result in improvements in impairments such as muscle weakness[7,8,27,28] and abnormal muscle tone.[27,29]

Coordination impairment is an underlying cause of gait deficits after stroke.[30] Dyscoordination prevents the normal execution of the coordinated movements required in normal gait, including swing phase hip, knee, and ankle flexion excursion and timing; swing phase knee extension; and stance phase pelvic and knee control.[25,26] However, very few studies describe interventions that actually focus on the problem of dyscoordination and show improvements in these coordinated gait components after interventions. Rather, more general treatments are applied such as treadmill training and harness unweighting systems.

Gait Training Response to Treadmill and Unweighting Systems

In response to gait training with available interventions, some researchers have reported gains in muscle strength, single joint coordination, gait speed, and temporal gait characteristics. However, few have reported improvements in the complex coordinated movement components that compose the gait pattern.

There are two general categories of reported RCTs of gait training studies. First, in studies comparing no treatment versus treadmill training (TT) or overground (OG) walking,[31–34] there was a significantly greater gain for treatment versus control, according to results of the 6-minute walk test,[31,32] walking velocity,[31–33] and Functional Independence Measure (FIM) subscales for bathing and dressing but not for the FIM subscale of walking mobility.[33] A significant gain in coordinated gait components was either not obtained or not reported.[31–33]

Second, in most comparisons among TT, OG, and body weight–supported treadmill training (BWSTT), there was no significant difference among gait training methods as shown by walking speed; BWSTT was comparable to a variety of other gait training methods, even when 11 studies (485 participants) were combined.[35] For moderately impaired and middle-aged patients, BWSTT was comparable to conventional methods,[36,37] as was TT.[38] In a comparison of TT with BWSTT, BWSTT was superior to TT alone[39]; however, in two studies, this was the case for only those who were more disabled or who were older adults.[36,37] These data suggest that the results of these studies were mixed. Notably, these studies reported no gains in coordinated gait components.[35–38,40]

There is a dearth of RCTs studying treatment response pertaining to the coordinated gait components comprising gait. In an animal study, coordination training was superior to both TT and no treatment, as shown by coordinated leg movements during walking tasks;[39] but in a study of humans, researchers reported no significant difference in measurements of gait coordination.[41]

The lack of success using TT, OG, and BWSTT methods for restoring coordinated gait components could result from an inability of these methods to train coordinated gait components. In contrast, FES-assisted coordination and gait training can provide some advantages. Coordination practice and coordination skill acquisition can be enhanced by using key motor learning principles such as the practice of close-to-normal movements;[42,43] muscle activation driving practice of movement; focused attention,[44] and repetition of desired movements.[45–48] Functional electrical stimulation can provide an electrically induced muscle contraction, thereby satisfying these principles.

Response of Impairment Measures to Functional Electrical Stimulation Gait Training

In prior studies, surface FES showed some promise in improving general mobility[49,50] and temporal gait variables including gait speed, but disadvantages of surface multichannel gait training precluded more widespread study and clinical use. A recent RCT was conducted using a two-channel implanted stimulator system. The results showed an improvement in an EMG measure of tibialis muscle function during the swing phase but showed no therapeutic effect in terms of gait speed when the FES was not activated during walking.[2]

Response of Coordinated Gait Components to Functional Electrical Stimulation

In recent work, an RCT of 32 people (>12 months poststroke) showed a statistically significant advantage in gait training using an eight-channel, percutaneous FES system (with implanted electrodes) plus conventional therapy versus conventional therapy alone. Conventional therapy was composed of coordination exercise, OG gait training, and BWSTT. The advantage of FES training was demonstrated in measures of both knee joint flexion coordination and coordinated gait components,[51] as well as coordination of relative hip/knee movements of the involved limb during walking.[4] These measures were obtained during volitional walking with the FES system deactivated, illustrating recovery of volitional coordinated components of gait.

The training protocol in these studies used FES-assisted practice of volitional gait component movements that could approximate the normal movement. Functional electrical stimulation was used alone in the event of absent volitional function or together with any volitional movement that was present. As volitional control improved, the FES assistance was decreased to demand practice of as much volitional effort as was present. These FES gait training methods were consistent with a task-oriented approach to motor learning,[52] and FES was used in such a manner as to provide practice of coordinated components of gait that would not have been possible without FES-assisted practice.

Types of Functional Electrical Stimulation Systems

Functional electrical stimulation systems can be categorized as follows: surface FES, in which electrodes are placed on the surface of the skin; percutaneous FES, in which the electrodes are placed beneath the skin and the electrode lead wires exit the skin and connect with an externally worn stimulator; and totally implantable FES, in which both the electrodes and stimulator are implanted beneath the skin (no lead wires exit the skin).

Surface Functional Electrical Stimulation

A number of studies have demonstrated that the use of surface FES is efficacious in recovery of upper limb functional movement components and functional task performance.[18,13,20] The evidence is incomplete regarding the relative benefits of surface FES in shoulder pain reduction.[3]

In addition, single- or double-channel surface FES systems for ankle dorsiflexion show some promise. There are at least four ankle surface FES systems that are currently commercially available. Studies are currently under way that will provide more conclusive evidence regarding the success of these systems for gait assistance and gait recovery.

In contrast, multichannel surface FES for gait training has proven more difficult. The following disadvantages for surface FES were reported for gait training application: difficulty obtaining joint movement in response to an FES stimulus that was within a comfort level; difficulty obtaining a limb movement that would be productive for gait training (i.e., difficulty obtaining close-to-normal gait practice or for safe walking using FES-assisted gait);[53] difficulty activating all but the most superficial muscles;[50,53] inadequate consistency of muscle activation from day to day since the surface electrodes had to be reapplied each day;[50,53] the application of electrodes for multiple muscles for a given session was too time-consuming;[50,53] and multichannel systems were not practical since they were not portable for gait practice.[27,50,53]

Implanted Functional Electrical Stimulation

Single- and Double-Channel Systems for Ankle Gait Training and Gait Assist

To our knowledge, there has not been a direct comparison of surface FES versus implanted FES single- and double-channel systems. Most control groups in studies of surface FES systems received gait training without FES or used an ankle-foot orthosis.

In early case studies or cohort studies, the feasibility and safety of implantable FES was confirmed for a gait system with a peroneal nerve cuff electrode and an implanted stimulator.[23,54] With the FES system activated, there was a statistically significant increase in walking speed. A recent single case study[55] supported the use of a dual-channel implanted microstimulator for drop foot correction, with the FES system activated according to measures of physiological cost index and gait speed. No recovery of volitional function was reported.

A cohort study of 20 subjects (4 months–9 years) showed that an implanted peroneal nerve stimulator was safe for a long period (over 17 months for one individual) according to nerve-conduction velocities and radiographs. The system was externally triggered with a sole force sensor and controlled via a radiofrequency device, allowing for the advantage of no lead wires exiting the skin.[56] According to a visual analysis of gait during the use of the stimulator, equinovarus was improved. A new two-channel, implanted stimulator system was recently introduced, and an RCT showed improved muscle contraction function but no therapeutic effect in terms of gait speed.[2]

Key Points

A number of clinical scientists have shown that surface FES can improve muscle strength, reduce spasticity, and improve isolated joint movement coordination after stroke.

Three different clinical scientists have shown that surface FES can improve arm/hand strength and coordination sufficient to produce gains in functional movement components and functional tasks after stroke.

For improvements of function to occur, surface FES should be applied within each individual's comfort level and at sufficient duration of weeks and hours per day.

Shoulder pain reduction after stroke has been demonstrated in response to implantable FES electrodes.

Recovery of the coordinated components of gait after stroke was shown in response to gait training using an FES system with implantable electrodes.

System with Multichannel, Epimysial Electrodes

In an early study of three cases, Waters *et al.*[23] found better results for an implanted FES system than for a surface system in terms of hip stability practice during walking. Their implanted system was composed of epimysial electrodes (surgically attached to the muscle epimysium), with percutaneous leads exiting through the skin and connecting with an external stimulator. They made an incision and implanted each of the electrodes for the following muscles: iliacus, sartorius, adductor magnus, quadriceps, gluteus medius, semimenbranosus, and the short head of the hamstrings. Stimulation was provided using an externally worn device. The authors reported greater joint movement and walking capability, as shown by hip gait components, than was otherwise volitionally possible. However, FES-assisted gait did not improve hip and knee flexion during walking without the FES.[23]

Studies Using Injectable Scheiner Electrodes

More recently, researchers used a multichannel, percutaneous system with intramuscular Scheiner electrodes[57] for gait training. The advantage of the Scheiner wire electrodes was that they could be injected with a hypodermic needle injection technique, eliminating the need for an incision. Electrodes were inserted at the motor point of up to eight separate paralyzed or paretic leg muscles,[58] under monitored anesthesia care.

The FES external stimulator was portable and was worn on a belt.[58] The finger switch controller was operated by either the therapist or the patient during walking. Subjects showed gains at the end of treatment in a test of voluntary walking (no FES activated during gait testing), as per measures of strength, coordination, and coordinated gait components performed volitionally, for a series of case studies.[21,59,60] An RCT showed a therapeutic effect of statistically significant gains in measures of strength, coordination, balance, and coordinated gait components.[4,59] In a 10-year study of 17 subjects, an analysis of safety and performance of the system showed a zero infection rate, 99% electrode survival rate, and excellent acceptance and patient satisfaction, with the system deemed comfortable by the patients.[60]

Conclusion

The recovery of coordination and motor control after a stroke is a form of motor skill acquisition or motor learning. Motor skill acquisition is based on activity-dependent plasticity, which is the modification of brain neural structure and function in response to motor activity practice or use. For the past decades, researchers have established that brain plasticity occurs in association with neurite outgrowth in the peri-infarct region,[61,62] synaptogenesis,[62] axonal sprouting,[63] increased neuronal excitability,[64,65] the reorganization of sensorimotor maps,[66,67] and neuronal pathway remodelling.[68,69]

For brain plasticity to occur, the required principles of motor learning must be met. Some studies of FES-assisted motor learning have incorporated these principles to good effect[4,13,20,18,51]; FES-assisted motor learning was used to activate muscles in the proper timing/sequence for practising the coordinated movement components that compose upper limb functional tasks or gait. Other currently available motor learning methods do not provide the full array of practice characteristics that FES-assisted motor learning affords.

The different types of FES systems each have advantages and disadvantages. The selection of the type of FES system for a given application should be

Clinical Pearls

Each patient is different, and surface FES treatment should be individualized for the patient's comfort and for the intended purpose.

Surface FES is most successful if used in conjunction with a motor learning program.. The user's attention must be focused on the desired training movement and their simultaneous volitional effort should be titrated to assist the FES in the movement training, but volitional effort should not produce abnormal compensatory strategies.

made according to the practical system characteristics relative to the application, the published evidence regarding benefits, and the availability. Functional electrical stimulation system technology development is ongoing and promises to bring more sophisticated delivery of coordination practice, more refined gait assistance, and more clinically practical systems in the future. Surface FES systems can best be fitted to the patient and used for motor learning and gait training by a licensed physiotherapist. For implantable FES systems, a surgeon is best qualified to place the electrodes and the stimulator. After the FES system is provided to the patient, a licensed physiotherapist is best qualified to utilize the FES system for treatment. Surface FES systems can be purchased directly from the four companies listed above (but currently deleted) or from their distributors. Implanted FES systems are currently in the research phase of development. ga

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References

1. Liberson W, Holmquest H, Scot D, et al. Functional electrotherapy: stimulation of the peroneal nerve synchronized with the swing phase of the gait of hemiplegic patients. Arch Phys Med Rehabil 1961;42:101–5.
2. Kottink AIR, Hermens HJ, Nene AV, et al. Therapeutic effect of an implantable peroneal nerve stimulator in subjects with chronic stroke and footdrop: a randomized controlled trial. Phys Ther 2008;4:437–48.
3. Chae J, Shaffler L, Knutson J. Neuromuscular electrical stimulation for motor restoration in hemiplegia. Top Stroke Rehabil 2008;5:412–26.
4. Daly JJ, Sng K, Fredrickson E, et al. Usefulness of an intralimb coordination measure in response to innovative gait training for stroke survivors. Gait Posture 2007;25:412–8.
5. Glanz M, Klawansky S, Stason W, et al. Functional electrostimulation in poststroke rehabilitation: a meta-analysis of the randomized controlled trials. Arch Phys Med Rehabil 1996;77:549–3.
6. Bowman BR, Baker LL, Waters RL. Positional feedback and electrical stimulation: an automated treatment for the hemiplegic wrist. Arch Phys Med Rehabil 1979;60:497–502.
7. Winchester P, Montgomery J, Bowman B, et al. Effects of feedback stimulation training and cyclical electrical stimulation on knee extension in hemipratic patients. Phys Ther 1983;63:1096–1103.
8. Merletti R, Zelaschi F, Latella D, et al. A control study of muscle force recovery in hemiparetic patients during treatment with functional electrical stimulation. Scand J Rehabil Med 1978;10:147–54.
9. Powell J, Pandyan AD, Granat M, et al. Electrical stimulation of wrist extensors in poststroke hemiplegia. Stroke 1999;30:1384–9.
10. Lagasse PP, Rogy MA. Functional electrical stimulation and the reduction of co-contraction in spastic biceps brachii. Clin Rehabil 1989;31:111–6.
11. Dimitrijevic MM, Stokic DS, Wawro AW, et al. Modification of motor control of wrist extension by mesh-glove electrical afferent stimulation in stroke patients. Arch Phys Med Rehabil 1996;77:252–8.
12. Hummelsheim H, Maier-Loth ML, Eickhof C. The functional value of electrical muscle stimulation for the rehabilitation of the hand in stroke patients. Scand J Rehabil Med 1997;29:3–10.
13. Alon G, Sunnerhagen KS, Geurts AC, et al. A home-based, self-administered stimulation program to improve selected hand functions of chronic stroke. Neurorehabilitation 2003;18:215–25.
14. Chae J, Yu DT, Walker ME, et al. Intramuscular electrical stimulation for hemiplegic shoulder pain: a 12-month follow-up of a multiple-center, randomized clinical trial. Am J Phys Med Rehabil 2005;84:832–42.
15. Yu DT, Chae J, Walker ME, et al. Intramuscular neuromuscular electrical stimulation for post-stroke shoulder pain: a multi-center randomized clinical trial. Arch Phys Med Rehabil 2004;85:695–704.
16. Chae J, Ng A, Yu DT, et al. Intramuscular electrical stimulation for shoulder pain in hemiplegia: does time from stroke onset predict treatment success? Neurorehabil Neural Repair 2007;16:16.
17. Chae J, Bethoux F, Bohine T, et al. Neuromuscular stimulation for upper extremity motor and functional recovery in acute hemiplegia. Stroke 1998;29:975–9.
18. Ring H, Rosenthal N. Controlled study of neuroprosthetic functional electrical stimulation sub-acute post-stroke rehabilitation. J Rehabil Med 2005;37:32–6.
19. Popovic MB, Popovic DB, Sinkjaer T, et al. Clinical evaluation of functional electrical therapy in acute hemiplegic subjects. J Rehabil Res Dev 2003;40:443–53.
20. Daly JJ, Hogan N, Perepezko EM, et al. Response to upper-limb robotics and functional neuromuscular stimulation following stroke. J Rehabil Res Dev 2005;42:723–36.
21. Daly JJ, Barnickle K, Kobetic R, et al. Electrically induced gait changes post stroke. J Neurorehabil 1993;1:17–25.
22. Waters RL, Campbell JM, Thomas L, et al. Energy cost of walking in lower extremity casts. J Bone Joint Surg 1982;64:896–9.
23. Waters RL, Campbell JM, Nakai R. Therapeutic electrical stimulation of the lower limb by epimysial electrodes. Clin Orthop Relat Res 1988;233:44–52.
24. Mayo N, Wood-Dauphinee ES, Ahmed S. Disablement following stroke. Disabil Rehabil 1999;21:1258–68.
25. Moseley AM, Wales A, Herbert R, et al. Observation and analysis of hemiplegic gait: stance phase. Aust J Physiother 1993;39:259–67.
26. Moore S, Schurr K, Wales A, et al. Observation and analysis of hemiplegic gait: wing phase. Aust J Physiother 1993;39:271–78.
27. Yan T, Hui-Chan CW. Functional electrical stimulation improves motor recovery of the lower extremity and walking ability of subjects with first acute stroke. Stroke 2005;36:80–5.
28. Alfieri V. Electrical treatment of spasticity. Reflex tonic activity in hemiplegic patients and selected specific electrostimulation. Scand J Rehabil Med 1982;14:177–82.
29. Veltink PH, Ladouceur M, Sinkjaer T. Inhibition of the triceps surae stretch reflex by stimulation of the deep peroneal nerve in persons with spastic stroke. Arch Phys Med Rehabil 2000;81:1016–24.
30. O'Sullivan SB, Schmitz TJ. Physical Rehabilitation: Assessment and Treatment. Philadelphia (PA): F.A. Davis Company; 1999.
31. Ada L, Dean CM, Hall JM, et al. Treadmill and overground walking improves walking after stroke. Arch Phys Med Rehabil 2003;84:1486–91.
32. Dean CM, Richards CL, Malouin F. Task-related circuit training improves locomotor tasks, chronic stroke. Arch Phys Med Rehabil 2000;81:409–17.
33. Wade DT, Collen FM, Robb GF, et al. Physiotherapy intervention later after stroke. Bio Med J 1992;304:609–3.
34. Werner RA, Kessler S. Effectiveness of outpatient rehabilitation for postacute stroke. Am J Phys Med Rehabil 1996;75:114–20.
35. Moseley AM, Stark A, Cameron ID, et al. Treadmill training and body weight support for walking after stroke. Cochrane Database Syst Rev 2003;(3):CD002840.
36. Kosak MC, Reding MJ. Comparison of weight-support versus bracing. Neurorehabil Neural Repair 2000;14:13–9.
37. Barbeau H, Visintin M. Optimal outcomes obtained with weight-support in stroke. Arch Phys Med Rehabil 2003;84:1458–65.
38. Liston R, Mickelborough J, Harris B, et al. Conventional physiotherapy and treadmill re-training for higher-level gait disorders in CVA. Age Ageing 2000;29:311–8.
39. Ding Y, Li J, Lai Q, et al. Motor balance and

coordination training enhances functional outcome in rate with transient middle cerebral artery occlusion. Neuroscience 2004;123: 667–74.
40. Visintin M, Barbeau H, Korner-Bitensky N, et al. A new approach to retrain gait in stroke through weight-support. Stroke 1998;29:1122–8.
41. Kwakkel G, Wagenaar RC. Effect of duration of upper- and lower-extremity rehabilitation sessions and walking speed on recovery of interlimb coordination in hemiplegia. Phys Ther 2002;82:432–48.
42. Nudo RJ, Milliken GW, Jenkins WM, et al. Use-dependent alterations of movement representations in primary motor cortex adult squirrel monkeys. J Neurosci 1996;15:785–807.
43. Nudo RJ, Wise BM, Sifuentes F, et al. Neural substrates for the effects of rehabilitative training on motor recovery after ischemic infarct. Science 1996;272:1791–4.
44. Singer R, Lidor R, Cauraugh JH. To be aware or not be aware? What to think about while learning and performing a motor skill. Sport Psychologist 1993;7:19–30.
45. Butefisch C, Hummelsheim H, Denzler, P, et al. Repetitive training of isolated movements. J Neurol Sci 1995;130:59–68.
46. Dean CM, Shepherd RB. Task-related training improves performance of seated reaching tasks after stroke: a randomized controlled trial. Stroke 1997;28:722–8.
47. Elbert T, Pantev C, Wienbruch C. Increased cortical representation of the fingers of the left hand in string players. Science 1995;270:305–7.
48. Pascual-Leone A, Torres F. Plasticity of the sensorimotor cortex representation of the reading finger in Braille readers. Brain 1993;116(Pt 1):39–52.
49. Bogataj U, Gros N, Malezic M, et al. Restoration of gait during two to three weeks of therapy with multichannel electrical stimulation. Phys Ther 1989;5:319–27.
50. Bogataj U, Gros N, Kljajic M, et al. The rehabilitation of gait in patients with hemiplegia: a comparison between conventional therapy and multichannel functional electrical stimulation therapy. Phys Ther 1995;6:490–502.
51. Daly JJ, Roenigk K, Holcomb J, et al., A randomized controlled trial of functional neuromuscular stimulation in chronic stroke subjects. Stroke 2006;1:172–8.
52. Van Peppen RPS, Kwakkel G, Wood-Dauphinee S, et al. The impact of physical therapy on functional outcomes after stroke: what's the evidence? Clin Rehabil 2004;18:833–62.
53. Stanic U, Acimovic-Janezic R, Gros N, et al. Multichannel electrical stimulation for correction of hemiplegic gait. Methodology and preliminary results. Scand J Rehabil Med 1978;2:75–92.
54. Waters RL, McNeal D, Perry J. Experimental correction of footdrop by electrical stimulation of the peroneal nerve. J Bone Joint Surg Am 1975;8:1047–54.
55. Weber DJ, Stein RB, Chan KM, et al. Functional electrical stimulation using microstimulators to correct foot drop: a case study. Can J Physiol Pharmacol 2004;82:784–92.
56. Strojnik P, Acimovic R, Vavken E, et al. Treatment of drop foot using an implantable peroneal underknee stimulator. Scand J Rehabil Med 1987;19:37–43.
57. Scheiner A, Polando G, Marsolais EB. Design and clinical application of a double helix electrode for functional electrical stimulation. IEEE Trans Biomedical Eng 1994;44:425–31.
58. Borges G, Ferguson K, Kobetic R. Development and operation of portable and laboratory electrical stimulation systems for walking in paraplegic subjects. IEEE Trans Biomedical Eng 1989;7:798–801.
59. Daly JJ, Ruff RL. Electrically induced recovery of gait components for older patients with chronic stroke. Am J Phys Med Rehabil 2000;4:349–60.
60. Daly JJ, Kollar K, Debogorski AA, et al. Performance of an intramuscular electrode during functional neuromuscular stimulation for gait training post stroke. J Rehabil Res Dev 2001;5:513–26.
61. Ng SC, de la Monte SM, Conboy GL, et al. Cloning of human GAP-43: growth association and ischemic resurgence. Neuron 1988;1:133–9.
62. Stroemer RP, Kent TA, Hulsebosch CE. Neocortical neural sprouting, synaptogenesis, and behavioral recovery after neocortical infarction in rats. Stroke 1995;26:2135–44.
63. Carmichael ST, Wei L, Rovainen CM, et al. New patterns of intracortical projections after focal cortical stroke. Neurobiol Dis 2001;8:910–22.
64. Schiene K, Bruehl C, Zilles K, et al. Neuronal hyperexcitability and reduction of GABAA-receptor expression in the surround of cerebral photothrombosis. J Cereb Blood Flow Metab 1996;16:906–14.
65. Redecker C, Luhmann HJ, Hagemann G, et al. Differential down regulation of GABAA receptor subunits in widespread brain regions in the freeze-lesion model of focal cortical malformations. J Neurosci 2000;20:5045–53.
66. Frost SB, Barbay S, Friel KM, et al. Reorganization of remote cortical regions after ischemic brain injury: a potential substrate for stroke recovery. J Neurophysiol 2003;89:3205–14.
67. Gharbawie OA, Gonzalez CL, Williams PT, et al. Middle cerebral artery (MCA) stroke produces dysfunction in adjacent motor cortex as detected by intracortical microstimulation in rats. Neuroscience 2005;130:601–10.
68. Dancause N, Barbay S, Frost SB, et al. Extensive cortical rewiring after brain injury. J Neurosci 2005;25:10167–79.
69. Napieralski JA, Butler AK, Chesselet MF. Anatomical and functional evidence for lesion-specific sprouting of corticostriatal input in the adult rat. J Comp Neurol 1996;373:484–97.