Health and Fitness Benefits of Functional Electrical Stimulation-Evoked Leg Exercise for Spinal Cord–Injured Individuals: A Position Review

Nur Azah Hamzaid and Glen M. Davis

Purpose: To investigate the potential health and fitness benefits of lower extremity functional electrical stimulation (FES) exercise for people with spinal cord injury (SCI). **Method:** Systematic review strategy conducted from electronic databases from 1830 until July 2008. Studies with randomized and/or controlled designs were highlighted for analysis, but all relevant literature was described to develop an overall position statement. Study selection: (1) leg FES-evoked exercise for (2) people with SCI and (3) effects on health and fitness outcomes. **Result:** One study was identified as a randomized controlled trial, and 32 investigations were quasi-experimental trials. Six outcome categories were identified on the topic of potential health and fitness benefits for people with SCI. Evidence from FES-evoked exercise studies demonstrated (a) positive changes within skeletal muscle, (b) enhanced cardiovascular and peripheral blood flow, (c) altered metabolic responses and increased aerobic fitness, and (d) improved functional exercise capacity. Bone mineral density changes and alterations of psychosocial outlook were less consistently reported or outcomes were deemed equivocal. **Conclusion:** Randomized and/or controlled studies reporting on the potential benefits of FES-evoked exercise are sparse. The available literature suggested that across a variety of outcome domains FES-evoked leg exercise promotes certain health and fitness benefits for people with SCI. **Key words:** *exercise, functional electrical stimulation, position review, spinal cord injury, systematic technique*

Since the 1960s, functional electrical stimulation (FES)-evoked leg muscle contractions have been widely employed as a rehabilitation therapy or as an exercise regimen using the paralyzed lower limbs of individuals with spinal cord injury (SCI). FES is defined as the use of electrical currents to induce muscle contractions by an external controller, thereby bypassing the central nervous system to evoke limb movements.[1,2] Paralyzed muscles, although atrophied after upper motor nerve spinal cord lesions, are still able to produce muscle contractions under FES control and thus generate force, power, and motion. Therapeutic stimulation commonly uses transcutaneous FES, whereby electrical current is applied via electrodes on the skin surface located over the individual's paralyzed or paretic muscles. Alternative approaches may use percutaneous electrodes or fully implanted FES leads whereby neurostimulation is directed into muscles or the spinal roots to evoke movements.[3]

FES has been used to produce hand grasp in patients with tetraplegia and to generate

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an upright posture and locomotion in patients with paraplegia.[1,4] Other FES applications have included partial bladder control, muscle re-education, strength training, and wound healing.[5] The technique has been reported to reduce muscle spasticity, promote blood circulation in skin and muscle, assist with pain management, and reduce pressure sores in people with SCI. For more than 20 years, FES-evoked leg exercise, particularly cycling, has been popular as a technique for maintaining health and fitness after traumatic SCI.[6] FES exercise may lead to other physiological adaptations that may be advantageous for wheelchair-based individuals.[7]

Despite numerous literature reviews,[8–16] there has not been a careful systematic approach toward documenting possible health and fitness benefits of FES-evoked exercise for individuals with SCI. This deficit is probably because the majority of published research studies lack consistency of approach, deploy small group sizes, and are often neither randomized nor controlled. Despite many years of clinical use and numerous research studies, there is still insufficient evidence to formulate a systematic review. In the current position review, we have used systematic techniques to survey available peer-reviewed literature to support a hypothesis that FES-evoked lower-limb exercise after SCI might promote certain health and fitness benefits amongst its users.

We articulated the question, "Does FES-evoked exercise of the lower limbs promote health and fitness benefits for the SCI population, and, if so, to what extent?"

Method

A systematic search of published sources was performed using Ovid MEDLINE (1966 to July 31, 2008), Ovid MEDLINE Daily Update, PREMEDLINE, Ovid OLDMEDLINE (1950–1965), SPORTDiscus (1830 to July 31, 2008), and Web of Science (1900 to July 31, 2008). A search for reviews on the topic was also performed using the Cochrane Library and Cochrane Database for Systematic Reviews. In addition, FES-specific annual international conference archives with known peer-review criteria were hand-searched for published studies. Studies were limited to human research, but they could be in any language, as long as English abstract translations describing clear and categorical outcomes were provided. All scientific findings were screened by the authors to ensure that they met certain inclusion criteria, as defined by the key search terms.

The inclusion criteria for this review were as follows: (1) functional electrical stimulation (FES) or functional neuromuscular stimulation (FNS) exercise, (2) lower limbs of neurologically disabled people, and (3) health and fitness. By *exercise* the authors referred to predominantly lower-limb physical training activities including cycling, rowing, walking, standing, muscle contractions, limb extension, or isometric muscle stimulation. In this review, FES-evoked lower extremity movements that might have involved concurrent upper extremity exercises were not excluded, even though the effects of such combined exercise could not fully attribute physiological responses to either the lower limb FES-evoked activities or the patient's voluntary upper body effort during exercise. The physiological responses could be from the combined effort (i.e., hybrid activity) Studies conducted on functional applications of FES or technological developments were included if there were secondary health and fitness insights within the study. *Func-*

tional studies comprised those that involved the use of FES for daily activities, such as grasping, bladder control, casual walking, or standing, but without scheduled exercise training for purely health and fitness benefits. *Technological development* studies included control approaches, analyses of FES stimulation parameters and controller performance, simulation and modeling studies, or any research into the technological domain of FES but without any intent to describe possible physiological benefits to subjects.

Key words used for the search were (a) FES, functional electrical stimulation, FNS, functional neuromuscular stimulation, functional electric stimulation, electrostimulation, electrical stimulation, functional stimulation, neuro stimulation, neurostimulation, neuromuscular stimulation; (b) exercise, training, cycling, rowing, walking, ambulation, standing, contraction, extension, stimulation, stimulated; (c) spinal cord, SCI, paraplegic, paraplegia, tetraplegics, tetraplegia, quadriplegic, quadriplegia, paralyzed, paralysed, paralyze, paralyse, paralysis, disabled; (d) human, man, people, person, patient, subjects; and (e) cardiovascular, blood flow, metabolic, muscle, endurance, strength, bone, physiological, psychosocial, cardiorespiratory, aerobic, blood, biochemistry, morphology, histochemistry.

We manually scanned the titles of all computer-generated search results to identify appropriate studies for inclusion. After the first search round, only one randomized controlled trial (RCT) was identified. Therefore, a second search round was conducted to include quasi-experimental research, specifically studies that adopted either randomization or controlled methodologies. Another 32 articles were identified that were considered of good quality meeting the broader criteria. By *controlled studies,* we considered investigations that included SCI participants in a treatment and control group. Studies that used able-bodied people as the control group were not categorized as controlled studies.

The collective conclusions of the RCT and quasi-RCT literature were not sufficient to answer the proposed question categorically, because the research designs of those studies were so widely varied. We finally included other nonrandomized or controlled studies, such as those with cross-sectional or crossover designs, which often comprised clinical trials and patient surveys, to encompass all available scientific evidence pertaining to FES-induced exercise. Nevertheless, the RCT and quasi-RCT studies were given greater emphasis in this position review, while the others were used to provide supporting facts to complete the picture about the topics in question.

Health and fitness outcomes were a priori divided into six broad categories: (a) skeletal muscle morphology and biochemistry; (b) cardiovascular and hemodynamic responses; (c) generalized metabolic responses, including aerobic fitness; (d) bone mineral density and stiffness; (e) functional changes in exercise capacity; and (f) psychosocial outlook.

Some studies crossed over two or more categories. In these cases, each study was primarily classified into its dominant category, but discussion of findings was considered more broadly within each outcome area.

Results

Figure 1 summarizes the search strategy for the studies selected for review and analysis. From over 1,122 potentially relevant titles and abstracts up to July 2008, 192

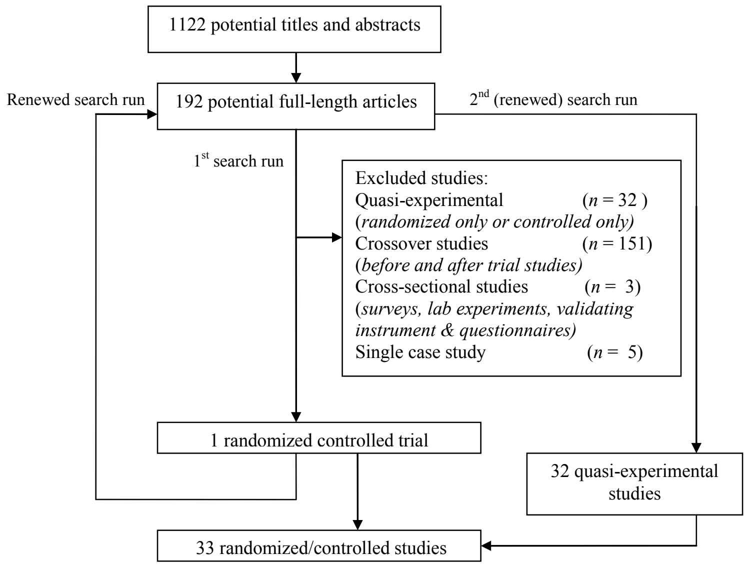

Figure 1 Article search flowchart.

fulfilled the primary inclusion criteria. These included peer-reviewed journal articles and refereed conference proceedings. Only one study was an RCT,[17] and an additional 32 quasi-experimental investigations were identified.

Together, the 33 papers comprised health and fitness outcomes in the domains of skeletal muscle morphology and biochemistry (**Table 1**), cardiovascular and haemodynamic responses (**Table 2**), metabolic responses and aerobic fitness changes (**Table 3**), bone mineral density and stiffness (**Table 4**), functional changes of exercise capacity (**Table 5**), and psychosocial outlook (**Table 6**).

Skeletal muscle morphology and biochemistry

Muscles denervated after SCI lose mass and contractile force. Participation in FES-evoked leg exercise programs over several years may reverse or ameliorate muscle atrophy and after such training muscle fibers can attain similar characteristics to sedentary nondisabled individuals.[18–20] This section presents evidence from six selected studies informing positive and negative outcomes on reversal of muscle atrophy as well as the effects of load and stimulation frequency on muscle properties. Such changes in muscle properties may include changes in muscle fiber, cross-sectional area, and muscle mass or volume.

A well-designed RCT study by Baldi and colleagues[17] demonstrated that muscle atrophy could be prevented in motor complete SCI participants through 6 months of FES cycling compared to FES-evoked isometric contractions or no training at all. Their research revealed significant reductions in total and lower limb lean body mass including gluteal mass in an SCI control group and for subjects who performed FES-induced

Table 1. Randomized/controlled studies of functional electrical stimulation (FES) exercise effects on muscle morphology and biochemistry

Author	Sample	Duration, intervention	Main result and conclusions	Quality considerations
Baldi et al, 1998[17]	*N* = 26, C4-T12 Frankel A/B	3 or 6 months, FES cycling or FES isometric contraction	FES cycling, but not FES isometric contractions, prevents muscle atrophy. Controls lost muscle mass.	Controlled study, randomly assigned subjects to trials.
Crameri et al, 2004[21]	*N* = 6, C6-T7 complete	10 weeks, FES load applied leg extension	Load applied during FES training increased amount of muscle force and fiber adaptation.	6 weeks self-control period, randomized muscle biopsies before intervention.
Demchak et al, 2005[25]	*N* = 10, C4-T8 ASIA A/B	13 weeks, FES cycling	Muscle biopsies of leg muscle in intervention group showed larger fiber cross-sectional area compared to control group.	Controlled study.
Harridge et al, 2002[22]	*N* = 9, C7-T10	9 weeks, FES leg contractions against an isometric dynamometer	FES trained leg showed increase in muscle fatigue resistance. No change in composition of myosin heavy chain was detected.	Controlled study, one leg control, one leg trained. No information on randomization.
Kern et al, 2004[24]	*N* = 22, lower motor neuron lesion	6 months, FES knee extension	FES exercise reversed muscle atrophy and increased paralyzed leg muscle mass.	Controlled study (11 control, 11 intervention).
Skold et al, 2002[39]	*N* = 15, unspecified lesion level ASIA A/B	6 months, FES cycling	Subjects undergoing FES cycling experience increased lower extremity muscle volume.	Controlled study.

Note: Frankel classification A = clinically complete upper motor neuron lesions without preserved motor or sensory function; Frankel classification B = absence of volitional motor function below the level of lesion, but some preserved sensation; ASIA = American Spinal Injuries Association classification.

Table 2. Randomized/controlled studies of functional electrical stimulation (FES) exercise effects on cardiovascular and haemodynamic responses

Author	Sample	Duration, intervention	Main result and conclusions	Quality considerations
Davis et al, 1990[66]	*N* = 12 T5-L2	Single day, FES-evoked leg muscle contraction	FES-evoked leg muscle contraction on paraplegics increased venous return and improved cardiovascular responses during submaximal exercise.	Controlled study, subjects' allocation depended on responsiveness to FES, randomized order of trial.
Nash et al, 1995[72]	*N* = 6 C5-C6 Frankel A/B	30 minutes each, FES cycling or continuous passive movements	FES cycling modified cardiac and metabolic functions from rest. Cardiac output in FES cycling was primarily due to increased heart rate.	Trials conducted on randomized nonconsecutive days.
Nash et al, 1996[96]	*N* = 20 T4-T11 ASIA A Frankel A/B	Single day, FES cycling	FES trained tetraplegics have greater lower extremity blood flow and hyperaemic responses to occlusion.	Controlled study (10 trained, 10 untrained), 10 able-bodied, blinded cross-sectional comparison
Petrofsky et al, 1992[73]	*N* = 8 T4-T11 complete	6 months, FES ergometer cycling at different work rates	FES cycling resulted in greater cardiovascular responses, including blood pressure, cardiac output, heart rate, and power endurance.	Randomized order of trials at different power outputs.
Raymond et al, 1999[68]	*N* = 10, T5-T12	Single day, arm cranking and FES cycling	FES-cycling + arm-cranking exercise increased stroke volume, i.e., reduced venous pooling and increased cardiac volume loading.	Trials conducted on randomized nonconsecutive days.
Raymond et al, 2002[89]	*N* = 10 T4-T9 ASIA A	Single day, 5 FES cycling and 3 passive cycling	On-transient response of FES cycling showed immediate and sustained increase in MAP in high-lesion subjects but only a small increase in MAP in low-lesion paraplegics.	Randomized order of trials.

Note: *Note:* Frankel classification A = clinically complete upper motor neuron lesions without preserved motor or sensory function; Frankel classification B = absence of volitional motor function below the level of lesion, but some preserved sensation; ASIA = American Spinal Injuries Association classification; MAP = mean arterial pressure.

Table 3. List of randomized/controlled studies of metabolic responses and aerobic fitness

Author	Sample	Duration, intervention	Main result and conclusions	Quality considerations
Davis et al, 1990[66]	*N* = 12 T5-L2	Single day, FES-evoked leg muscle contraction	FES evoked leg muscle contraction on paraplegics increased venous return and improved cardiovascular responses in submaximal exercise.	Controlled study, subjects allocated depending on responsiveness to FES, randomized order of trial.
De Carvalho et al, 2005[116]	*N* = 21 C4-C8 complete	6 months, FES-assisted treadmill training	FES-assisted treadmill training among quadriplegics increased VO_2 and energy expenditure.	Controlled study, subject allocated according to complete or incomplete lesion.
De Carvalho, 2006[118]	*N* = 21 C4-C8 ASIA A	6 months, FES treadmill gait training	Treadmill gait with FES increases metabolic stress and aerobic capacity more efficiently compared to normal physiotherapy.	Controlled study, subjects allocated to control group according to participation.
Hooker et al, 1995[104]	*N* = 8 C5-L1 Frankel A	19 weeks, FES ergometer cycling	Improvement in VO_2 was detected. FES-evoked exercise can increase cardiorespiratory fitness.	Randomized block repeated measures, before and after training measurement.
Jacobs, 1998[117]	*N* = 9 T4-T10	Single day, FES walking or arm cranking	At matched subpeak levels of VO_2, FES walking showed greater endurance. No significant difference in peak metabolic responses between arm cranking or FES walking.	Randomized order of trials.

Laskin et al, 1993[114]	$N = 8$ C6-T6	Single day, 3 different trials of FES rowing	Combined arm and leg FES rowing in paraplegia produced significant increase in oxygen consumption.	Self-controlled subjects, randomized order of trials.
Mutton et al, 1997[107]	$N = 11$ C5-L1 complete	18 weeks, FES cycling with arm exercise	FES cycling with simultaneous arm exercise improved aerobic capacity of SCI patients.	Self-controlled study, nonrandomized subject allocation to test.
Phillips et al, 1995[108]	$N = 8$ C6-T12 Motor complete or incomplete, or some degree of sensation	Single day study, arm cranking with no FES and with FES at high & low current stimulation	FES can increase submaximal arm-cranking exercise oxygen uptake and the increments were enhanced at higher level of electrical stimulation and workload.	Random application of three stimulation currents (no stimulation, low stimulation, and high stimulation).
Raymond et al, 1999[68]	$N = 10$ T5-T12	Single day, arm cranking and FES cycling	Combined FES-cycling and arm-cranking exercise produced greater metabolic stress compared to arm cranking alone.	Trials conducted on randomized nonconsecutive days.

Note: FES = functional electrical stimulation; Frankel classification A = clinically complete upper motor neuron lesions without preserved motor or sensory function; ASIA = American Spinal Injuries Association classification.

Table 4. List of randomized/controlled studies of bone mineral density (BMD) and stiffness

Author	Sample	Duration, intervention	Main result and conclusions	Quality considerations
Bloomfield et al, 1996[143]	*N* = 9 C5-T7 Frankel A/B	9 months, FES ergometry cycling	BMD of lumbar spine increased with FES cycle ergometry training among SCI patients.	Self-controlled study, non-randomized trial.
Eser et al, 2003[142]	*N* = 38 C5-T12 ASIA A / B	6 months, FES cycling (19 control, 19 intervention)	BMD in FES cycling intervention group reduced at slower rate than control group.	Controlled study, nonrandomized due to ethical concern; subjects are comparable between groups.
Hangartner et al, 1994[144]	*N* = 37 C5-T10 complete/ incomplete	12 weeks, FES cycling and FES knee extension resistance exercise	Rate of bone loss in FES exercise group was less than expected from regression lines of bone density loss. FES exercise intervention revealed positive rehabilitation effect for SCI.	Controlled study (15 SCI in intervention group), nonrandomized assignment of subjects to groups.
Carvalho et al, 2006[138,139]	*N* = 21, C4-C8 chronic	6 months, treadmill gait training with NMES	Gait group had increase in bone formation markers and a decrease in bone resorption markers. Gait training with NMES improve bone mass.	Controlled study (11 in gait group), complete lesion in gait group, incomplete in control.
Shields et al, 2007[140]	*N* = 4 T12 and above ASIA A	6 to 11 months, unilateral soleus training	No changes on BMD were observed between the trained and untrained leg, before or after study.	Within-subject controlled. Non-stimulated leg served as control condition.
Clark et al, 2007[141]	*N* = 33, C4-T12 acute ASIA A-D	5 months, FES tetanic muscle contraction, knee flexion/extension	Total body BMD differed significantly between control and intervention group up to 3 months but not thereafter. No changes in hip and spine BMD throughout experiment.	Nonrandomized, controlled, repeated measures.

Note: FES = functional electrical stimulation; NMES = neuromuscular electrical stimulation; Frankel classification A = clinically complete upper motor neuron lesions without preserved motor or sensory function; Frankel classification B = absence of volitional motor function below the level of lesion, but some preserved sensation; ASIA = American Spinal Injuries Association classification.

Table 5. List of randomized/controlled studies of functional changes of exercise capacity

Author	Sample	Duration, intervention	Main result and conclusions	Quality considerations
Eser et al, 2003[167]	N = 19 C5-T10 complete lesion	30 min each, FES cycling at 30, 50, or 60 Hz stimulation frequencies	Power outputs of exercise were greater at higher frequency stimulation. No muscle fatigue was detected at any tested frequencies within 30 minutes.	Trials conducted on randomized nonconsecutive days.
Fornusek et al, 2004[182]	N = 9 T4-T9 ASIA A	Single day, FES cycling at different pedaling cadence	Exercise torque production at lower cadence decayed more slowly. Fatigue rate also decreased at lower pedaling cadence.	Different cadence trials conducted on randomized order.
Petrofsky et al, 2000[172]	N = 90 T4-T11 complete lesion	10 weeks, FES isokinetic exercise	Training for 3 days a week for 30 minutes a day proved optimal for strength and endurance training with 50:50 work to rest ratio.	Controlled study with 9 groups of 10 subjects. Matched subjects between groups.
Petrofsky et al, 2004[170]	N = 45 T3-T12 complete	6 weeks, FES ergometry cycling	Weight training concurrently and before FES cycle ergometry increased training endurance among SCI subjects.	Controlled study, nonrandomized subject allocation to trials.
Postans et al, 2004[156]	N = 14 C4-T8 ASIA C / D	4 months, treadmill walking with partial weight bearing and FES	FES augmented partial weight bearing increases walking endurance and speed.	Self-controlled subjects with 4 weeks control period, randomized intervention-control sequence.
Rabischong et al, 1992[171]	N = 25 T2-T10 complete	2 months, FES knee extension training	Muscle strength improved significantly with training but fatigue resistance remained at low level.	Controlled study, nonrandomized group.
Shields et al, 2007[140]	N = 4 T12 and above ASIA A	6 to 11 months, unilateral soleus training	Fatigue index and torque-time integral of the FES-trained leg improved significantly compared to the untrained leg. Peak torque demonstrated by the untrained leg increased together with the peak torque of the trained leg. Performance indicators related to training compliance.	Within-subject controlled. Non-stimulated leg served as control condition.

Note: FES = functional electrical stimulation; Frankel classification A = clinically complete upper motor neuron lesions without preserved motor or sensory function; ASIA = American Spinal Injuries Association classification.

Table 6. Randomized/controlled studies of psychosocial outlook

Author	Sample	Duration, intervention	Main result and conclusions	Quality considerations
Bradley, 1994[204]	$N = 60$ unspecified lesion level	3 months, mixed post-rehab FES exercise program.	Subjects with unrealistic expectation of FES have higher depression scores than ones with realistic expectations.	Controlled study, nonrandomized due to factors such as high cost, insurance coverage, and commitment.

Note: FES = functional electrical stimulation.

isometric contractions. In contrast, SCI participants who performed FES cycling showed no reduction in their lower limb lean body mass and gluteal lean body mass after 3 months of exercise training. After 6 months, the lower limb and gluteal lean body masses had increased significantly in the cycle-training group.

Factors that affect muscle properties during FES exercise include external loading and neuromuscular stimulation frequencies. A controlled study by Crameri et al[21] demonstrated that the external load applied on completely paralyzed muscles during electrical stimulation exercise was important to subsequent morphologic and biochemical adaptations. Isometric training, which evoked high external load upon a muscle, revealed significantly increased muscle fiber cross-sectional areas, higher percentage of type I fibers, enhanced citrate synthase activity, and greater relative oxygenation compared to dynamic load training.

In Harridge and colleagues' controlled study,[22] they demonstrated that there was a relationship between low-frequency stimulation isometric training and the development of muscle fatigue resistance after SCI (C7-T10). Following FES-evoked training, the subjects' fatigue index increased by 75%, but no change was detected in the contralateral (control) leg that received no FES muscle training. Gerrits et al[23] did not observe this result in their complete SCI subjects (C5-T9), so the precise relationship between stimulation frequency and muscle adaptations in paralyzed human tissue remains unclear.

Muscle fiber diameter and cross-sectional area increased after FES exercise. Kern and co-workers[24] reported in their controlled study that long-term denervated muscles expressed more than 50% of myofibers with diameters less than 10 μm, whilst muscles that underwent consistent FES training contained more than 50% myofibers with diameters greater than 30 μm. Similarly, a controlled study by Demchak et al[25] noted from muscle biopsies that larger fiber cross-sectional areas in vastus lateralis muscles were observed in motor complete SCI individuals who performed FES cycling. Other quasi-experimental evidence[26–29] has supported these findings. Yet, it is worth noting that some researchers who have investigated changes in muscle fibers after FES training reported conflicting conclusions.[30–38]

Increased muscle cross-sectional area lead to increased muscle bulk, volume, and circumference. A controlled study by Skold and colleagues[39] investigated body composition after FES exercise in motor complete SCI participants. They reported increased leg muscle volume without changes in total body mass among SCI individuals who participated in FES-evoked cycling exercise for 6 months, but these outcomes were not observed in nonexercise controls. Their study agreed with a large number of quasi-experimental crossover investigations that have reported positive effects on body composition, including muscle mass after FES-evoked cycling,[37,38,40–44] FES-evoked knee extension,[45–50] FES-induced walking,[51–53] or other combined modes of FES exercise.[33,54,55] Only two studies failed to detect any changes at all in muscle mass and circumference.[56,57]

In terms of altered muscle biochemistry after FES exercise, two crossover studies reported changes in muscle size and protein synthesis.[58,59] FES cycling training was observed to increase protein expressions of glucose transporter GLUT-1 and GLUT-4 content in paralyzed muscles,[38,60] increased glycolytic and mitochondrial oxidative enzymes,[61] increased collagen turnover,[62] and increased endothelin and creatine kinase composition.[63]

All these studies suggested that FES-evoked cycling was highly effective for promoting muscle hypertrophy in individuals with thoracic SCI, particularly when external load was applied during such exercise. Positive changes were reported about the physical properties of muscles, such as their mass and volume, and also about altered muscle morphology and biochemistry. Unfortunately, based on a lack of empirical evidence, we cannot claim that these benefits might also apply to high-lesion SCI individuals (i.e., tetraplegia), because most RCT studies that have posited positive health benefits on muscles have used SCI participants with lower lesion levels.

In summary, one randomized controlled study, five randomized or controlled investigations, and numerous quasi-experimental trials all generally demonstrated positive changes to skeletal muscle morphology and biochemistry in adherents to exercise programs involving FES training. These data lend support to our position statement that such exercise promotes peripheral muscle health and fitness benefits for the SCI population.

Cardiovascular and haemodynamic responses

In able-bodied people, changes in cardiovascular responses during exercise are modulated by neural feedback arising from exercising muscles. This mechanism may not be operant after SCI, whereby functioning afferent neural circuits from peripheral muscles do not transcend the spinal lesion to higher order cardiovascular control centers in the brain. Thus, cardiovascular and haemodynamic responses during FES-evoked exercise may be dissimilar to voluntary exercise responses. This section reports on six selected studies and some corroborating evidence that have investigated this question.

During FES-evoked physical activities, cardiovascular and metabolic variables such as heart rate (HR), oxygen consumption (VO_2), and stroke volume (SV) have been observed to increase in individuals with SCI in a similar fashion to their able-bodied cohorts undertaking voluntary exercise.[64] Yet, SCI individuals' cardiac output (Q) responses have sometimes been increased during FES-exercise significantly more than observed for equivalent able-bodied exercise.[65]

One explanation for this finding was suggested by Davis et al[66] who proposed that SCI individuals' central haemodynamic responses might be augmented by FES-evoked movements improving venous return from the dependent limbs. In the controlled study, they observed that persons with paraplegia who performed FES-evoked leg extension during arm-cranking exercise had no different steady-state HR responses, but their SV and Q increased compared to arm exercise alone. This finding suggested that an increase in venous return from the FES-contracted lower limb muscles contributed to greater cardiovascular performance during such hybrid (i.e., arm + leg) exercise.[67] Submaximal arm-cranking exercise induced similar HR, Q, or power output compared to hybrid effort but at a significantly lower VO_2 and SV. During peak exertion, hybrid exercise demonstrated larger VO_2 compared to arm cranking alone, as reported by Raymond et al's randomized trial.[68]

Inconsistent responses of exercise HR have been reported amongst studies. Some studies have reported a normal exercise-induced tachycardia, whereas others have observed no change of HR during FES-evoked muscle contractions. Thomas and co-authors[69] and Kjaer and colleagues[70] proposed a hypothesis whereby, after SCI, blood circulation might play a role in evoking "pseudo-normal" HR response during leg exercise when muscle neural feedback and central command were not operant.[69,70] Supporting the lack of central command concept, Raymond et al[71] demonstrated that FES cycling did not reset the carotid sinus baroreflex to operate around a higher sinus pressure, as occurs during voluntary exercise. They posited this explanation for their observation of inconsistent HR responses during FES cycling, because the carotid baroreflex still responded to blood pressure fluctuations at rest and at similar carotid sinus pressures.[71]

A randomized trial by Nash and colleagues[72] observed that Q in persons with tetraplegia increased during FES exercise via elevated HR only, with no detected change in SV. In contrast, another randomized study by Petrofsky and Stacy[73] noted decreased HR after 3 months of FES cycling. Further inconsistent evidence of cardiovascular responses during or following FES-evoked exercise in SCI individuals has been reported in other published studies.[65,74–83] It is interesting to note that patients with SCI who walk with FES assistance and use voluntary muscles in their arms to stabilize their gait pattern have always demonstrated augmented cardiovascular responses or reduced cardiac stress.[51,52,84–86] The key message is that FES-evoked lower-limb exercise has poorly understood command and control effects on whole-body cardiovascular responses, partly because the modality has uncertain components of central neural command, absent peripheral afferent feedback, and unquantified blood-borne neurohumeral drive components.

Apart from the central cardiac adaptations previously described, SCI individuals who exercise via FES might also experience certain peripheral haemodynamic adaptations. Vascular or haemodynamic responses of the lower extremity have generally accompanied central cardiovascular responses in SCI individuals undertaking FES-induced training.[80–83,87,88] For example, a randomized study by Raymond et al[89] investigated transient onset responses during FES-induced cycling in spinal cord–injured patients with paraplegia. Low-lesion (T7-T9) and high-lesion (T5-T6) individuals revealed different responses of blood pressures during evoked leg exercise. In persons with high-lesion paraplegia, blood pressures were increased instantly and were sustained for several minutes. The increment in blood pressure was immediately accompanied by a concomitant reduction in HR. On the other hand, blood pressure of persons with low-lesion paraplegia demonstrated a small rise at the beginning of exercise but quickly returned to near resting levels, without significant alterations in HR during exercise onset. Other supporting quasi- experimental evidence has generally reported improved blood flow during FES standing,[49] hybrid training,[56] or FES leg extension,[90,91] and all these studies have proposed there is reduced venous pooling during leg muscle contractions. Yet, notwithstanding the strong empirical evidence for enhanced blood flow during FES, a study by Olive et al pointed out that the increase in blood flow during FES-induced muscle contractions was five times slower than for able-bodied individuals and that this slow increase of blood flow escalated their fatigue more than in able-bodied individuals.[92]

Muscle blood flow is altered after SCI, but adaptations that naturally occur following paralysis also include changes to blood vessel properties. Because paralyzed muscles are tonically inactive, reduced blood flow leads to peripheral circulatory adaptations such as decreased vessel diameter, decreased femoral artery compliance, and increased shear stress in blood vessels. Three longitudinal FES-training studies revealed significant reversal of these negative sequelae after SCI.[93–95] A controlled study by Nash and colleagues[96] assessed lower extremity blood flow and responses to occlusion ischemia in FES-trained versus sedentary tetraplegics. The authors observed a greater lower extremity blood flow in the trained subjects and greater hyperaemic responses to occlusion compared to the sedentary subjects. They proposed this finding was due to a larger vascular bed in the conditioned muscles. Other cross-sectional studies also reported similar occlusion responses.[51,97] Total peripheral resistance in lower limbs also was reduced after FES-induced exercise,[75,98,99] with increased resting diameter of femoral arteries.[100]

In summary, there have been inconsistent findings concerning HR and blood pressure responses during FES-evoked muscle contractions, likely due to poorly understood mechanisms of cardiovascular control. However, other cardiovascular and haemodynamic responses during and after FES exercise have supported, through randomized, controlled, or quasi-experimental evidence, the view that such exercise promotes positive adaptations. The observation of increased

SV, Q, and VO_2, as well as improved vascular adaptations within peripheral musculature, positively positions the argument that FES exercise promotes cardiovascular and haemodynamic health and fitness for wheelchair-bound individuals.

Metabolic responses and aerobic fitness

The expression of an individual's peak aerobic fitness during exercise reflects an interaction of peripheral muscle metabolism (oxygen demand) and central cardiovascular responses (oxygen supply). Accordingly, any potential improvement of whole-body metabolism and aerobic fitness following FES exercise reflects adaptations transpiring within both the peripheral musculature and cardiovascular system. The nine randomized or controlled studies reported herein relate to generalized metabolism and/or aerobic fitness changes during and after FES-evoked exercise.

The whole-body metabolic responses of SCI individuals during leg exercise are quite different from the able-bodied population due to their considerably smaller leg muscle mass and the inherent differences of FES-evoked muscle contractions compared to voluntary muscle activation.[37,101,102] SCI does not affect the ability of the central nervous system to elicit metabolic responses during FES exercise,[69] particularly those dependent upon baroreflex activity during voluntary effort.[103] However, some studies that have investigated submaximal and graded FES exercise have revealed different metabolic responses among SCI subjects.[74,75,77] A good quality randomized study of 19 weeks of graded FES-cycle training by Hooker and colleagues[104] showed significant increases of peak VO_2 at the end of training, in the absence of differences in maximal work rate, HR, and expired ventilation (VE). In the same study, the authors also reported no significant changes in metabolism during submaximal exertion.

In a similar fashion to the cardiovascular responses, when FES leg exercise was combined with upper body activity (hybrid exercise), whole-body metabolism was increased.[105,106] An early controlled study by Davis and co-workers[66] did not observe significant changes of VO_2 between FES and no FES conditions, suggesting that its individual contribution to whole-body metabolism was very small. However, later self-controlled investigations by Mutton and colleagues,[107] Phillips and Burkett,[108] and a randomized trial by Raymond et al[68] all clearly demonstrated that hybrid exercise using the paralyzed legs provided greater potency for aerobic fitness development compared to FES leg cycling or arm exercise alone. Further empirical evidence from crossover studies supported the viewpoint that combined upper body voluntary exercise and FES-evoked leg exercise produced enhanced metabolic responses, which included higher peak VO_2[56,109–111]; increased posttraining measurements of HR, VO_2, VE, and Q[67,99,112]; larger SV; greater arteriovenous oxygen extraction[98]; and increased peak power output.[42] The level of whole-body metabolism (METS) during FES alone was less than 50% of that observed during arm plus leg exercise,[113] and blood-borne lactic acid was also highest during hybrid exercise likely due to the larger muscle mass involved in such exercise.[113]

In a self-controlled randomized trial of SCI individuals who performed FES-assisted rowing, Laskin and co-workers[114] observed that arm plus leg rowing evoked significantly higher VO_2 compared to FES leg stimulation only or voluntary manual rowing only. Respiratory exchange (VCO_2/VO_2) and HR were both lower during hybrid compared to arms-only rowing. These results were supported in a later investigation into FES-assisted rowing by Wheeler et al.[115]

A popular form of hybrid exercise where the legs contribute most of the whole-body metabolism is FES-assisted walking, especially on a motor-driven treadmill. De Carvalho and Cliquet[116] performed a controlled analysis of energy expenditure at rest and during FES-assisted treadmill gait training in persons with tetraplegia, who had 30%–50% of their body weight supported by a harness. The participants who underwent FES-assisted gait training demonstrated greater VO_2 and energy expenditure compared to those who performed knee extension training. These data reinforced the view that external load carriage is an important determinant of generalized metabolism during exercise. On the other hand, in Jacobs' randomized trial,[117] Parastep® training did not alter VO_{2peak} or other metabolic responses during an arm ergometer test, suggesting that most metabolic adaptations after FES walking occur in the legs. A more recent controlled study by De Carvalho et al[118] investigated 6 months of FES-induced treadmill gait training among persons with tetraplegia. The authors observed that FES treadmill gait training increased metabolic stress and aerobic fitness more than usual physiotherapy treatment in control subjects who did not receive FES. In addition, FES ambulation has also demonstrated the potential to enhance cardiorespiratory fitness and efficiency[119] without increasing shoulder joint dysfunction,[120] to improve physical conditioning, and to increase time to fatigue.[121,122] As a caveat, some investigations into the energy cost of FES-induced walking compared to passive walking have reported conflicting results.[123,124]

Evidence that did not adhere either to randomization or controlling the treatment has explored FES-evoked exercise responses among persons with tetraplegia[38,41,72,125]; children with SCI[126]; and an individual's fatigue responses,[23,127] gas exchange kinetics during exercise involving aerobic and anaerobic metabolism,[128–132] and muscle deoxygenation and leg metabolism.[29,76,82,101,133] A consistent finding in this less rigorous research has been the observation that work rate and load of exercise are important determinants of metabolic responses[55,73,110,134] and, in particular, the power output production of the legs.[42,64,65,130]

In general, and in agreement with the prior two categories of physiological outcomes, the empirical evidence lends support to positive metabolic responses and increased aerobic fitness for people with SCI who participate in FES-induced exercise training programs. Randomized, controlled, and quasi-experimental investigations of different modes of FES-evoked training contribute to this conclusion.

Bone mineral density and stiffness

Osteoporosis, a commonly occurring condition amongst spinal cord–injured people with paralyzed limbs, creates an associated risk of bone fracture during activities of daily living. One case of bone fracture after FES knee-extension exercise has been reported, which was likely associated with severe osteoporosis.[135] Cases of bone fractures have been reported to be dramatically reduced after FES training by one author,[136] but contrary findings have also been noted.[137]

Primary evidence that has suggested positive effects of FES leg exercise on bone mineral density (BMD) has been observed in a single controlled study,[138,139] whereas four have reported equivocal results.[140–143] Carvalho and co-workers[139] reported improved bone formation after FES treadmill walking in a sensorimotor complete SCI group compared to the incomplete control group. In a parallel finding,[138] the authors followed their FES treadmill walking group for 6 months, and they reported a significant increase of BMD of lumbar spine, femoral neck, trochanteric area, and total femur compared to the SCI control group. These findings suggested that FES-evoked treadmill walking might be better for bone health than isometric or isotonic FES leg muscle contractions wherein the subjects are seated or supine without body-weight support.

In an earlier study, Eser and colleagues[142] undertook a 6-month prospective controlled clinical trial of FES cycling on tibiae BMD in recently injured motor complete SCI subjects. Nonexercisers revealed a greater rate of BMD loss compared to the FES-exercise intervention group, but this difference was not statistically significant. The authors concluded that bone mineral loss was unrelated to spinal lesion level or time since injury but was greater in subjects with higher initial BMD and older age.

Other evidence of bone density adaptations has also been equivocal. A controlled study by Hangartner and co-workers[144] sought to determine if tibial bone loss could be reduced through lower limb movements evoked by standardized FES exercise. They reported no changes of measured bone density amongst differing weekly frequencies of exercise. However, by using regression-modeling techniques, the authors alleged a potential reduction of bone density loss between estimated values in subacute SCI subjects without exercise compared to the group who undertook FES-evoked exercise.

Similarly, Bloomfield et al,[143] using X-ray absorptiometry, found a small BMD increment at the lumbar spine but no changes of bone density in femoral neck, distal femur, or proximal tibia after FES leg training. The subjects in this study were 6 years motor complete post-SCI who had undergone FES knee-extension training and FES cycling for about 9 months. The authors also reported increases in distal femur and proximal tibia bone density for subjects who exercised at high power ($\geq$18 W) compared to low power ($\leq$12 W) for at least 3 months.

Clark and co-authors[141] reported a significant difference of the total body BMD after nonresisted isotonic FES muscle contractions in the first 3 months post injury. Yet, a longer follow-up could not detect significant BMD differences between an FES exercising group and a nonexercise control group. Shields et al[140] conducted a within-subject controlled study training the soleus muscles via isometric FES muscle contractions. No changes in BMD were observed between the trained and untrained leg, before or after the study. Whereas Clark et al investigated complete and incomplete subjects, Shields et al investigated only motor-sensory complete subjects.

Other nonrandomized and controlled investigations have revealed disparate or conflicting outcomes concerning the efficacy of FES-evoked exercise on BMD and stiffness. A few studies have supported the effectiveness of FES-evoked exercise to enhance bone density,[111,145–151] but more numerous investigations have failed to show any positive outcomes of FES exercise on bone health.[43,51,58,152–154]

In conclusion, bone health improvements after FES-evoked leg training were reported positive only on some localized areas of bones, particularly in the hips or in the knee area and shank, with FES-induced treadmill walking delivering more positive outcomes compared to other modalities of FES exercise. This may be due to the effect of body mass support by the pelvis and legs during stepping, as well as by the effect of muscle contractions that impart loading forces around the bones. In contrast, studies that used FES-evoked cycling or leg extension training did not note as significant changes in BMD, because the loading forces during such exercise were certainly lower than for FES stepping. Generally, the evidence for positive bone health adaptations is scarce, and conclusions from available research studies are neither consistent nor suggestive of any conclusion. To date, no claim can be made that FES-induced exercise has the potential to reduce osteoporosis or promote bone health.

Functional changes in exercise capacity

Increased muscle mass and volume following electrically stimulated exercise directly lead to improved strength and endurance of the muscles.[73,155] These outcomes have resulted in increased functional exercise capacities such as longer training time or endurance, longer FES-assisted walking distances, increased training repetitions, or greater exerted load during FES exercise. It is worth noting that endurance has been often described to be one of the most improved functional capacities, not only after FES-assisted walking but also following FES-evoked knee extension or cycling. For instance, persons with paraplegia or tetraplegia who were only able to exercise for only a few seconds at the beginning of a training period could perform up to 60 minutes of exercise against a load of up to 9.8 N at the end of 2 years of training.[136]

A recent within-subject controlled study by Shields[140] investigated the longitudinal effects of FES-evoked exercise on the shank muscles. The authors observed significantly improved fatigue index and torque-time interval of the FES-trained leg compared to the untrained leg. It is interesting that the peak torque elicited by the untrained leg increased together with that of the trained leg. This study also revealed that these performance measures were closely related to the subjects' training compliance over the 6- to 11-month training period.

A controlled study by Postans et al[156] investigated the performance of SCI individuals performing FES-augmented partial weight support gait training. When evaluated against a 4-week control period, wherein subjects received the usual physiotherapy and performed gait-training activities, they demonstrated improved endurance and walking speed with FES assistance.

Clinical evaluation of FES-evoked knee-extension training after SCI has reported increases in strength[46,47] and endurance.[157] Other examples of improved functional endurance were reported through FES-induced knee-extension studies that produced significant improvements in load resistance and repetitions,[158] range of motion,[159] increased generated torque,[147,160,161] force impulse,[162,163] voluntary strength and leg function,[48] and increased muscle fatigue resistance.[57,164] In addition to improvements of endurance, increased work rate and power output throughout training also implied enhanced functional exercise capacity, such as power production, strength, endurance,[25,37,75,77,99] and mechanical efficiency.[130] Increments in cycling load, mean work rate, and duration of exercise further exemplify the increase in functional capacity.[43,60] Mechanical efficiency during FES cycling in persons with paraplegia however was reported to be still lower than able-bodied voluntary cycling efficiency.[165]

From a technical perspective, stimulation frequencies can modify the torque and work production.[166] Eser and colleague's randomized trial demonstrated that power outputs during FES exercise were greater at higher stimulation frequencies (i.e., 50 and 60 Hz) .[167] In contrast, low frequency and stimulation voltage might delay the onset of neuromuscular fatigue.[168] Nevertheless, high- (50 Hz) and low-frequency (10 Hz) stimulation both increased strength by the end of training in SCI individuals.[31]

Additionally, previous training had shown positive effects on exercise endurance.[169] Petrofsky et al,[170] in his controlled study, reported that any strength training of thigh muscle groups contributed toward better FES cycling endurance, and longer strength training duration prior to undertaking FES cycling resulted in greater increase of muscle endurance during it. Similarly, a controlled study by Rabischong and Ohanna[171] reported an increase in muscle strength following FES training, but they did not detect improvements in fatigue resistance.

With a view to optimizing FES training, some researchers have investigated the best protocol for conducting exercise to maximize gains of functional capacity. A controlled study by Petrofsky et al[172] determined that the optimum protocol of FES-evoked isokinetic strength training for quadriceps muscles in persons with paraplegia to augment their strength and endurance was 3 days per week for 30 minutes per day, with a work to rest ratio of 50:50. Optimal stimulation of paralyzed muscles resulted in positive changes of muscle and increased endurance.[173] Besides varying the training period,[174] investigators had mechanically constrained the SCI pedaling to be forced-smoothed,[175] varied the stimulation current intensity,[176] varied the flywheel resistance,[177] and applied other combinations of modes of exercise to augment the exercisers' functional capacity.[54,58,59,178]

For FES-cycling exercise, pedal cadence also affects force production and power output. Slow cadence isokinetic FES cycling was observed to produce greater muscle force,[179,180] as the muscle's force-velocity relationship holds valid even for artificially induced FES-evoked contractions.[179,181] A randomized trial by Fornusek et al[182] investigated the effects of movement velocity on muscle fatigue, torque production, and power output. The authors found that higher pedal cadence (50 rev $\cdot$ min^{-1}) lead to quicker muscle fatigue, which limited the potency of FES exercise training. Higher cadence evoked greater initial power output, but this significantly decreased after the first minute to be lower than the power output produced at a slower cadence. The slower cadence cycling (15 or 20 rev $\cdot$ min^{-1}) also revealed greater peak and average torques, with slower onset of fatigue. In short, slower cadence will generate more muscle force but at a lower power output.

In addition to FES-evoked cycling and leg extension, a number of crossover research studies on standing and ambulation have highlighted changes of functional exercise capacity.[51–53,121,123,124,183–196] Investigators found increased muscle size, increased torque production in the quadriceps muscle,[183] improved walking speed and distance,[124,184,186,187,197,198] reduced fatigue index,[52] greater cadence and stride length,[199] and increased strength and reduced physiological cost.[185,200] Some of the SCI participants were able to achieve independent ambulation.[51,53,188] Peak work load of graded peak arm exercise also increased as the effect of ambulation training.[121] Notably, there was no reported evidence of joint destruction due to FES exercise and walking.[189,190] One experimental study addressed the increased functional capacity and strength of FES-assisted rowing. The study however acknowledged that FES-evoked rowing was unable to produce an efficient rowing stroke among SCI adherents.[201]

In conclusion, seven controlled and randomized studies, supported by several other investigations, promoted the proposition that FES-induced training contributed positively toward strength and endurance, among other indicators of functional exercise capacity.

Psychosocial outlook

Just like any other physical activity, FES-evoked exercise may contribute positively to SCI individuals' well-being and psychosocial outlook. One of the most oft-studied elements of psychosocial adaptation after SCI has been subjects' depression level.[202] Apart from depression, the psychosocial outlook of FES exercisers has been described in terms of their general well-being, their physical self-concept, and their perception of their appearance.

Exercise adherents have generally revealed reduced depression after training.[202,203] The only controlled study addressing this psychological outcome was a study of FES hybrid training (i.e., voluntary arm plus FES leg exercise) conducted by Bradley.[204] Bradley reported that SCI subjects with unrealistic expectations (i.e., the desire to walk independently without assistance) experienced significantly increased depression compared to subjects with realistic expectations (such as the desire to improve physical conditioning and appearance). Other nonrandomized or controlled studies that investigated depression levels used indicators such as levels of plasma beta endorphin immunoreactivity and cortisol levels,[205] Tennessee Self-Concept Scale and Beck Depression Inventory scores,[51,206] and physical self-concept scores.[188]

Several other noncontrolled studies investigated FES users' perceptions about performing various types of FES exercise activities. One of the investigations observed the use of a hybrid FES-assisted rowing trainer,[114] which was perceived to be more natural than arm-ergometer and cycling hybrid exercise. A study investigating the perception of long-term users of an FES-implanted system[207] and FES-assisted orthosis[208] for standing, exercise, and transfers concluded uniformly that the system increased overall health and general well-being and perceived the system to be safe, reliable, and easy to use. FES cycle ergometer users[209] also reported to have increased their endurance, and they perceived better self-image, better appearance, and reduced lower extremity oedema. One study on participation in home FES cycling[210] reported the users' perceived benefits, including increases in endurance and muscle bulk, changes in spasticity, and changes in neurogenic pain and lower limb swelling. The reasons for less usage however were lack of preparation assistance, long preparation time, skin irritation, and lack of motivation.

An extensive self-report by Fitzwater,[211] as an individual with SCI and an FES cyclist, suggested that for FES cycling to be more beneficial for SCI individuals, researchers should make it more enjoyable and convenient. He claimed that FES cycling, even during the clinical inpatient phase of rehabilitation, was better than hand- and arm-dependent exercise that might potentially cause upper limb injuries. The author further confirmed that, with his increase in muscle bulk, he achieved better body image and reduced pressure sores. The size of nonstimulated muscles increased less than stimulated muscles. He also recognized increments in bone density, greater cardiovascular health and fitness, mood improvements, and greater leg forces and strength. The disadvantage of FES cycling from his point of view was the boredom of indoor exercise and the extra time needed to prepare for such exercise, specifically to apply and remove the electrodes.

Overall, the only study that adhered to a controlled research methodology in this outcome domain suggested positive effects of FES-evoked exercise on SCI users' depression levels. Despite limited quasi-experimental evidence that cumulatively added strength to our hypothesis, we find insufficient support for the viewpoint that FES-exercise users' perceptions show positive attitudes toward health and fitness benefits of regular FES-evoked exercise.

Discussion

Although the benefits of FES-evoked exercise may depend on the subjects' lesion level, degree of injury, or time since injury, the randomized and/or controlled studies presented in this article did not suggest any link between lesion level and degree of injury upon the capacity of the subjects to gain or reduce clinically evident effects of FES-evoked exercise. Other factors were more significant, including an individual's tolerance to electrical stimulation and the frequency of training. Because most subjects who were assigned to FES interventions possessed sensorimotor complete spinal lesions, they could tolerate higher electrical stimulation and evoke stronger muscle contractions than incomplete individuals. However, definitive conclusions about the relationship between degree or level of SCI and physiological or psychosocial outcomes could not be drawn, because many studies did not consistently report their subjects' spinal injury characteristics. This inconsistency was also confounded by the reporting period that spanned a transition from Frankel to ASIA classification schemes.* Although not within the scope of this article, further analyses should be conducted to determine which type of FES-evoked exercise is best for specific individuals with varying levels and degree of SCI.

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*The ASIA standards were endorsed as the recommended international standard in 1920 by the International Medical Society of Paraplegia (IMSOP), now known as ISCoS, at their Annual Scientific Meeting in Barcelona, Spain, on September 7, 1992. The RCT studies reported in this article still described Frankel classifications until 1998, by Baldi et al's RCT study. ASIA classifications were earliest reported in our RCT study by Raymond et al in 2002 (**Table 2**). Some other RCT studies mentioned subjective classifications or did not note any classification at all. We presume researchers were still in the midst of transition from Frankel to ASIA classification schemes during the period from which the papers were selected for this position review.

Nevertheless, to answer the primary question, as to whether or not FES-evoked exercise promoted health and fitness among SCI exercisers, we concluded that positive outcomes after FES-evoked exercise have been identified for individuals with SCI across multiple domains of health and fitness. Exercise adherents were reported to gain enhanced cardiovascular and metabolic responses during the FES-evoked physical activity, however changes in aerobic fitness (e.g., VO_{2peak}) were still lower than for the able-bodied population who undertook voluntary leg exercise. Certainly, the available evidence strongly supported improved health in other fitness domains, particularly for skeletal muscle adaptations and strength and endurance improvements leading to better functional outcomes.

Investigations into bone health after FES exercise were adequate in number, yet controlled studies did not universally conclude that such exercise was effective to induce positive adaptations that might protect against osteoporosis-related bone trauma. In contrast, quantitative evidence of psychosocial improvements among FES exercise participants was rare. Even though some investigations supported the use of FES-evoked exercise, there was only one controlled study and some encouraging quasi-experimental research that demonstrated this. In summary, changes of BMD in the legs and alterations of FES exercisers' psychosocial outlook were found to be equivocal, and it cannot be claimed that such exercise promotes these positive outcomes after SCI. Clearly, there is a need for well-designed studies to strengthen the evidence within these two key domains of health and fitness.

Even though the greater plurality of research findings strongly supported the use of FES-evoked exercise, primarily the randomized and controlled studies, the extent to which these benefits can be generalized to the wider population of SCI individuals must be interpreted with caution. Such caution is necessary due to the small number of participants in most trials, and sample sizes were often too underpowered to represent the larger cohort with SCI adequately. Moreover, the results of all studies could not be pooled to construct a valid meta-analysis due to the diversity of research designs, small number and diversity of subjects, and widely varied research questions. The next sections elaborate upon inherent problems in the nature of FES-exercise research to-date and the quality of evidence presented therein.

Nature of research

Based on all 33 randomized and/or controlled studies, we can describe the common approaches when researchers design their studies, primarily how investigators have implemented randomization and how they have defined their control groups. The most common control group in any RCT assigns subjects either to placebo or no intervention while other individuals are assigned to an intended intervention, such as FES-evoked exercise. In general, the control groups of the controlled studies described herein were either non-FES exercise or usual physiotherapy sessions of another group of people. Some studies performed within-subject control whereby a nonexercise period was assigned to the same subjects before or after an FES intervention, or alternatively one of the subject's legs was subjected to FES exercise but not the other. Presumably, most investigators did not use another group of control participants during their study implementation because the available pool of possible individuals was already very small compared to the requisite sample size for a statistically sound treatment effect size. Therefore, any available SCI subjects who were recruited as study participants were frequently assigned to the FES intervention, so that its effect could be perceived as more potent; this represents a common bias within most FES studies.

For the studies that did use control groups, these either divided subjects into sensorimotor complete SCI or incomplete SCI to serve as control and intervention groups or separated subjects according to their responsiveness to FES, their participation, or by matched age and lesion level between groups. Other investigations used able-bodied people in the control group, which did not accurately reflect treatment effect potency on the target group of individuals with SCI. Apart from a few studies that randomized the order of trial or intervention, only Baldi et al[17] randomized subjects between a control and intervention group. Often investigators avoided randomizing subjects between treatment and control groups, because they expressed concern about ethical issues and compliance factors faced by the generally sedentary SCI population.

After collectively examining all FES-evoked exercise studies, the common number of SCI subjects in each trial varied from a single individual to 20 subjects. Few investigations used more than 20 people. The test period ranged from a single day to 4 years. Usually, the majority of the trials were conducted within a single day, although some performed studies within 4 weeks up to 4 years. The most common durations of longitudinal investigations were 6 months, 12 weeks, 8 weeks, and 6 weeks, respectively.

Given the challenging nature of FES trials with SCI individuals, but especially the paucity of subjects who were responsive to and could tolerate FES, the available studies were able to make analysis of the topic with an average of 14 SCI subjects each. Often, the small number of subjects was compensated by lengthening the duration of intervention and by ensuring greater compliance within study participants. Another way to increase statistical power is to use interventions that are more robust. Nevertheless, FES technology itself is still undergoing research and development and has yet to reach the optimal standard and treatment efficiency, especially for FES-evoked standing and walking.[212]

Another way to improve the quality of research and strengthen the statistical power is by decreasing the variability within samples. Although not impossible, this approach is deemed difficult because it requires low dropout rates and the recruitment of a homogenous sample of subjects. Dropout events among FES intervention studies with SCI individuals have been high, because they have increased risks of health complications that were unrelated to the study or had limited accessibility and compliance. Maintaining sample homogeneity was more complicated. Each SCI subject is often very different from another; each person may have a similar lesion level, weight, and age but their secondary health has a great effect on the subjects' physiological performance and may limit the group's homogeneity. This increased the variability in effect and responsiveness within a group.

Challenges to quality of evidence

As a rehabilitation technique, FES exercise bears similar issues and challenges to other standardized treatments used with patient groups. As noted by Turner-Stokes,[213] even though RCT studies are commonly acknowledged as the most scientifically valid evidence, they are not always practical or feasible. Research into rehabilitation efficacy makes RCT studies less practicable for many reasons, including the diversity of goals and conditions, as well as the hardly achievable uniform approach.

The lack of RCT studies in FES-exercise research among people with SCI has similarly limited this position review from achieving the gold standard of scientific evidence.[214] Due to the challenges in implementing a "statistically appropriate" sample size, lack of statistical power failed to detect significant differences among people with SCI. The concept of statistical power should be reconsidered, because in this research domain, even small, statistically nonsignificant improvements may translate into meaningful clinical outcome for people with SCI. The other challenge was in demonstrating the effectiveness of FES-exercise interventions, because most individuals with SCI dropped out from ongoing investigations due to other health problems that were not related to the research. Other challenges included selecting measurements that are responsive to exercise interventions and identifying meaningful treatment endpoints.

Investigators were encouraged to include the outcome measures of both statistical and clinical significance.[214] To increase the value of trials further, clinicians may consider the value of nonrandomized designs, by using quasi-experimental designs to assign volunteers to experimental conditions based on their attendance barriers, and to consider the definitions of dropout and compliance. In short, researchers may find practical ways to advance knowledge in this field despite the challenges. There is little doubt that the changes and improvements seen in SCI subjects during nonrandomized trials were the effect of the FES-evoked exercise.

Investigators may attempt to adhere more closely to the highest quality of research criterion despite the limitations and challenges associated with the nature of this research area. Although investigators can reanalyze the traditional approach to RCTs, we recommended researchers in clinical trials focus more on adhering as much or as close as possible to the evidence-based methods. These may include the adherence to blinded assessment, adequate follow-up duration, and the use of appropriate measurements, which is valid, sensitive, reliable, and relevant.[213] This is to ensure that the experiments, trials, and analysis are well accepted as randomized controlled trials. Adherence to study design quality will contribute toward the value of systematic review in this field, so that significant conclusion and resolution can be made by health care providers, consumers, policy makers, and researchers, who need reliable and standardized trials as evidence and a basis for making rational decisions regarding FES rehabilitation therapy for SCI individuals. After performing the review, we realized that, despite the challenges, there are in fact numerous possibilities for trials and experiments to be administered by the evidence-based methods.

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