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The Performance of Aerobic Exercising by Spinal Cord Injury Patients Through the Application of Functional Electrical Stimulation

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Evoking a muscular response using Functional Electrical Stimulation onto paralyzed muscles will allow patients with spinal cord damage at the level of C4-L1 to perform aerobic and strengthening exercise training. The provoked activity will improve body strength, body composition, mitigate disuse atrophy, and enhance metabolic and cardiopulmonary function. The higher the injury of the spinal cord, the more severe the extent of paralysis. Higher cervical nerves at the level of C4 and above can result in a patient having complete paralysis in their arms, hands, trunk, and legs causing quadriplegia. Lower spinal cord injury will spare the function in the upper body resulting in paraplegia. Lower cervical spinal cord injuries from C5 and below may end up with partial paralysis in the upper and lower body. Injuries to the lower lumbar spinal cord retains the upper body function and results in some loss of function in the hips and legs. For the purposes of this study, the C4-L1 level is focused on to hone in on subjects who have the potential ability to restore previous functioning having damages from a lower section of the cervical spinal cord and a higher lumbar spinal cord segment. The study designs included case report, case control, case series, pre-clinical and post-clinical intervention and outcomes measure, clinical trial, prospective cohort study, cross-sectional, and longitudinal repeated measures design. The statistical methods and methods of data analysis used were ANOVA, ASIA impairment scores, α level and p-value, mean ± standard error, r^2, Student paired t-test, PASW statistics, Spearman rank correlation coefficient, Mann-Whitney U test, regression analysis, and Wilcoxon signed-rank test. The outcome of the study showed an increase in muscle thickness, strength, and lean muscle mass. Results yielded a positive effect on cardiorespiratory functioning with a significant increase in peak oxygen consumption and peak heart rate from the baseline level. FES-trained individuals also exhibited an increase in cardiac output and stroke volume in comparison to FES-untrained subjects. There was also a reduction in inflammatory markers, such as CRP, IL-6, and TNF-α, which are associated with cardiovascular disease. Body strength was improved with a slight increase in bone density, however, this was only a significant finding when the training protocol was more intense and longer in duration. Additional parameters were looked at to show the positive impact FES induced exercising had on metabolic function. Both insulin and glucose levels were decreased post-training thereby improving insulin sensitivity and glucose tolerance. The lipid panel, however, did not show any significant changes. Oxygen-Hemoglobin was also increased after active cycling. Subjects were able to perform more intense exercising as the training regime had progressed and further proves the positive effect on body strength and body composition. Subjects displayed the maximum cycling power and work done in the later stages of their training. Depending on the administration of continuous or variable electrical stimulation, subjects had varied evoked torque due to differences in muscle fiber activity. The significance of these findings shows a potential way to improve the health of subjects with spinal cord injury, but also to recover and eventually regain the use of the muscles that were once paralyzed. Functional electrical stimulation therapy will introduce physical activity to a population that is normally found to be inactive.

Keywords: Functional electrical stimulation, spinal cord injury, FES-cycling, FES-rowing, rehabilitation, exercise training

Spinal cord injury (SCI) can result in drastic damages that have permanent repercussions which alter one's ability to function in their daily life. This disruption prevents the communication between the brain and the body which leads to the paralysis of muscles and the disuse of the associated limbs. People who undergo injuries to the spinal cord often adapt a more sedentary lifestyle which begins to impact their health (Bakkum, 2015) and increase the risks of co-morbidities such as cardiovascular disease (van der Scheer, 2016), type 2 diabetes (Jeon, 2010), obesity, osteoporosis and bone fractures. A preventative measure evokes the use of the paralyzed muscles to stimulate the unused limbs to provide therapeutic benefits to the patient.

In recent medical advancement, electrical stimulation has become a clinically significant method to improve the management of patients suffering from SCI by restoring useful functioning of their body. Individuals can regain the use of their limbs and manage their daily activities by repairing the activity of the paralyzed muscles. Applying Functional Electrical Stimulation (FES) to stimulate the paralyzed muscles will induce functional muscle movement which can allow an aerobic exercise like rowing to become possible again. It also enables the recovery process after SCI. Progression in SCI management will allow patients to not only regain mobility, but will also reduce their dependence on caregivers and enhance the patient's quality of life overall.

Current studies show ample evidence favoring the use of aerobic exercise during the rehabilitation process. This study specifically focuses on the use of FES-cycling and FES-rowing. FES-rowing involves both hand strokes to propel the body forward along with lower leg movement to test the strength of both the upper and lower limbs functioning simultaneously. The use of FES-induced leg exercise is preferred over voluntary arm exercise due to the involvement of larger muscle mass which activates the venous muscle pump of the legs and enhances circulation (Bakkum, 2015). After SCI there is an accumulation of intramuscular adipose tissue, this contributes to inflammation and makes patients susceptible to cardiometabolic risks and hinders cardiovascular performance (Galea, 2017). Cardiometabolic health benefits are closely associated with skeletal muscle tissue metabolism, and the

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introduction of exercising in patients who are normally inactive will potentially improve cardiovascular functioning.

It is crucial to establish ways to prevent the deterioration of musculoskeletal tissue through rehabilitation to initiate neurological recovery (Galea, 2017). Recent literature using FES-induced exercising has reported an increase in muscle mass and muscle fiber size (Jeon, 2010). The biochemical changes seen included an increase in expression of glucose transporter-4 and hexokinase II activity and an alteration in muscle composition due to changes in muscle fiber type. Aerobic exercise has been shown to improve the overall health of patients by progressively enhancing metabolic activity by reducing glucose levels, fasting plasma insulin levels, and leptin levels (Jeon, 2010). Sufficient training which employs exercises with adequate intensity and frequency is required to maximize potential changes in body composition and overall therapeutic advantages (van der Scheer, 2016).

The purpose of this study was to investigate how the application of electrical stimulation allows patients suffering from SCI to undergo rehabilitation to regain proper and normal functioning of their spinal cord. I hypothesized that the application of FES to paralyzed muscles will allow patients with spinal cord damage at the level of C4-L1 to perform aerobic and strengthening exercise training. This muscle usage will enhance body strength, body composition, prevent disuse atrophy, and improve metabolic and cardiopulmonary function.

Methods:

The literature chosen for this analysis focused on studies that were centered around patients undergoing rehabilitation after SCI for a duration of more than a year postinjury and recruited for the studies from rehabilitation hospitals and clinics. The criteria stressed on subjects having SCI for more than a year to eliminate patients who are undergoing muscle fiber changes which may alter the results and give unreliable findings. Studies were picked based on the subjects that were gathered for the study and limited to patients with damage at the level of C4-L1 as classified by the American Spinal Injury Association (ASIA) class A-C including both complete and incomplete SCI. The strategy used during publication searches was to stay within a limitation where studies shared similarities and could be generalized. The findings of the research were to be compared to gather evidence on the topic of focus, this was primarily done by finding studies using similar study protocols and shared inclusion/ exclusion criteria.

Databases were used to find relevant literature on the study and included PubMED, MeSH, EBSCOhost, Ryerson online database, PEDro, and Google Scholar. The study excluded studies prior to 2007 which limited the study range to within the last ten years to ensure the most recent research regarding this topic would be explored. Search keywords included: electrical stimulation, FES-rowing, FES-cycling, spinal cord injury, SCI rehabilitation, aerobic exercise in SCI and a more thorough search was done using specific search phrases such as: 'spinal cord rehabilitation', 'electric stimulation in muscle paralysis', 'electric stimulation for strength training in paralyzed muscles', and 'spinal cord rehabilitation with electrical stimulation'.

Inclusion criteria selected studies with an exposure of interest in strengthening exercise training prior to FES aerobic exercising. Subjects needed to be assessed for pre-existing medical conditions and tested for response to electric stimulation. This was part of the criteria to verify the accuracy of the results of publications that screened for patients to be excluded from the study. Publications with different study designs were used, evidence proved by the studies were analyzed and correlated by looking at the sample size of the subjects and the data analysis used in the study. This allowed for this study to incorporate different aspects examined by each study design so that inferences made from the findings were not limited. Studies picked were conducted from USA, France, Ireland, Switzerland, Australia, UK, and Korea, to get a diverse population of subjects from studies employing similar protocols. To maintain a homogenous study, the inclusion criteria ensured that subject selection was consistent across studies. Subjects ranged in age between 16-65 years old and included both males and females.

Therapy or exposure was restricted to either cycling or rowing (Figure 1) as a form of aerobic exercising. This limited any variability which arises from different techniques required to manipulate the equipment used to gather data. The duration of the study was also looked at to pick studies that ranged from 3 weeks to up to 18 months. This variability was imperative to infer if the findings were seen only after a short duration or if it persisted after a long period of time. Lastly, studies were chosen based on the factors being monitored such as bone density, muscle architecture, body composition, peak oxygen consumption (Vo2 peak), metabolic and cardiorespiratory adaptations, muscle strength, and caloric expenditure. These criteria allowed the study to focus on the positive benefits of this therapy and to determine whether this can be a long-term approach for SCI patients in the future.

The method of data synthesis and analysis included comparison tables to summarize findings concisely, further supported by qualitive and/or quantitative data from each study. The similarities and differences were analyzed across the literature to form a conclusive statement regarding the benefits of the selected therapies. Figures and graphs were also used to visually understand how the training altered body composition and strength from the baseline level to the end of the study. Table 1 shows the study designs used in this analysis, this accounted for accuracy of the data by making comparisons across multiple designs contributing to methodological heterogeneity. The study population was relatively similar across the studies analyzed, Table 2 breaks down the specific data used in picking appropriate studies.

Table 3 summarizes the studies which shared similar forms of outcome assessment. The major similarities include the type of stimulator used for the training, the devices used to measure oxygen consumption, equipment used to monitor any changes in cardiorespiratory functioning post-training, and lastly the Borg scale which was used for perceived exertion. The use of similar equipment allows for comparison of data across studies and reduces any error caused by equipment and measuring devices.

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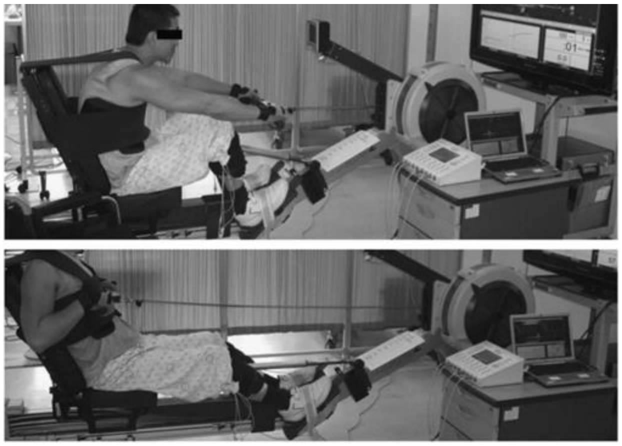

Figure 1. FES-rowing equipment (D-I Kim, 2014)

Table 1. Study Design

Study Design	No. of Studies
Case Report	1
Case Control	2
Case Series	4
Preclinical and Post-clinical Intervention and Outcomes measure design	2
Clinical Trial	2
Prospective Cohort study	1
Cross Sectional	1
Longitudinal Repeated measures design	1

Table 2. Study Population

Study	Avg. Age (yrs.)	Injury level	Avg. Time postinjury (yrs.)	Gender	ASIA class
1	36	T4-T5*	2	F$^{\alpha}$	A
2	40	C4-T7	11	M/F	-
3	< 40	T4-T9*	< 18	M$^{\alpha}$	A
4	45.08	T2-T11*	11.22	M/F	A-B$^{\beta}$
5	41.8	T3-T12*	10.7	M/F	A
6	42.5	T4-T9*	13.4	M/F	A
7	35	T5-T12*	3	M$^{\alpha}$	A
8	36	C6-L1	11.4	M/F	A-C$^{\beta}$
9	34.83	C6-T4	7.67	M/F	A
10	44	C5-T6	> 1	M/F	A-B$^{\beta}$
11	35.7	C4-T10	8.99	M/F	A-B$^{\beta}$
12	45.1	C4-T11	13.4	M/F	A-B$^{\beta}$
13	33.9	C5-T12	9.5	M/F	A-B$^{\beta}$

* – SCI at the thoracic level only
α – Single gender study
β – Incomplete SCI under the ASIA impairment scale

Table 3. Outcome Assessment

Study	Outcome Assessment
1	Odstock Salisbury stimulator, Isokinetic dynamometer, Biopac Systems Inc, B-mode ultrasonography, linear-array probe, tape measure, DEXA, heart rate monitor, K4b^2 (gas exchange), Borg scale
2	Ergys2, ASIA test, OGTT, Basic One Touch blood glucometer, ^{125}I radioimmunoassay, immunoturbidimetric assay, ELISA, microplate reader
3	Odstock Salisbury stimulator, open circuit spirometry, paramagnetic O_2, infrared CO_2 analyzer, pneumotachograph, heart monitor, Borg scale
4	Battery powered muscle stimulator, Borg scale
5	Salisbury Odstock 4 channel stimulator, 8 channel Stanmore Stimulator, low dead space portable system (gas exchange), fingertip sensor: Datex-Ohmeda 3000 pulse oximeter system, user interface (Matlab), non-phase shifting low-pass filter
6	Stanmore Stimulator, portable ergospirometric system (Metamax)
7	ERGYS-1, metabolic cart, electrocardiogram, NIRS-based photometer, pneumatic tourniquet
8	4 channel stimulator MEGA XP, Polar Beat apparatus, portable K4b2 gas analyzer, hand held dynamometer, Inbody S20 (body composition)
9	Concept2 ergometer, linear string potentiometer, Odstock Salisbury stimulator, open circuit spirometry, paramagnetic O_2, infrared CO_2 analyzer, heart rate monitor, NI LabVIEW software, Matlab software
10	RT300 FES bike, isokinetic dynamometer chair, battery operates electrical stimulation unit, K4b2 portable metabolic unit COSMED (energy expenditure), heart rate monitor,
11	Transducer on a commercial ultrasound system, electrocardiogram
12	Portable electrical stimulation unit, NIRS, arterial occlusion cuff, ultrasound B-mode imaging, MRI
13	Isokinetic dynamometer, biphasic square pulses with Compex 2 stimulator

Results:

In general, the studies looked at how training in aerobic exercising played a role in altering metabolic functioning, body composition, oxygen consumption, cardiorespiratory functioning, and strength through various training therapies. While most of the studies found similar evidence to strengthen the findings of the topic, there were also data opposing some of the major significant findings. The focus of this study encompassed SCI patients who underwent pulses of electric stimulation through surface electrodes or muscle stimulators to a group of muscles on paralyzed limbs to elicit muscle use during exercising using FES-rowing or FES cycling equipment. Various measurements were taken prior to the onset of training and compared to levels upon completion of the study. Some factors that were looked at included peak oxygen consumption, changes in glucose and insulin levels, muscle thickness or composition of the muscles like hemoglobin levels, and lastly the improvement in the level of intensity the subject was able to withstand as training progressed. A look at the evidence table provided in the appendix under Table 4 briefly discusses the publications that were examined for this review.

Table 4. Evidence Table.

First Author	Year	Study Design	Level of Evidence	Study Population/ Level of Spinal Cord Damage	Therapy or Exposure- Form of Strengthening Exercise Training	Outcome/ Results
Gaëlle Deley	2017	Case report	4	36-year-old female with SCI between T4-T5	FES-strengthening and FES-rowing	FES-strengthening and FES-rowing benefitted the test subject and parameters tested showed an increase after regular aerobic exercise.
Adina Draghici	2017	Case control	3	6 Adults with SCI between C5-T12 (5 males and 1 female) & 6 Able-bodied subjects who were former varsity athletes in rowing or currently training individually (2 males and 4 females)	FES-rowing	FES-rowing allows for whole body exercise in patients with SCI, however, the kinetics and kinematics differs from able-bodied subjects. FES resulted in higher ATP consumption and led to quicker muscle fatigue and lower leg strength. It can potentially benefits SCI patients with bone health by slowing down bone loss.
D-I Kim	2014	Preclinical and post-clinical intervention and outcomes measure design	4	12 subjects with SCI (10 males and 2 females) between C6-L1	Motor driven FES-rowing exercise	After the 6-week exercise training using motor driven FES-rowing, there was an increase in muscular strength of the upper extremity along with improvement in cardiopulmonary fitness and body composition.
Satoshi Muraki	2007	Case control	3	4 male patients with SCI between T5-T12 and 6 able-bodied subjects	ES- stimulated cycling (passive and active)	Passive cycling had little effect on cardiorespiratory responses in comparison to active ES cycling. With the onset of ES cycling there was deoxygenation of the muscles, however, after a delay it reached an equilibrium point between oxygen demand and oxygen delivery after prolonged ES-cycling.
Helen Russell Berry	2008	Case series	4	10 male and 2 female subjects with SCI between T3-T12	ES-cycle training	Endurance of cycle training increased from 10 minutes to 60 minutes of continuous pedaling. Significant improvement in cardiorespiratory functioning and cycling power output.
J. Andrew Taylor	2011	Clinical trial	2	6 male patients younger than 40 years old with SCI between T4-T9	Hybrid FES-rowing vs. arms only rowing	Whole body aerobic training with FES-row training can increase aerobic capacity to normal levels of able bodied individuals.
L. Griffin	2009	Case series	4	18 subjects (5 females and 13 males) with	FES-cycling	Lean muscle mass increased but bone and adipose mass did not change. Blood glucose and insulin levels were lower with OGTT after
Ashraf Gorgey	**2014**	**Case series**	**4**	**10 subjects (9 males and 1 female) with SCI between C5-T10**	**FES-cycling**	**Different pulse duration of acute bouts of FES-cycling did not affect cycling VO2 or energy expenditure, however, a higher pulse duration may augment energy expenditure during the FES cycling. Acute bout of FES-cycling can lead to delayed onset muscle fatigue.**
Amanda Carty	2012	Prospective cohort study	2	14 subjects (11 men and 3 women) with SCI between T4-T11	Novel NMES system	Improved aerobic fitness in SCI patients living an inactive lifestyle: improvement in both Vo2 peak and HR peak.
Claudio Perret	2010	Case series	4	8 subjects (7 males and 1 female) with SCI between T3-T9	FES-cycling	FES-cycling was an alternative form of upper body exercising for caloric expenditure and to maintain health benefits in patients with spinal cord injury.
RS Gibbons	2016	Cross-sectional, longitudinal repeated measures design	4	14 subjects with SCI between C4-T10 ASIA scale A or B	FES-rowing	FES-rowing resulted in cardiac remodeling. After training these subjects had cardiac structure and function more like non-SCI subjects.
Melissa Erickson	2017	Pre- vs. post-test study design	4	14 subjects with SCI between C4-T11 with ASIA scale A or B	NMES training	After training there was an increase in muscle contractions. Increase in skeletal muscle oxidative capacity but no changes seen in metabolic or lipid profiles, and no significant changes in muscle composition.
Gaelle Deley	2015	Clinical Trial	2	10 subjects with SCI between C5-T12 ASIA scale A or B	Variable frequency trains or constant frequency trains	VFT offsets muscle fatigue and allows exercising at higher intensity and longer duration than ES that is applied constantly.

Training time had significantly impacted the fitness of patients across all studies. The duration of ride time was statistically greater and reached up to 30 min in 12 out of 18 subjects as the training progressed in weeks, in comparison to the baseline level of 0.22-30 min with only 5 subjects reaching 30 min. When it came to studies looking at FES-rowing, aerobic capacity was 20.0 ± 1.9 mL/kg/min when patients underwent rowing with FES in comparison to arms only rowing which was 15.7 ± 1.5 mL/kg/min with a statistically significant difference at $p = 0.01$ (Taylor, 2011).

Results varied depending on the compliance of exercise regime which ranged from 67% to 86%. Figure 2 shows three subjects with varying aerobic capacity, subject 2 was more consistent with a compliance of 82% and had approximately a 50% increase in aerobic capacity from 18.3 to 27.1 mL/kg/min. However, subject 1 had only a 30% increase at the end of 18 months due to varying adherence to the exercise sessions with a compliance of 75%. Subject 3 showed no change in peak aerobic capacity after training for only 6 months duration and had an average weekly exercise intensity of 1698 watts*min. This was well below the averages of subjects 1 and 2 which was 1878 ± 157 and 2986 ± 185 watts*min, respectively. Training protocols with varying pulse durations (200, 350, and 500 microseconds) showed no difference on relative oxygen uptake, cycling energy expenditure, or muscle fatigue (Gorgey, 2014). The change in energy expenditure between rest and exercise was 42% greater with a pulse duration of 500 and 350 microseconds than in 200 microseconds where $p = 0.07$. Continuous cycling capacity showed an increase from 10 to 60 minutes of pedaling during the training process for all the subjects (Berry, 2008).

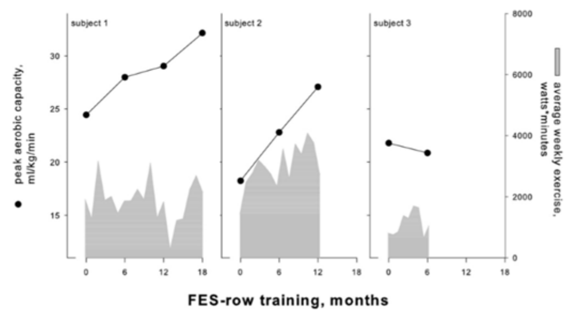

Figure 2. Changes in aerobic capacity and weekly total work in FES row training (Taylor, 2011)

Body composition and muscle structure was seen to change after the training procedure. Muscle thickness increased by 136% along with thigh circumference by 14% from baseline levels to the end of 12 months of training (Deley, 2017). The total body mass and lean muscle mass significantly increased from 153.22 ± 9.32 to 157.76 ± 9.11 lb. and 96.8 ± 5.61 to 100.0 ± 5.47 lb., respetively (Griffin, 2009). Evidence from another study also showd an increase in lean mass from 50.4 ± 9.4 to 53.3 ± 10.0 kgwhere $p = 0.001$, but percent body fat was reduced from 239 ± 8.5 to 20.4 ± 7.9 % where $p = 0.028$ after 6 weeks of trainig (D-I Kim, 2014). Muscle area (left: $p = 0.9$, right: $p = 0.48$),fat area (left: $p = 0.63$, right: $p = 0.73$), and intramuscular fat (left: $p = 0.62$, right: $p = 0.81$) of the left and right quadriceps muscle did not significantly change in response to neromuscular electrical stimulation training (Erickson, 2017).

Although bone mineral density showed an increase by 19.4% post-training in a study conducted by Deley et al. (2017), Griffin et al. (2009) concluded there was no significant difference in bone or adipose tissue following 10 weeks of training. Near the end of cycling training, the change in oxygen-Hemoglobin (oxy-Hb) after active cycling differed between able-bodied and SCI patients. SCI patients had increased oxy-Hb by 92.2% where $p < 0.05$, and twice as much of that seen in able bodied subjects who had an increase of +35.0% where $p > 0.05$ (Muraki, 2007). Deoxy-Hb was also significantly higher throughout active cycling, however, after recovery both SCI subjects and able-bodied subjects had similar levels. Glucose levels at 30, 60, and 120 min after dextrose consumption were lower post-test, along with significantly lower insulin levels at 60 and 120 min compared to the pre-test levels (Griffin, 2009). After neuromuscular electrical stimulation training, there was a 3% average reduction in hemoglobin A_{1C} (HbA_{1C}) from 5.6 ± 0.4 to 5.4 ± 0.5 % where $p = 0.03$ (Erickson, 2017). CRP, IL-6, and TNF-

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alpha improved following training with a statistically significant difference at $p < 0.05$, but cholesterol, LDL, and triglyceride levels did not show much change with a slight reduction in HDL where $p < 0.05$ (Griffin, 2009). Maintaining approximately 4-8 hours of FES-cycling was needed to reach the weekly recommended expenditure of calories of 1000-2200 kcal (Perret, 2010).

Oxygen consumption measured during FES-rowing increased from the first month of training to the twelfth month from 18.1 to 28.6 $mL \cdot min^{-1} \cdot kg^{-1}$ (Deley, 2017). When comparing arms only rowing to rowing with FES, peak ventilation was similar for both exercises. However, peak respiratory exchange ratio for rowing with FES was 1.17 ± 0.03 and was higher for arms only rowing which was 1.28 ± 0.16 where $p = 0.14$ (Taylor, 2011). Application of neuromuscular electrical stimulation also showed a statistically significant increase in peak oxygen consumption (VO_2 peak), from -1.1% to 57.2% where $p = 0.001$, and peak heart rate (HR peak), where $p = 0.032$ from the baseline levels (Carty, 2012). Another study found that after neuromuscular electrical stimulation training, there was an increase in skeletal muscle oxidative capacity which changed from 0.49 ± 0.15 to 1.01 ± 0.49 min^{-1} where $p = 0.019$ (Erickson, 2017). Significant changes in VO_2 during cycle training occurred between 3-6 months where $p = 0.003$, and changes seen over the first 6 months were related to total training hours completed where $p = 0.012$ and $r^2 = 0.52$ (Berry, 2008). The HR peak also increased by 13% after 6 months where $p = 0.008$, but by 12 months there was no significant increase where $p = 0.057$. The same pattern was seen with peak O_2 pulse which had a statistically significant increase by 6 months where $p = 0.002$, but after this there was no significant increase and $p = 0.85$.

VO_2 in both SCI (PARA) subjects and able-bodied (AB) subjects was increased compared to resting levels and reached a steady state plateau phase after 10 minutes of cycling. After about 40 minutes of exercise, the increase in VO_2 levels above baseline levels were about the same between both groups where PARA group reached 546 ± 139 $mL \cdot min^{-1}$ and AB group reached 575 ± 51 $mL \cdot min^{-1}$ (Muraki, 2007). Respiratory exchange ratio (RER) in PARA subjects increased until the 10th minute of cycling with a significant difference of 1.36 ± 0.05 in comparison to 0.90 ± 0.10 in AB subjects. RER then decreased until the end of the exercise after 40 min to 0.99 ± 0.02 in the PARA group and 0.85 ± 0.04 in the AB group. Heart rate (HR) in the PARA group was shown to increase after 10 min and 40 min of exercise, going from the baseline level of 60 ± 5 beats/min to 83 ± 11 and 105 ± 20 beats/min, respectively. HR did not return to resting levels after 10 minutes of recovery time and remained at 99 ± 29 beats/min displaying cardiovascular drift (Figure 3).

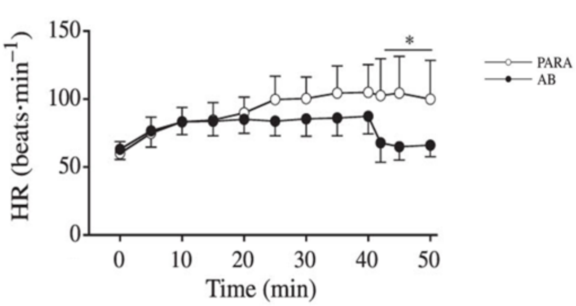

Figure 3. Heart rate during active cycling using electrical stimulation or voluntary cycling at similar oxygen consumptions (Muraki, 2007)

Stroke volume increased significantly by 20 mL where $p < 0.05$ only in AB subjects after 40 min of exercise, but these results showed a non-significant trend in higher values (Muraki, 2007). Another study found that stroke volume was significantly lower in FES-untrained subjects, which was 36 ± 5 mL in females and 42 ± 8 mL in males, compared to FES-trained males who had 67 ± 7 mL and $p < 0.05$ (Gibbons, 2016). Gibbons et al. (2016) found that resting HR was higher in FES-untrained subjects (73 ± 17 $beats \cdot min^{-1}$ in females and 63 ± 15 $beats \cdot min^{-1}$ in males) compared to FES-trained males (53 ± 6 $beats \cdot min^{-1}$). Cardiac output was lower in FES-untrained subjects (2.6 ± 0.3 $L \cdot min^{-1}$ in females and 2.6 ± 0.2 $L \cdot min^{-1}$ in males) in comparison to FES-trained males (3.6 ± 0.8 $L \cdot min^{-1}$). Oxygen saturation in PARA subjects reduced to 72% ± 28% of resting muscle oxygenation at the start of exercise and again at the end of exercising to 72% ± 19%, with a spike to 86% ± 23% from 5-7 minutes after the onset of exercise (Muraki, 2007).

FES-rowers had lower oxygen consumption and performed less work in comparison to able-bodied subjects, however, oxygen consumption increased in both groups through exercise training. FES-rowers were less efficient with a value of 0.101 ± 0.022 in comparison to 0.199 ± 0.006 (total work)/ VO_2 where $p < 0.01$ and performed less external work relative to increase in oxygen consumption (Draghici, 2017). In a study conducted by D-I Kim et al. (2014), there was no significant changes in VO_2 peak after rowing training which changed from 17.2 ± 3.8 to 19.4 ± 4.7 $mL \cdot kg^{-1} \cdot min^{-1}$ where $p = 0.099$. After 8 weeks of FES-rowing training there was a significant increase in left ventricular internal diameter in diastole (LVIDd), which changed from 4.34 ± 0.13 to 4.56 ± 0.05 cm. There was also an increase in left ventricular mass (LVM) which changed from 110 ± 6 to 118 ± 2 g, and a decrease in relative wall thickness in diastole (RWTd) which went from 0.37 ± 0.01 to 0.35 ± 0.01 cm (Gibbons, 2016).
Evoked torque had a big increase at the onset of rowing training during the first three months by 154%, and a small decrease was seen in the last three months by -11% in a 12-month training procedure (Deley, 2017). When constant frequency trains (CFT pattern) was used as the first pattern for training, it needed a lower stimulus intensity (76 ± 5 mA) to produce 50% of the maximal force (Figure 4) compared to using variable frequency trains (VFT pattern) as the first pattern for training (112 ± 3 mA) where $p < 0.05$ (Deley, 2015). When the CFT pattern was administered second, it required a similar stimulus intensity to VFT (113 ± 5 mA compared to 110 ± 9 mA) and $p = 0.19$. When the CFT pattern was used first, it resulted in less contractions before torque failed to reach its target (3.5 ± 0.2) than when the VFT pattern was initially used (6.7 ± 0.8) where $p < 0.05$. Starting with the VFT pattern resulted in 10.3 ± 1.2 contractions compared to starting with the CFT pattern which produced 6.9 ± 1.1 contractions where $p < 0.05$. Deley et al. (2015) concluded that the total work produced with the initial use of the VFT pattern followed by the CFT pattern was 1218.1 ± 211.0 $Nm \cdot s$, the opposite produced a total work of 696.7 ± 120.2 $Nm \cdot s$ where $p = 0.01$. Both CFT and VFT resulted in a

decrease in torque between the first and last contractions, which went from 41.8 ± 7.2 to 21.4 ± 3.0 N·m and 43.6 ± 7.4 to 29.6 ± 5.1 N·m, respectively and $p < 0.05$.

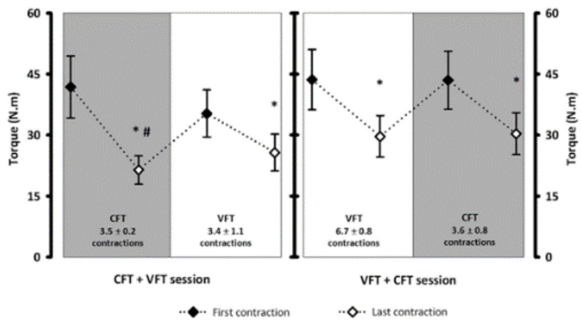

Figure 4. Torque measured during the first and last contractions stimulated by constant frequency trains (CFT) and variable frequency trains (VFT). # Significant difference from last contraction across stimulation patterns. * Significant difference from first contraction within stimulation pattern (Deley, 2015).

Cycling power and work done were greater in the later weeks reaching a power of 0.71-10.51 W after persistent training in comparison to the onset of training during week 1 with a power of 0 (Griffin, 2009). The greatest increase in peak power output (PO peak) was seen in the first 3 months of exercising with a statistically significant difference of $p = 0.02$ with values ranging from 6.7 to 35.6 W. The increases seen in the first 6 months of training between 0.77 and 20.82 W was related to the training hours completed ranging between 59 and 114 hours with $p < 0.001$ and $r^2 = 0.84$ (Berry, 2008). In PARA subjects during cycling, the power output dropped until the tenth minute and after 15 minutes of exercise training reached steady state (Figure 5). This was lower than that of AB subjects who also had higher mechanical efficiencies of 12.6% in comparison to the 1.3% seen in PARA subjects where $p < 0.05$ (Muraki, 2007).

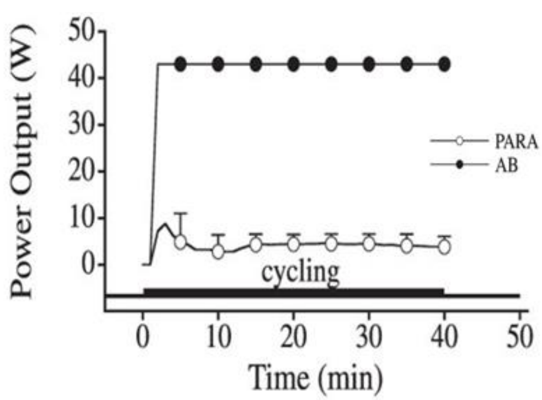

Figure 5. Power output during active cycling in PARA and AB subjects (Muraki, 2007)

Upper body muscle strength was increased after rowing training in shoulder flexion ($p = 0.002$), extension ($p = 0.010$), abduction ($p = 0.002$), adduction ($p = 0.003$), and elbow extension ($p = 0.002$) and flexion ($p = 0.004$) (D-I Kim, 2014). Able-bodied subjects performing rowing exercise coordinated their lower body, trunk, and upper body so that it moved simultaneously, whereas SCI subjects undergoing FES-rowing had their arms initiate the rowing and had the legs following uncoordinatedly (Draghici, 2017). These subjects exerted a higher force using their upper body, which was 0.30 ± 0.11 body weight (BW), in comparison to the force applied by the lower body, which was 0.22 ± 0.10 BW, where $p = 0.01$ (Figure 6). Able-bodied individuals showed the opposite pattern and favored the lower body for stronger forces during rowing by reaching 0.97 ± 0.17 BW in comparison to an upper body force of 0.81 ± 0.12 BW where $p < 0.01$. Overall, able-bodied subjects achieved higher forces for both upper and lower body compared to SCI subjects where $p < 0.01$.

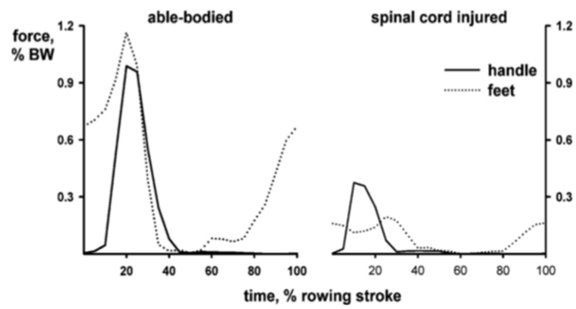

Figure 6. External force output at the handle and at the feet (Draghici, 2017)

Although both able-bodied and FES-rowing subjects had a constant drive time, the FES-rowing subjects spent more time during recovery phase as the peak % workload (relative intensity) increased and had a drive to recovery ratio of 0.81. Recovery time where $p = 0.05$ decreased in able-bodied individuals which allowed for a higher stroke rate with increasing intensity ($p = 0.02$) and a drive to recovery ratio of 1.13. It was also noted that as workload increased, able-bodied rowers increased foot force with $p < 0.01$, whereas FES-rowers had a constant foot force of about 20% BW with $p = 0.15$ despite the increased load. The findings were similar in upper body peak handle force which had increased for both groups where $p < 0.01$ (Draghici, 2017). The lower extremity total ASIA scores changed from 137.94 ± 16.22 to 147.24 ± 16.83, the motor and sensory part of the ASIA test were also higher following cycling training with a statistically significant difference at $p < 0.05$ (Griffin, 2009).

Discussion:

This study determines whether administration of electrical stimulation is an improvement to the sedentary life of SCI patients by encouraging exercise of unused muscles to yield therapeutic benefits. The variance in the answer to this question can be attributed to the difference in training regimes, those which employed a longer duration in training along with greater intensity found a more positive outcome at the end of the study. Taylor et al. (2011) found that there was a positive relationship between the duration of training and an increase in aerobic capacity reaching normal values as those of able-bodied individuals. A likely reason why stimulation of electricity to unused muscles yielded significant results is a possible use of alternative routes that remained intact after the injury, this constant repetitive stimulation may have strengthened these pathways and allowed for partial recovery (Griffin, 2009). Previous studies have suggested the use of passive exercise to stimulate neuroplasticity caudal to the injury, whereas actively exercising promotes plasticity both rostral and caudal to the injury (Taylor, 2011).

The use of larger electrodes in a study conducted by Carty et al. (2012) using neuromuscular electrical stimulation may have stimulated a larger proportion of muscle tissue, this allows for simultaneous stimulation of different groups of muscles producing more metabolic demand. This may be accountable for why application of FES showed varying results between SCI subjects and able-bodied individuals, the use of FES electrodes was of smaller size and restricted to stimulating only the quadriceps and hamstrings. The use of neuromuscular electrical stimulation improved skeletal muscle oxidative capacity which caused a corresponding increase in muscle contractions at the end of training (Erickson, 2017). However, there was a lack of change in muscle composition and no improvement was seen in metabolic and lipid profiles possibly because of the low frequency used to elicit contractions. The level of ease of the training procedure played a role in compliance of exercising. FES training was time consuming which may have reduced compliance and overall reduction in the duration of training which may have hindered the progressive improvement. Training with acute bouts of FES cycling limited to twice a week resulted in delayed onset muscle fatigue which lasted 48-72 hours after cycling, this may be a way to avoid muscle damage with repetitive bouts of stimulation (Gorgey, 2014).

An increase in muscle thickness implies there has been protein synthesis due to muscle training causing hypertrophy of the muscle groups involved after repetitive contractility. The increase in muscle work and power may be due to the increase in lean muscle mass post-training. Although there is alteration in the muscle composition, it may not reach levels of able-bodied subjects due to muscle disuse atrophy, increased intramuscular fat, and changes in muscle architecture and fiber type after SCI which may not be sufficient to produce maximal work (Berry, 2008). Another cause for variation may be the disorderly manner the axons are recruited through transcutaneous stimulation. Although disorganized, an increase in motor unit recruitment is suggested to be the cause of an increase in peak oxygen consumption post-training through actin-myosin cycling attachments (Gorgey, 2014). The recruitment of muscle fibers is done through electric stimulation rather than physiologically, and FES uses a higher frequency in comparison to that of physiological activation which is possibly the cause of quicker muscle fatigue and faster ATP and oxygen consumption (Draghici, 2017). Lastly, the major type of muscle fibers is Type IIx, which is fast and fatigable, but after training there is improvement in endurance possibly due to a transformation of muscle fibers into Type I fatigue-resistant type (Berry, 2008). SCI patients are more prone to fatigue as they have more fast twitch fibers. On the other hand, able-bodied subjects recruited less fatigable slow twitch fibers when switching from CFT to VFT pattern (Deley, 2015). This explains why there was significant fatigue and a reduction in torque in SCI subjects between the first and last contractions.

Current research looking at motor unit recruitment changes as a function of stimulation frequency found that VFT reduced fatigue, this allowed subjects to exercise for a longer time and with greater intensity than training with CFT (Deley, 2015). Applying electrical stimulation causes the muscle fibers in that region to experience fatigue with continuous contractile activity with a decrease in force production. When there are changes in the intensity and frequency of stimulation, this allows new muscle fibers to depolarize at different locations from the site of the electrode and explains why VFT reduced fatigue. Deley et al. (2015) suggested that using a VFT pattern lowers the metabolic cost of contractions, which increases the work that can be produced before fatigue. This is due to the first pulse causing the muscle to stretch, and when a second pulse is administered it causes a force response that is much greater with successive pulses. This explains why starting with the VFT pattern resulted with a higher total number of contractions in a session.

Although the studies analyzed for this review did not show any significant alteration in bone mineral density post-training despite seeing an increase in lean muscle mass, previous studies with training regimes with a longer duration and more intense protocol saw a significant increase in bone density. Insufficient evidence may be tested with a modified procedure since muscle volume in SCI patients generally correlates with bone mineral content and cortical bone volume (Griffin, 2009). Also, a study conducting FES walking saw a reduction in urinary hydroxyproline/ creatine ratio which signifies bone loss. Improvement in bone density requires 150% bone weight loading or substantial axial loading onto the long bones. Draghici et al. (2017) found that in a hybrid FES-rowing training, there was low force generated by the lower body preventing enough loading of the legs which may have limited improvement in bone formation. Deley et al. (2017) however did find an increase in bone mineral density after 12 months of FES rowing, this may be due to a more intense training procedure with increased bone loading and a longer duration. Perret et al. (2010) found that there is higher physical and caloric demand doing FES-rowing in comparison to FES-cycling suggested by a higher peak oxygen consumption value.

Both glucose and insulin levels decreased post-training due to increased expression of glucose transporter-4 and enzymes involved in glucose clearance along with a reduction in TNF-α, which is linked to insulin resistance and type 2 diabetes (Griffin, 2009). D-I Kim et al. (2014) suggest improvements in insulin sensitivity and glucose tolerance due to reduction in percent body fat and an increase in lean mass. A shift to insulin sensitive type I and type IIa fibers and reduced type IIb fibers was also seen after training in FES cycling. Improvement in plasma lipids were not observed in a study conducted by Griffin et al. (2009), however, this may be due to subjects already having lipid profiles in the normal rang at the onset of the study. Also, HDL levels were shown to have been reduced after training and may be due to variation in patient genetics or diet.

Markers of inflammation, such as CRP, IL-6, and TNF-α, are associated with atherosclerotic plaques and heart disease, and those who maintain a physically active lifestyle have a reduction in inflammation. The use of FES allows for SCI patients to be more physically active, Griffin et al. (2009) found a reduction in inflammatory markers after FES training which reduces cardiovascular disease in these patients. The use of hybrid FES training, involving both the upper arms and the FES stimulated legs, using large muscle groups and increased stress allows for a greater forward flow of blood from the skeletal muscle back to the heart (Taylor, 2011). Since the legs are not innervated, there is no sympathetic vasoconstriction in the inactive legs. Instead, with the training regime there is an increase in active muscle mass which acts as a venous muscle pump to promote return of blood back to the heart. This improves power output and oxygen consumption through an increase in cardiac output and systemic flow and oxygen extraction from the active muscle.

Current research shows SCI patients have cardiac structure and function comparable to the lower values obtained from non-SCI subjects. As these patients trained with FES-rowing, their cardiac structure and function underwent adaptation and remodeling to resemble reported values for non-SCI patients (Gibbons, 2016). Actively exercising causes an increase in muscle mass in these subjects and simultaneously increases volume loading of the heart, this increases both stroke volume and cardiac output. The smaller left ventricular chamber size seen in FES-untrained subjects may be due to the insufficient muscle pump in the leg causing blood pooling and reduced blood volume going back to the heart. Also, the higher levels of RWTd seen in FES-untrained individuals may imply there is cardiac hypertrophy secondary to circulatory hypertension.

Able-bodied patients were found to have low oxy-Hb values throughout the exercise, this may be due to muscle compression of the blood vessels limiting the blood flow into the actively exercising muscle. SCI patients had a low oxygen saturation and high levels of deoxy-Hb at the onset of exercising, this may be the result of the absence of central command which regulates exercise induced changes in circulation to maintain proper oxygenation (Muraki, 2007). This suggests SCI patients have a delay in aerobic metabolism and primarily depend on anaerobic metabolism, this is supported by a greater increase in blood lactate concentrations. After 10 weeks of training, along with an increase in muscle oxygenation was an increase in type I fiber, citrate synthase levels, and capillary to fiber ratio. Muraki et al. (2007) also suggested fatigue inducing metabolites or prolonged exercise induced vasodilation improving muscle oxygenation and increased levels of oxy-Hb. It was also suggested that the reduced oxygen saturation may be implying FES exercise is highly intense requiring more oxygen extraction by the SCI subjects, this can be compared to able-bodied subjects performing a prolonged and highly intense exercise.

Limitations:

Future research needs to conduct studies on subjects with consistent spinal cord injuries. A limitation in this study was the extensive range of the level of spinal cord damage. After SCI, patients muscle architecture changes differently and it is difficult to control for all these aspects when choosing subjects for the focus on SCI rehabilitation. An additional factor is the difference in manifestations depending on injuries occurring at C-Spine, T-Spine, or L-Spine. Another limitation found in this study was lack of compliance with the training procedure which reduced the adequacy of the exercising regime. Even after training, patients were not guaranteed to improve in the same manner, and multiple factors contributed to how effective the therapy would be. The study protocol only lasted for a few months which limited seeing how sufficient the FES induced exercising would benefit a patient long term. The size of the electrodes used for FES did not stimulate a lot of muscle groups and this may have limited the peak level of exercising possible.

There is need for future research on this topic since it can help the SCI population in enhancing their overall wellbeing, and a change from a sedentary lifestyle to incorporating regular physical activity. Future research should look at more intense hybrid exercising regimes which will increase the force used by the lower body to enhance bone health in SCI patients. Further studies exploring rehabilitation techniques should use equipment which will be easier to handle to increase the compliance of training and yield more accurate results which is more representative of the employed therapy. Lastly, future work can monitor how longer duration of training and less frequency of training can prevent overuse muscle damage, which may hinder rehabilitation, and positively alter the progressive outcomes revealed by current research.

The chosen primary literature used in the analysis of this study strengthens the hypothesis that was being tested. The studies found evidence to correlate with one another which supported the claims of the hypothesis being looked at. Data which were skewed or opposed the main findings gave supporting evidence to prove this was due to a weak point in the conducted study, or rather due to a more developed procedure which allows room for improvement in future research. Overall, these publications impacted the research question by providing supportive evidence needed to confirm that the findings in current research proved the positive benefits of this type of therapy.

Conclusion:

The use of FES induced exercising was found to improve the health of SCI patients living an inactive life. Progressive exercising allowed the muscle composition and architecture to transform to be more like normal muscle. Improvements in strength, metabolic functioning like glucose metabolism, cardiorespiratory functioning, and bone mineral density were some of the few changes seen post-training. Although levels reached by SCI individuals were not as high as those achieved by able-bodied subjects, there is room to enhance the training procedure in future research which can address the areas of weakness in the current studies. Using electrical stimulation was found to enhance the health benefits of SCI patients by improving oxygen consumption and muscle oxygenation over the training period. The positive outcomes found from recent literature may promote the use of this therapy to help these patients over time, and eventually regain use of their paralyzed limbs. Although current stages of research are showing improvement after these interventions are applied for a temporary period, recovery is still not complete, and more understanding is necessary to progress in the use of this therapy.

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