Review

Functional electrical stimulation cycling in youth with spinal cord injury: A review of intervention studies

Tanja A. Mayson^{1,2}, Susan R. Harris²

¹Shriners Gait Lab & Therapy Department, Sunny Hill Health Centre for Children, Vancouver, BC, Canada,

²Department of Physical Therapy, University of British Columbia, Friedman Building, Vancouver, BC, Canada

Context: Preliminary research suggests that functional electrical stimulation cycling (FESC) might be a promising intervention for youth with spinal cord injury (SCI).

Objective: To review the evidence on FESC intervention in youth with SCI.

Methods: Systematic literature searches were conducted during December 2012. Two reviewers independently selected titles, abstracts, and full-text articles. Of 40 titles retrieved, six intervention studies met inclusion criteria and were assessed using American Academy for Cerebral Palsy and Developmental Medicine Levels of Evidence and Conduct Questions for Group Design.

Results: The study results were tabulated based on levels of evidence, with outcomes categorized according to the International Classification of Functioning, Disability, and Health framework. Evidence from the six included studies suggests that FESC is safe for youth with SCI, with no increase in knee/hip injury or hip displacement. Results from one level II randomized controlled trial suggest that a thrice weekly, 6-month FESC program can positively influence VO₂ levels when compared with passive cycling, as well as quadriceps strength when compared with electrical stimulation and passive cycling.

Conclusions: FESC demonstrates limited yet encouraging results as a safe modality to mitigate effects of inactivity in youth with SCI. More rigorous research involving a greater number of participants is needed before clinicians can be confident of its effectiveness.

Keywords: Adolescent, Bicycling, Child, Electrical stimulation, Spinal cord injuries

Introduction

Spinal cord injury (SCI) affects approximately two of every 100 000 youth (children and adolescents).¹ Youth with SCI face the same health challenges as age-mates in the general population but also experience the neuromuscular effects of the injury.² In adults following SCI, muscle atrophy occurs quickly and, with age, continues at a rate above and beyond that of the general population.³ As well, SCI significantly increases the risk of cardiovascular disease, including myocardial infarction and hypertension,⁴ as well as the risk of metabolic syndrome and diabetes mellitus.^{4,5} Cardiovascular disease is one of the leading causes of mortality in people with SCI.^{6,7}

In addition, youth and adults with SCI (or adults with childhood onset SCI) must cope with loss of bone mineral density which can significantly increase fracture risk.⁸ Authors of a recent systematic review of SCI in the pediatric population reported that children who sustain a SCI before their growth spurt have a greater likelihood of developing scoliosis than adolescents or adults with SCI.⁹ Hip subluxation/dislocation is also relatively common in pediatric SCI, especially in children under the age of 10 years.¹⁰ With recent medical advances, youth with SCI have increased life expectancy, making it important to mitigate the neuromuscular effects of SCI in order to optimize quality of life and minimize health care costs.²

Exercise is one way to address the neuromuscular effects of SCI¹¹; cycling, in particular, provides an ideal way for individuals with SCI to exercise and

Correspondence to: Tanja A. Mayson, Therapy Department, Sunny Hill Health Centre for Children, 3644 Slocan St. Vancouver, BC, Canada, V5M 3E8. Email: tmayson@cw.bc.ca

address the long-term consequences of SCI by targeting the lower extremity muscles.¹² Cycling with the addition of functional electrical stimulation (FES) is another option available to individuals with SCI. FES involves using electrical current to activate muscles through the stimulation of intact peripheral motor nerves to promote functional activities.¹³ By using FES across a certain sequence of muscle groups, a cycling motion can be produced; this use of FES is called FES cycling (FESC).¹⁴

In adults with SCI, FESC has led to improvements in muscle cross-sectional area, lean body mass, voluntary and electrically induced muscle force,^{15,16} and muscle endurance.^{17,18} FESC in adults has led also to reported improvements in energy expenditure^{19–22} as well as in heart rate, stroke volume, and cardiac output during exercise and at rest.²³ Finally, improvements have also been observed in decreasing spasticity.^{24,25} Effects on bone mineral density have, however, been conflicting.^{26–30} When comparing results of studies using FESC to those using passive cycling in adults with SCI,^{31–33} FESC appears to have greater benefits in decreasing spasticity and muscle atrophy and improving cardiac output and stroke volume.

The purpose of this review is to examine the quality and quantity of published evidence on the use of FESC in youth with SCI.

Methods

Data sources and searches

We conducted a comprehensive review of the literature to identify relevant articles. Searches of the SCI scientific literature were conducted in nine databases from their inception to December 2012: CDSR, CINAHL, DARE, EMBASE, ERIC, MEDLINE, PEDro, PsychINFO, and Sport Discus. A sample search strategy used for MEDLINE (including keywords and combinations) appears in Appendix 1. All other search strategies are available from the corresponding author.

Study selection

Inclusion criteria for the review were that each study had to (1) pertain to FESC; (2) include only participants under age 21 years of age; and (3) include children and adolescents with a diagnosis consistent with having a SCI. The review was limited to peer-reviewed studies published in English-language journals. Studies published only in abstract or dissertation form were excluded.

Both authors independently reviewed studies identified from the literature search at all stages of study selection. Studies were initially screened based on title,

then abstract, and then full-text reviews to confirm inclusion in the systematic review. At the title review stage, any title selected by either reviewer was included in the abstract review. For the abstract and full-text reviews, we used checklists with inclusion criteria to record decisions for each reviewer; disagreements were resolved by consensus.

Data extraction and quality assessment

To assess the level of evidence for each study design, we used the American Academy for Cerebral Palsy and Developmental Medicine (AAPCDM) Levels of Evidence for Group Design scale (Appendix 2).³⁴ Secondly, to rate the methodological quality of each study, the 7-point American Academy for Cerebral Palsy and Developmental Medicine (AAPCDM) Conduct Rating Scale for Group Design was used (Table 1).³⁴ We scored each study independently and resolved disagreements by consensus.

The primary author extracted descriptive and outcome data from the included studies, which were then fact-checked by the second author. These data included number of participants in each study, level of SCI and American Spinal Injury Association classification, age of participants, intervention characteristics, frequency, and duration of intervention sessions, and specific parameters of FESC (see Table 2).

Data synthesis

To synthesize the six included studies, the authors created a descriptive summary table (Table 2). We then created an outcomes table for results listed in each study (Table 3) and classified them according to the AAPCDM's levels of evidence for group design³⁴ (see Appendix 2). In addition to classifying the studies by levels of evidence, we used the International Classification of Functioning, Disability and Health (ICF)³⁵ to determine whether the study outcomes were at the level of Body Structures and Functions or Activity and Participation (Table 3).

Results

Search results

Six studies met the inclusion criteria for this review.^{36–41} Fig. 1 shows the search process and results of each review step. Of the 40 studies resulting from the literature search, 27 received full-text review. After full-text review, 21 studies were excluded (reasons for exclusion are listed in Fig. 1; citations excluded at the full-text review stage are listed in Appendix 3). Cohen's kappa was used to examine inter-rater inclusion/exclusion

Table 1 AACPDm conduct questions for group design

	Intervention studies					
	Johnston ³⁶	Johnston ³⁷	Lauer ³⁸	Johnston ³⁹	Johnston ⁴⁰	Castello ⁴¹
(1) Were inclusion and exclusion criteria of the study population well described and followed?	Yes	Yes	Yes	Yes	Yes	Yes
(2) Was the intervention well described and was there adherence to the intervention assignment? (For 2-group designs, was the control exposure also well described?) Both parts of the question need to be met to score "yes"	Yes	Yes	Yes	No	Yes	No
(3) Were the measures used clearly described, valid and reliable for measuring the outcomes of interest?	Yes	Yes	Yes	Yes	No	Yes
(4) Was the outcome assessor unaware of the intervention status of the participants (i.e. were the assessors masked)?	No	No	Yes	No	No	No
(5) Did the authors conduct and report appropriate statistical evaluation including power calculations? Both parts of the question need to be met to score "yes"	Yes (P < 0.05)	Yes (P < 0.05)	Yes (P < 0.05)	Yes (P < 0.05)	N/A	N/A
(6) Were dropout/loss to follow-up reported and less than 20%? For 2-group designs, was dropout balanced?	Yes	Yes	Yes	Yes	Yes	No
(7) Considering the potential within the study design, were appropriate methods for controlling confounding variables and limiting potential biases used?	Yes	Yes	No	Yes	No	No
Total score	6	6	6	5	3	2

AACPDm, American Academy for Cerebral Palsy and Developmental Medicine³⁴; N/A: not applicable.

Conduct Question Categories¹

S: Strong (well conducted) 6 to 7

M: Moderate (fairly conducted) 4 to 5

W: Weak (poorly conducted) 3 or less.

agreement with substantial to perfect levels of agreement⁴² ($k = 1.00$ at full-text review stage).

An intervention study uses a specific therapeutic intervention over a period of time to improve health or health-related outcomes. Six publications (albeit from only two different studies) were classified as FESC intervention studies.^{36–41}

Methodological quality of the studies

Table 1 summarizes the results of the quality analysis conducted with the AACPDm Conduct Rating Scale for Group Design. Scores of 5–7 indicate strong studies (well conducted), 4–5 moderate studies (fairly conducted), and 0–3 weak studies (poorly conducted).³⁴

Description of the studies

Table 2 provides an overview of the six included studies (published from 2008 to 2012) using FESC as an intervention,^{36–41} including levels of evidence, conduct rating scores, sample sizes and age ranges, levels and American Spinal Injury Association classifications of SCI, intervention characteristics, treatment intensity, and FESC parameters.

Each study included between four and 30 participants; the age span across studies was 5–20 years with injury levels between C3 and T11, and American Spinal Injury Association classifications A, B, and/or C.

Quality of evidence of FESC

Table 3 summarizes the levels of evidence (as per consensus rating) supporting outcomes as described in the studies. Measurement in all six of the intervention studies involved outcomes only in the body structure and function dimension of the ICF.^{36–41} Only the Castello *et al.*⁴¹ pilot study included a quality-of-life outcome measure.

Adverse events

None of the intervention studies reported occurrence of adverse events.^{36–41}

Intervention studies

Authors of the randomized controlled trial^{36–39} examined the effects of FESC on cardiorespiratory and vascular health in youth ages 5–13 years. Participants were randomly assigned to one of three groups: (1) FESC (2) passive leg cycling, or (3) electrical stimulation (ES) therapy. Participants in both cycling

Table 2 Levels of evidence and quality scores for functional electrical stimulation cycling intervention studies

First author	Study design	AACPDM level of evidence	AACPDM quality rating score ¹	Sample	Sample size and age range	SCI injury level/ASIA	Intervention	Treatment intensity	FES cycling parameters
Johnston ³⁶	RCT	II	6/7 – S	Same sample	N = 30 (ages 5–13 years)	C4 to T11 ASIA A, B, C	<ul style="list-style-type: none"> • FES cycling (n = 10) • Passive leg cycling (n = 10) • ES only (n = 10) 	1 hour sessions 3 x /week For 6 months	<ul style="list-style-type: none"> • Applied to: quadriceps, hamstrings, gluteal muscles • Frequency: 33 Hz • Pulse duration: 150, 200, 250 or 300 µs
Johnston ³⁷ Lauer ³⁸ Johnston ³⁹			6/7 – S 6/7 – S 5/7 – M						<ul style="list-style-type: none"> • Amplitude: <140 mA • Resistance adjusted by 0.14 nm to maintain 50 rpm
Johnston ⁴⁰	Case series (subgroup from RCT ^{34–37})	IV	3/7 – W	Subset of children from above sample ^{34–37})	N = 4 (ages 7–11 years)	C7 to T6 ASIA A	<ul style="list-style-type: none"> • FES cycling (n = 2) • Passive leg cycling (n = 2) 	1 hour sessions 3 x /week For 6 months	<ul style="list-style-type: none"> • Applied to: quadriceps, hamstrings, gluteal muscles • Frequency: 33.3 Hz • Pulse duration: 250 µs • Amplitude: 70–120 mA • 45–50 rpm
Castello ⁴¹	Prospective case series	IV	2/7 – W	Unique sample	N = 6 (ages 9–20 years)	C3-T4 ASIA A, B, C	<ul style="list-style-type: none"> • FES Cycling (n = 6) 	0.5 hour sessions 3 x /week For 9 months	

AACPDM, American Academy for Cerebral Palsy and Developmental Medicine.

AACPDM Quality Rating Score: S, strong; M, moderate; W, weak.

ASIA, American Spinal Injury Association Impairment Scale.

btw, between; ES, electrical stimulation; FES, functional electrical stimulation; Hz, Hertz; mA, milliAmpere; RCT, randomized controlled trial; rpm, revolutions per minute; SCI, spinal cord injury; µs, microseconds.

Table 3 Intervention study outcomes by level of evidence according to International Classification of Functioning, Disability and Health³⁵

Level of evidence	Positive outcomes		No change or inconclusive		Negative outcomes	
	II	IV	II	IV	II	IV
Electrical stimulation						
Body structure and function						
Hip BMD			Lauer ³⁸			
Distal femur BMD			Lauer ³⁸			
Proximal tibia BMD					Lauer ³⁸	
Hip migration index			Johnston ³⁹			
VO ₂			Johnston ³⁶			
Triglycerides			Johnston ³⁶			Johnston ⁴⁰
Total cholesterol	Johnston ³⁶ (ES had greater decrease than FES cycling)		Johnston ³⁶ (%) pre/post change)			
HDL			Johnston ³⁶	Johnston ⁴⁰		
LDL			Johnston ³⁶			Johnston ⁴⁰
Resting heart rate			Johnston ³⁶			
Forced vital capacity			Johnston ³⁶			
Overall quadriceps muscle volume	Johnston (compared with FES cycling and passive cycling) ³⁷					
Vastus lateralis muscle volume	Johnston (compared with FES cycling and passive cycling) ³⁷					
Biceps head muscle volume	Johnston (compared with FES cycling and passive cycling) ³⁷					
Average percentage change in quadriceps muscle volume	Johnston (% pre/post change) ³⁷					
Average percentage change in hamstrings muscle volume			Johnston ³⁷ (pre/post % change)			
Stimulated quadriceps muscle strength			Johnston ³⁷ (pre/post % change)			
Stimulated hamstrings muscle strength			Johnston ³⁷ (pre/post % change)			
Functional electrical stimulation cycling						
Body structure and function						
Hip BMD	Lauer ³⁸	Johnston ⁴⁰				
Distal femur BMD	Lauer ³⁸	Johnston ⁴⁰ Castello ⁴¹ (positive relationship between # FESC sessions and % change BMD pre/post as well as between # months of FESC and % change BMD pre/post)				
Proximal tibia BMD	Lauer ³⁸	Johnston ⁴⁰				
Hip migration index			Johnston ³⁹			

Continued

Table 3 Continued

Level of evidence	Positive outcomes		No change or inconclusive		Negative outcomes	
	II	IV	II	IV	II	IV
VO ₂ peak	Johnston ³⁶ (Significant % change in FES cycling vs. passive cycling)	Johnston ⁴⁰ (n = 1)	Johnston ³⁶ (% change pre/post)	Johnston ⁴⁰ (n = 1)		
Triglycerides			Johnston ³⁶			Johnston ⁴⁰
Total cholesterol			Johnston ³⁶			Johnston ⁴⁰
HDL		Johnston ⁴⁰ (n = 1)	Johnston ³⁶			Johnston ⁴⁰
LDL			Johnston ³⁶			(n = 1) Johnston ⁴⁰
Cholesterol/HDL ratio						Johnston ⁴⁰
Muscle volume		Johnston ⁴⁰				
Muscle strength		Johnston ⁴⁰				
Resting heart rate		Johnston ⁴⁰	Johnston ³⁶			
Peak heart rate				Johnston ⁴⁰		
Forced vital capacity			Johnston ³⁶			
Vastus lateralis muscle volume	Johnston (compared with passive cycling) ³⁷					
Average percent change in quadriceps muscle volume	Johnston (% change pre/post) ³⁷	Johnston ⁴⁰				
Average percent change in hamstrings muscle volume			Johnston ³⁷ (% change pre/post)			
Stimulated quadriceps muscle strength	Johnston (% pre/post change compared with passive cycling) ³⁷					
Stimulated hamstrings muscle strength			Johnston (% change pre/post) ³⁷			
Quality of life PedsQL		Castello (Positive relationship btw # months FESC and % change pre/post)				
Passive cycling						
Body structure and function						
Hip BMD	Lauer ³⁸	Johnston ⁴⁰ (femoral neck: n = 2)				
Distal femur BMD		Johnston ⁴⁰ (n = 1)	Lauer ³⁸			Johnston ⁴⁰ (n = 1)
Proximal tibia BMD		Johnston ⁴⁰ (n = 1)	Lauer ³⁸			Johnston ⁴⁰ (n = 1)
Hip migration index			Johnston ³⁹			
VO ₂			Johnston ³⁶	Johnston ⁴⁰		
Triglycerides			Johnston ³⁶	Johnston ⁴⁰		
Total cholesterol			Johnston ³⁶	Johnston ⁴⁰		
HDL		Johnston ⁴⁰	Johnston ³⁶			
LDL		Johnston ⁴⁰ (n = 1)	Johnston ³⁶			Johnston ⁴⁰ (n = 1)
Cholesterol/HDL ratio				Johnston ⁴⁰		
Muscle volume				Johnston ⁴⁰		
Muscle strength		Johnston ⁴⁰ (n = 1)				Johnston ⁴⁰ (n = 1)
Resting heart rate		Johnston ⁴⁰	Johnston ³⁶			

Continued

Table 3 Continued

Level of evidence	Positive outcomes		No change or inconclusive		Negative outcomes	
	II	IV	II	IV	II	IV
Peak heart rate				Johnston ⁴⁰		
Forced vital capacity			Johnston ³⁶			
Average percentage change in quadriceps muscle volume			Johnston ³⁷ (% change pre/post)			
Average percentage change in hamstrings muscle volume			Johnston ³⁷ (% change pre/post)			
Stimulated quadriceps muscle strength			Johnston ³⁷ (% change pre/post)			
Stimulated hamstrings muscle strength			Johnston ³⁷ (% change pre/post)			

Statistically significant results are indicated in bold.

ES, electrical stimulation; FES, functional electrical stimulation; BMD, bone mineral density; HDL, high-density lipoprotein; LDL, low-density lipoprotein; MRI, magnetic resonance imaging; PedsQL, Pediatric Quality of Life Inventory; btw, between; S, subject; VO₂, maximal volume of oxygen utilized in 1 minute.

Figure 1 Article inclusion/exclusion flow chart.

groups completed a 1-hour home exercise program, three times per week for 6 months. The FESC group received FES to the quadriceps, hamstring, and gluteal muscles. The ES group received 20 minutes each of stimulation to the quadriceps, hamstring, and gluteal muscles for a total of 60 minutes while in a supine position.

In this RCT, compared to passive cycling, the FESC intervention led to statistically significant improvements in percentage of VO_2 change,³⁶ vastus lateralis volume, and quadriceps muscle strength.³⁷ Non-significant increases in bone mineral density were noted in the hip, distal femur, and proximal tibia for the FESC group, whereas non-significant bone mineral density increase was noted only at the hip for the passive cycling group; the ES-only group had no bone mineral density increases at the hip or femur and a negative change at the tibia.³⁸ In the fourth study that was published from the randomized controlled trial, hip migration indices were assessed before and after the three 6-month interventions (FESC, passive cycling, and ES exercise without cycling); there were no changes in migration indices following any of the interventions, leading the authors to conclude that all three were likely safe for children with SCI as long as they were positioned to prevent adduction and internal rotation while cycling.³⁹

In the small case series that was a subset of the previously mentioned randomized controlled trial,^{36–39} a 6-month FESC program was compared to passive cycling alone.⁴⁰ For the children in both cycling programs, positive changes occurred in femoral neck bone mineral density and resting heart rate. In addition, the two children who completed FESC showed positive changes in all other measured bone mineral density values, muscle volume, and stimulated quadriceps strength.⁴⁰

In the sixth intervention publication, a prospective case series including six youths with spinal cord dysfunction (ages 9–20 years), the effect of 2–9 months of FESC (15–69 total sessions) on bone mineral density and quality of life was examined.⁴¹ The authors reported a tendency toward improved bone mineral density associated with frequency and duration (number of months) of cycling sessions, as well as greater improvement in quality of life with increasing months of cycling.⁴¹

Discussion

This review summarizes results of six publications^{36–41} examining the effects of FESC in children and adolescents with SCI. Levels of evidence for the included studies were relatively low with all but one study

(albeit resulting in four publications) at level IV. The quality of the studies was mixed with one study (four publications^{36–39}) stemming from the level II randomized controlled trial of moderate-to-strong quality.

Authors of all intervention studies^{36–41} concluded that FESC is safe for youth with SCI and does not lead to increased incidence of dysreflexia⁴¹ or hip subluxation.³⁹ FESC is therefore emerging as a safe method for children or adolescents with SCI. Although studies are limited, evidence from one level II randomized controlled trial^{36–39} suggests that FESC can positively influence VO_2 ,³⁶ as well as quadriceps muscle strength and volume.³⁷ FESC may also influence a variety of other physiological measures in the body structure and function dimension of the ICF, including the possibility of improving bone mineral density.^{38,40,41} However, ES alone may be more beneficial in reducing cholesterol levels³⁴ and increasing thigh muscle volume.³⁵

When considering the results of the randomized controlled trial that generated four papers,^{36–39} the highest evidence level and quality study included in this review, it is important to note study limitations. First, although there were no significant differences among groups for any baseline outcome measures, there were significant between-group differences in age, height, and weight. In addition, there is no mention of blinding assessors to group assignment for most outcome measures, which makes it possible for bias to have been introduced into the study. As per the authors of the randomized controlled trial, using dual-energy X-ray absorptiometry may have underestimated bone mineral density changes over the 6-month time period; other, more responsive measures, e.g. peripheral quantitative computed tomography, might have been preferable.³⁸

A concerning limitation in our review of these studies is that five of the six intervention papers^{36–40} involved multiple outcome measure analyses (across studies) for a very small sample of participants ($n = 30$). Consequently, generalizability of the results of 83% of the intervention studies conducted to date on FESC in youth with SCI are limited to youth with the same or similar characteristics.

Due to the limited number of intervention publications, five of which involved the same small sample, it is impossible to recommend optimal parameters for use of FESC in children and adolescents with SCI.

Implications for future research

Although a half-dozen recently published studies have examined the effectiveness of FESC in youth with SCI, evidence is still of a relatively low level and of

mixed methodological rigor.^{36–41} A further concern is the fact that the same 30 participants comprised the sample for five of the six intervention studies.^{36–40} In addition, results are limited to the body structure and function dimensions of the ICF, with no evidence as to the impact of FESC on the activity and participation dimensions. Although influencing physiological outcomes is important, measurement of participation level outcomes is crucial as they are the ultimate indicators of rehabilitation impact.⁴³ Inclusion of a pediatric quality-of-life measure in the pilot study by Castello *et al.*,⁴¹ albeit not an activity or participation measure *per se*, does provide the opportunity to look beyond physiological outcomes to examine emotional, social, and school functioning as well.

Research is also needed to evaluate the safety and effectiveness of FESC in youth with neurological disorders similar to SCI, e.g. meningomyelocele. A systematic review examining strengthening interventions for children with meningomyelocele reported some improvement in muscle torque as a result of ES to the quadriceps muscles⁴⁴; a recent pilot study of threshold nighttime ES showed improved strength in at least one lower extremity muscle group for the seven participants who completed 9 months of treatment.⁴⁵ However, no studies have been published examining the effects of FESC in this patient population.

Conclusion

Current research regarding the use of FESC in children with SCI is limited; however, available results suggest that FESC is a safe method for youth with SCI to modify the effects of inactivity. Data from one good-quality, level II study^{36–40} indicated that FESC can have a positive impact on certain outcomes at the body structure and function level of the ICF, e.g. VO₂, quadriceps muscle strength and volume.^{36,37} Results from a small level IV study tentatively suggest that FESC may also enhance bone mineral density and quality of life.⁴¹ Further research is needed to clarify the effects of FESC on other body structure and function measures (e.g. lipid profiles, muscle characteristics, and heart rate), as well as to determine whether FESC can also positively influence youth with SCI at the activity and participation levels of the ICF. It is therefore recommended that clinicians who use FESC should measure relevant outcomes before and after use of this intervention to document and monitor its effects.

Acknowledgment

The authors would like to thank Ms Lori Roxborough for her support and guidance in development of the paper.

Appendix 1: Sample search strategy

1. exp Spinal Cord Injuries/
2. spinal cord injur*.mp. [mp = title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
3. exp Electric Stimulation/
4. electric* stimulation.mp. [mp = title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
5. exp Bicycling/
6. cycling.mp.
7. bicycl*.mp. [mp = title, abstract, original title, name of substance word, subject heading word, protocol supplementary concept, rare disease supplementary concept, unique identifier]
8. 1 or 2
9. 3 or 4
10. 5 or 6 or 7
11. 9 and 10
12. 8 and 11
13. limit 25 to "all child"

Appendix 2: AACPDM:– Levels of evidence (December 2008) and grades of recommendation

Level	Group intervention studies
I	Systematic review of randomized controlled trials (RCTs)
II	Large RCT (with narrow confidence intervals) ($n > 100$) Smaller RCTs (with wider confidence intervals) ($n < 100$) Systematic reviews of cohort studies “Outcomes research” (very large ecologic studies)
III	Cohort studies (must have concurrent control group)
IV	Systematic reviews of case control studies Case series Cohort study without concurrent control group (e.g. with historical control group)
V	Case-control study Expert opinion Case study or report Bench research Expert opinion based on theory or physiologic research Common sense/anecdotes

AACPDM, American Academy for Cerebral Palsy and Developmental Medicine.

Appendix 3: List of excluded citations

1. Arnold PB, McVey PP, Farrell WJ, Deurloo TM, Grasso AR. Functional electric stimulation: its efficacy and safety in improving pulmonary function and musculoskeletal fitness. *Arch Phys Med Rehabil* 1992;73:665–8.
2. Ashe MC, Craven BC, Eng JJ, Krassioukov A. Prevention and treatment of bone loss after a spinal cord injury: a systematic review. *Top Spinal Cord Inj Rehabil* 2007;13:123–45.
3. Baldi JC, Jackson RD, Moraille R, Mysiw WJ. Muscle atrophy is prevented in patients with acute spinal cord injury using functional electrical stimulation. *Spinal Cord* 1998;36:463–9.
4. Decker MJ, Griffin L, Abraham LD, Brandt L. Alternating stimulation of synergistic muscles during functional electrical stimulation cycling improves endurance in persons with spinal cord injury. *J Electromyogr Kinesiol* 2010;20:1163–9.
5. Eser PC, Donaldson Nde N, Knecht H, Stüssi E. Influence of different stimulation frequencies on power output and fatigue during FES cycling in recently injured spinal cord injured people. *IEEE Trans Neural Syst Rehabil Eng* 2003;11:236–40.
6. Fornusek C, Davis GM. Cardiovascular and metabolic responses during functional electric stimulation cycling at different cadences. *Arch Phys Med Rehabil* 2008;89:719–25.
7. Hakansson NA, Hull ML. The effects of stimulating lower leg muscles on the mechanical work and metabolic response in functional electrically stimulated pedaling. *IEEE Trans Neural Syst Rehabil Eng* 2010;18:498–504.
8. Hakansson NA, Hull ML. Can the efficacy of electrically stimulated pedaling using a commercially available ergometer be improved by minimizing the muscle stress-time interval? *Muscle Nerve* 2012;45:393–402.
9. Hamzaid NA, Davis GM. Health and fitness benefits of functional electrical stimulation-evoked leg exercise for spinal cord-injured individuals: a position review. *Top Spinal Cord Inj Rehabil* 2009;14:88–121.
10. Hamzaid NA, Pithon KR, Smith RM, Davis GM. Functional electrical stimulation elliptical stepping versus cycling in spinal cord-injured individuals. *Clin Biomech (Bristol, Avon)* 2012;27:731–7.
11. Hooker SP, Scremin AM, Mutton DL, Kunkel CF, Cagle G. Peak and submaximal physiologic responses following electrical stimulation leg cycle ergometer training. *J Rehabil Res Dev* 1995;32:361–6.
12. Krause P, Szecsi J, Straube A. Changes in spastic muscle tone increase in patients with spinal cord injury using functional electrical stimulation and passive leg movements. *Clin Rehabil* 2008;22:627–34.
13. Janssen TW, Bakker M, Wyngaert A, Gerrits KH, de Haan A. Effects of stimulation pattern on electrical stimulation-induced leg cycling performance. *J Rehabil Res Dev* 2004;41:787–96.
14. McRae CG, Johnston TE, Lauer RT, Tokay AM, Lee SC, Hunt KJ. Cycling for children with neuromuscular impairments using electrical stimulation—development of tricycle-based systems. *Med Eng Phys* 2009;31:650–9.
15. Merli GJ, Herbison GJ, Ditunno JF, Weitz HH, Henzes JH, Park CH, *et al.* Deep vein thrombosis: prophylaxis in acute spinal cord injured patients. *Arch Phys Med Rehabil* 1988;69:661–4.
16. Nash MS, Tehranzadeh J, Green BA, Rountree MT, Shea JD. Magnetic resonance imaging of osteonecrosis and osteoarthritis in exercising quadriplegics and paraplegics. *Am J Phys Med Rehabil* 1994;73:184–92.
17. Reichenfelser W, Hackl H, Hufgard J, Kastner J, Gestaltner K, Gföhler M. Monitoring of spasticity and functional ability in individuals with incomplete spinal cord injury with a functional electrical stimulation cycling system. *J Rehabil Med* 2012;44:444–9.
18. Sloan KE, Bremner LA, Byrne J, Day RE, Scull ER. Musculoskeletal effects of an electrical stimulation induced cycling programme in the spinal injured. *Paraplegia* 1994;32:407–15.
19. Szecsi J, Fornusek C, Krause P, Straube A. Low-frequency rectangular pulse is superior to middle frequency alternating current stimulation in cycling of people with spinal cord injury. *Arch Phys Med Rehabil* 2007;88:338–45.
20. Szecsi J, Schiller M. FES-propelled cycling of SCI subjects with highly spastic leg musculature. *NeuroRehabilitation* 2009;24:243–53.
21. Wieler M, Stein RB, Ladouceur M, Whittaker M, Smith AW, Naaman S, *et al.* Multicenter evaluation of electrical stimulation systems for walking. *Arch Phys Med Rehabil* 1999;80:495–500.

References

- Vitale MG, Goss JM, Matsumoto H, Roye DP, Jr. Epidemiology of pediatric spinal cord injury in the United States: years 1997 and 2000. *J Pediatr Orthop* 2006;26(6):754–9.
- Vogel LC, Klaas SJ, Lubicky JP, Anderson CJ. Long-term outcomes and life satisfaction of adults who had pediatric spinal cord injuries. *Arch Phys Med Rehabil* 1998;79(12):1496–503.
- Castro MJ, Apple DF Jr, Staron RS, Campos GE, Dudley GA. Influence of complete spinal cord injury on skeletal muscle within 6 mo of injury. *J Appl Physiol* 1999;86(1):350–8.
- Wahrman K, Nash MS, Lewis JE, Seiger A, Levi R. Increased cardiovascular disease risk in Swedish persons with paraplegia: the Stockholm spinal cord injury study. *J Rehabil Med* 2010;42(5):489–92.
- Marayuma Y, Mizuguchi M, Yaginuma T, Kusaka M, Yoshida H, Yokoyama K, *et al.* Serum leptin, abdominal obesity and the metabolic syndrome in individuals with chronic spinal cord injury. *Spinal Cord* 2008;46(7):494–9.
- Thietje R, Pouw MH, Schulz AP, Kienast B, Hirschfeld S. Mortality in patients with spinal cord injury: descriptive analysis of 62 deceased subjects. *J Spinal Cord Med* 2011;34(5):482–7.
- Ahoniemi E, Pohjolainen T, Kautiainen H. Survival after spinal cord injury in Finland. *J Rehabil Med* 2011;43(6):481–5.
- Maïmoun L, Fattal C, Micallef JP, Peruchon E, Rabischong P. Bone loss in spinal cord-injured patients: from physiopathology to therapy. *Spinal Cord* 2006;44(4):203–10.
- Parent S, Mac-Thiong JM, Roy-Beaudry M, Sosa JF, Labelle H. Spinal cord injury in the pediatric population: a systematic review of the literature. *J Neurotrauma* 2011;28(8):1515–24.
- McCarthy JJ, Chafetz RS, Betz RR, Gaughan J. Incidence and degree of hip subluxation/dislocation in children with spinal cord injury. *J Spinal Cord Med* 2004;27(Suppl 1):S80–3.
- Dallmeijer AJ, van der Woude LH. Health related functional status in men with spinal cord injury: relationship with lesion level and endurance capacity. *Spinal Cord* 2001;39(11):577–83.
- Hettinga DM, Andrews BJ. Oxygen consumption during functional electrical stimulation-assisted exercise in persons with spinal cord injury: implications for fitness and health. *Sports Med* 2008;38(10):825–38.
- American Physical Therapy Association. Electrotherapeutic terminology in physical therapy. Section on clinical electrophysiology. American Physical Therapy Association: Alexandria, Virginia; 2000, p. 36.
- Newham DJ, Donaldson Nde N. FES cycling. *Acta Neurochir Suppl* 2007;97(Pt 1):395–402.
- Scremin AM, Kurtz L, Gentili A, Wiseman B, Perell A, Kunkel C, *et al.* Increasing muscle mass in spinal cord injured persons with a functional electrical stimulation exercise program. *Arch Phys Med Rehabil* 1999;80(12):1531–6.
- Hjeltnes N, Aksnes AK, Birkeland KI, Johansen J, Lannem A, Wallberg-Henriksson H. Improved body composition after 8 wk of electrically stimulated leg cycling in tetraplegic patients. *Am J Physiol* 1997;273(3 Pt 2):R1072–9.
- Chilibeck PD, Jeon J, Weiss C, Bell G, Burnham R. Histochemical changes in muscle of individuals with spinal cord injury following functional electrical stimulated exercise training. *Spinal Cord* 1999;37(4):264–8.
- Mohr T, Andersen JL, Biering-Sørensen F, Galbo H, Bangsbo J, Wagner A, *et al.* Long-term adaptation to electrically induced cycle training in severe spinal cord injured individuals. *Spinal Cord* 1997;35(1):1–16.
- Bhambhani Y, Tuchak C, Burnham R, Jeon J, Maikala R. Quadriceps muscle deoxygenation during functional electrical stimulation in adults with spinal cord injury. *Spinal Cord* 2000;38(10):630–8.
- Perret C, Berry H, Hunt KJ, Donaldson N, Kakebeke TH. Feasibility of functional electrical stimulated cycling in subjects with spinal cord injury: an energetic assessment. *J Rehabil Med* 2010;42(9):873–5.
- Hooker SP, Scremin AM, Mutton DL, Kunkel CF, Cagle G. Peak and submaximal physiologic responses following electrical stimulation leg cycle ergometer training. *J Rehabil Res Dev* 1995;32(4):361–6.
- Hooker SP, Figoni SF, Rodgers MM, Glaser RM, Mathews T, Suryaprasad AG, *et al.* Physiologic effects of electrical stimulation leg cycle exercise training in spinal cord injured persons. *Arch Phys Med Rehabil* 1992;73(5):470–6.
- Faghri PD, Glaser RM, Figoni SF. Functional electrical stimulation leg cycle ergometer exercise: training effects on cardiorespiratory responses of spinal cord injured subjects at rest and during submaximal exercise. *Arch Phys Med Rehabil* 1992;73(11):1085–93.
- Sköld C, Lönn L, Harms-Ringdahl K, Hulting C, Levy R, Nash M, *et al.* Effects of functional electrical stimulation training for six months on body composition and spasticity in motor complete tetraplegic spinal cord-injured individuals. *J Rehabil Med* 2002;34(1):25–32.
- Jacobs PL, Nash MS. Modes, benefits and risks of voluntary and electrically induced exercise in persons with spinal cord injury. *J Spinal Cord Med* 2001;24(1):10–18.
- Fornusek C, Davis GM. Cardiovascular and metabolic responses during functional electrical stimulation cycling at different cadences. *Arch Phys Med Rehabil* 2008;89(4):719–25.
- Chen SC, Lai CH, Chan WP, Huang MH, Tsai HW, Chen JJ. Increases in bone mineral density after functional electrical stimulation cycling exercises in spinal cord injured patients. *Disabil Rehabil* 2005;27(22):1337–41.
- McDonald JW, Becker D, Sadowsky CL, Jane JA Sr, Conturo TE, Schultz LM. Late recovery following spinal cord injury: case report and review of the literature. *J Neurosurg* 2002;97(2 Suppl):252–65.
- Sloan KE, Bremner LA, Byrne J, Day RE, Scull ER. Musculoskeletal effects of an electrical stimulation induced cycling programme in the spinal injured. *Paraplegia* 1994;32(6):407–15.
- BeDell KK, Scremin AM, Perell KL, Kunkel CF. Effects of functional electrical stimulation-induced lower extremity cycling on bone density of spinal cord-injured patients. *Am J Phys Med Rehabil* 1996;75(1):29–34.
- Kakebeke TH, Lechner HE, Knapp PA. The effect of passive cycling movements on spasticity after spinal cord injury: preliminary results. *Spinal Cord* 2005;43(8):483–8.
- Muraki S, Ehara Y, Yamasaki M. Cardiovascular responses at the onset of passive leg cycle exercise in paraplegics with spinal cord injury. *Eur J Appl Physiol* 2000;81(4):271–4.
- Willoughby DS, Priest JW, Jennings RA. Myosin heavy chain isoform and ubiquitin protease mRNA expression after passive leg cycling in persons with spinal cord injury. *Arch Phys Med Rehabil* 2000;81(2):157–63.
- American Academy for Cerebral Palsy and Development Medicine Treatment Outcomes Committee. 2008. AACPDM methodology to develop systematic reviews of treatment interventions (Revision 1.2) 2008 version. Available from: http://www.aacpdm.org/membership/members/committees/treatment_outcomes_methodology.pdf [accessed 2011 August 23].
- World Health Organization. International classification of functioning, disability and health (ICF). World Health Organization: Geneva, Switzerland; 2001.
- Johnston TE, Smith BT, Mulcahey MJ, Betz RR, Lauer RT. A randomized controlled trial on the effects of cycling with and without electrical stimulation on cardiorespiratory and vascular health in children with spinal cord injury. *Arch Phys Med Rehabil* 2009;90(8):1379–88.
- Johnston TE, Modlesky CM, Betz RR, Lauer RT. Muscle changes following cycling and/or electrical stimulation in pediatric spinal cord injury. *Arch Phys Med Rehabil* 2011;92(12):1937–43.
- Lauer RT, Smith BT, Mulcahey MJ, Betz RR, Johnston TE. Effects of cycling and/or electrical stimulation on bone mineral density in children with spinal cord injury. *Spinal Cord* 2011;49(8):917–23.
- Johnston TE, Betz RR, Lauer RT. Impact of cycling on hip subluxation in children with spinal cord injury. *J Pediatr Orthop* 2009;29(4):402–5.
- Johnston TE, Smith BT, Oladeji O, Betz RR, Lauer RT. Outcomes of a home cycling program using functional electrical stimulation or passive motion for children with spinal cord injury: a case series. *J Spinal Cord Med* 2008;31(2):215–21.
- Castello F, Louis B, Cheng J, Armento M, Santos AM. The use of functional electrical stimulation cycles in children and adolescents

- with spinal cord dysfunction: a pilot study. *J Pediatr Rehabil Med* 2012;5(4):261–73.
- 42 Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977;33(1):159–74.
 - 43 Sakzewski L, Boyd R, Ziviani J. Clinimetric properties of participation measures for 5–13 year old children with cerebral palsy: a systematic review. *Dev Med Child Neurol* 2007;49(3):232–40.
 - 44 Dagenais LM, Lahay ER, Stueck KA, White E, Williams L, Harris SR. Effects of electrical stimulation, exercise training and motor skills training on strength of children with meningocele: a systematic review. *Phys Occup Ther Pediatr* 2009;29(4):445–63.
 - 45 Walker JL, Ryan SW, Coburn TR. Does threshold nighttime electrical stimulation benefit children with spina bifida? A pilot study. *Clin Orthop Rel Res* 2011;469(5):1297–301.