A The effects of a neuromuscular electrical stimulation training intervention on physiological measures in a spinal cord injured male: a case study

Mc Cormack K,¹ Carty A,^{1, 2} Coughlan GF,¹ Crowe LM,¹ Caulfield BM¹

¹ Stim XDP Research Group, Institute for Sport and Health, Newstead, University College Dublin, Belfield, Dublin 4, Ireland ² Physiotherapy Department, National Rehabilitation Hospital, Dun Laoghaire, Co. Dublin, Ireland.

12 ABSTRACT

2 3

4 5

6 7

8

9 10 11

13 Background: People with spinal cord injury (SCI) are exposed to the development of comorbidities secondary 14 to a decreased ability to exercise and pathological complications. Aerobic exercise has been advocated as a 15 means of preventing the development of these illnesses. Previous research has indicated that functional electrical 16 stimulation (FES) provides an appropriate aerobic stimulus in an SCI population to provide cardiovascular 17 fitness gains. However, FES devices are time consuming for both clients and medical staff in a rehabilitation 18 and home setting with devices often expensive. Our research group have developed a novel neuromuscular 19 electrical stimulation (NMES) system which may provide an alternative to FES and elicit a similar response. 20 Methods: A 40 year old male with a T6 incomplete SCI, undertook 6 weeks of NMES training for one hour, 21 five days per week. Pre and post intervention measures include a treadmill VO2 peak test, a DXA scan and 22 subjective feedback regarding the NMES device and training stimulus.

Results: Improvements in VO2 peak, heart rate and exercise tolerance were observed with minor decreases in total body fat mass. The participant reported that the NMES was an acceptable form of cardiovascular training.
 Conclusion: Our pilot case study has indicated that our NMES system is capable of eliciting an aerobic training effect in people with SCI, which could potentially improve their cardiovascular fitness. Further study with a greater number of participants is warranted in this population using a similar training program.

29
 30
 Keywords: Spinal Cord Injury, Neuromuscular Electrical Stimulation, Aerobic Capacity

Correspondence to: Dr Garrett Coughlan Email: garrett.coughlan@ucd.ie
 32

34 INTRODUCTION

33

35 The spinal cord serves as a bidirectional channel between the 36 brain and its motor, sensory and autonomic targets, allowing 37 the brain to communicate effectively with the rest of the body 38 resulting in healthy, normal human functioning.^{1, 2} A spinal 39 cord injury (SCI) occurs following an insult which disrupts the 40 spinal cord's conveyance of impulses and can be caused by 41 either a crushing, compressing or stretching insult to the cord 42 within the vertebral canal. 84% of SCI are as result of 43 trauma,³ including motor vehicle accidents (36–48%), violence 44 (5-29%), falls (17-21%), and recreational activities (7-16%),⁴ 45 whilst 16% of SCI are owing to non-traumatic causes,³ e.g. 46 tumours, infections, toxins, congenital and developmental 47 disorders, and results in temporary or permanent loss of 48 motor, sensory and autonomic control.³ The gravity of resultant 49 dysfunction will depend on the extent of injury to a particular 50 level of the cord as each level is responsible for a unique 51 bodily function. 52 Approximately, 13.1 per one million Irish people are 53 affected by SCI annually, and 50% of these injuries are due to 54 motor vehicle accidents.⁵ Following injury, those affected 55 experience significant changes in their physical, psychological

and social capacity. This includes their ability to engage and
profit from exercise due to muscle mass paralysis, sympathetic
autonomic impairment and decreased venous return.⁶
Considerable physical deconditioning generally results from

the effects of a SCI and contributes to secondary comorbidities

such as cardiovascular (CV) disease, reduced bone mineral density (BMD), increases in body fat and decreases in lean body tissue.⁷⁻⁹ Exercise attenuates the development of these comorbidities amongst those with SCI, highlighting the importance of making it routine for those affected.¹⁰ Employing exercise as part of daily activity may be hampered by reduced accessibility owing to a loss or impairment of functional movement and lack of wheelchair friendly sports facilities.¹⁰ Quadriplegics and paraplegics are also generally restricted to upper extremity exercise which are less effective than lower extremity exercise in generating the CV stress required to experience gains in fitness, whilst also predisposing them to greater risk of developing upper limb over-use injuries. The exercise difficulties surrounding this pathology can decrease this population's ability to perform daily activities, as well as increases their risk of developing medical complications is well supported by the literature.¹¹⁻¹³ Collectively, these concerns have evoked clients, clinicians and researchers to call for exercise initiatives for the paralysed lower limbs.

One such treatment, neuromuscular electrical stimulation (NMES), has been employed to train the paralysed muscles of individuals with SCI whereby an electric current, managed by an external controller, is applied to the skin over muscle to evoke an action potential in the nerve fibre in order to stimulate a muscle contraction similar to that of a cortically induced contraction. This technology, known as functional

electrical stimulation (FES), has been used since the 1960's as 2 an exercise tool for the paralysed muscles of individuals with 3 SCI.¹⁴ This exercise modality harnesses the original technique of NMES and applies it in a functional manner to evoke a 4 5 muscle contraction producing an otherwise unattainable dynamic movement. Examples include FES assisted cycling, 6 rowing, standing and stepping and studies in these areas, 7 although largely of low quality due to a lack of randomised 8 controlled trials, demonstrate that FES induced exercise is 9 10 capable of eliciting and maintaining CV fitness in this 11 population with 10-70% increases in VO₂ peak being reported.¹⁵⁻¹⁸ Despite these favourable trends, the improper 12 13 facilitation of correct muscle contractions during FES - leg 14 cycle ergometry (FES-LCE) has been reported to be a possible 15 reason for these metabolic increases.¹⁶⁻¹⁸ Therefore the true 16 efficacy of this intervention to improve fitness is inconclusive. 17 Added to this, FES induced exercise is hindered by the need 18 for expensive equipment which is cumbersome and assistance 19 of trained staff to operate them, therefore limiting its 20 application for home use for those with SCI.¹⁹ Whilst the 21 arrival of FES technology is encouraging for those with SCI, 22 the obstacles to training highlighted in the literature clearly 23 demonstrate that it is still far from the optimal type of training 24 for clients and clinicians. 25 In response to the evident limitations of FES based exercise, 26 we have developed a new method of using NMES technology 27 which could potentially evolve exercise opportunities for this 28 population in need of such fitness innovation. This novel 29 system develops previous FES induced exercise as it causes an 30 exercise response within users without loading the limbs or 31 joints or requiring external work.²⁰ It evokes rapid, rhythmical 32 NMES induced muscle contractions that mimics shivering, 33 causing a subsequent demand for oxygen in the large lower 34 limb muscles.²⁰ This physiological response is similar to that 35 achieved during physical exercise.²¹ In an earlier study which 36 explored the effects submaximal stimulation has on healthy 37 adults, the system triggered significant increases in VO2, heart 38 rate (HR) and minute ventilation which were comparable to 39 levels expected during light to moderate voluntary exercise.²² 40 Furthermore, physical fitness improved in sedentary adults 41 after 6 weeks of training with this system as recorded by 42 significant increases in VO2 peak, 6-minute walk test and quadriceps strength.²⁰ Additionally, this type of stimulation has 43 44 shown improvements in the same fitness parameters in people 45 with stable chronic heart failure (CHF).²³ This research 46 highlights the possibility that people with SCI, who also have 47 reduced CV fitness similar to that of sedentary adults and those 48 with CHF, could potentially benefit from NMES. Furthermore, 49 with the knowledge that improving CV fitness is necessary to 50 prevent the development of comorbidities and that new 51 exercise ingenuity is required to incorporate the lower limb 52 musculature and increase CV stress, further investigation into 53 the effects of this system is warranted. Therefore the objective 54 of this investigation was to evaluate if our novel NMES system 55 could improve the CV fitness in an SCI population. 56

57 METHODS

58 Design of study

59 This study was a pilot case study and was approved by the60 local university ethics committee.

В

Participant A 40 year old male, (height: 1.80 metres (m), weight: 83.3 kilograms (kg), Body Mass Index (BMI): 24.7 kg/m², SCI level: T6 incomplete, 5 years post injury), volunteered to participate in the study. Following an introductory session with the NMES device he read a participant information leaflet and gave written informed consent.

Aerobic Capacity

Following a review of the literature a protocol was designed and piloted by the research team to measure the participants VO₂ and HR peak response during an incremental treadmill test. This test was conducted both pre and post the intervention period. Aerobic capacity was evaluated using cardiopulmonary gas exchange analysis. The participant wore a facemask attached to a gas analysis system (Quark b², Cosmed, Rome, Italy) to measure oxygen and carbon dioxide concentration and volume. HR was also recorded throughout the test using a chest strap embedded with electrodes (Polar, Tampere, Finland) and synchronized with the gas analysis system. The protocol initially involved the establishment of the participant's baseline regular pushing speed whilst propelling on a treadmill (HP Cosmos Venus 200/100R, Germany). This baseline speed was ascertained by the participant as their normal everyday pushing speed were they outside'. A 3 minute warm-up at this speed at a 2% gradient was then conducted. Following a short break to apply the facemask, the initial test stage was 0.5 kmh-1 below the baseline regular pushing speed for a 1 minute duration. The speed was increased by 0.5 kmh⁻¹ for each additional 1 minute stage there after while gradient remained constant. Average HR and oxygen measurements were taken for the last 30 seconds of each stage. When VO₂ peak was reached i.e. when volitional exhaustion occurred, the treadmill test was immediately terminated by one of the investigators.

Bone mineral density and body composition

The Dual Energy X-ray Absorptiometry technique (DXA) (Lunar, DXA, GE Healthcare, USA) was used to evaluate BMD pre and post the intervention period using a DXA scanner. The DXA was used owing to its availability, reproducibility and good overall accuracy (5-8%).²⁴ Prior to each image the DXA machine was calibrated. Body Composition (BC) variables including total body fat percentage (TBF%), total body fat mass (TBFM) and total lean body tissue mass (TLBM) were also evaluated using this technique as DXA scanning has been reported to offer a reliable method of determining these components.^{25,26}

Subjective feedback

The participant filled out a modified version of the Perceived Discomfort in Running Scale (Tenenbaum et al, 1999) to help ascertain the extent of discomfort he experienced during NMES training. This scale lists 32 symptoms grouped into eight dimensions and it was originally designed to give to runners immediately after running a distance of between 2 km and 42 km to rate the level of perceived discomfort during running conditions. The 8 valid dimensions include: Proprioceptive symptoms (ten items, score range 10–50), leg symptoms (six items, range 6–30), respiratory difficulties (four

items, range 4-20), disorientation (two items, range 2-10), dryness and heat (two items, range 2–10), task completion 2 thoughts (three items, range 3-15), mental toughness (two 3 items, range 2–10), and head/stomach symptoms (three 4 items, range 3–15). Participants rate how intensely they felt 5 each of the symptoms on a 5-point Likert-type scale ranging 6 from '1' (not at all) to '5' (extremely). The score of each of the 7 eight discomfort symptoms is determined by the summation of 8 all items within each dimension. The higher the score, the 0 10 more the symptom is felt during performance of the task. It is 11 recognised that NMES training is not directly comparable to 12 running, however, this questionnaire was chosen to measure 13 NMES training discomfort due to the absence of similar 14 questionnaires specific to this type of exercise. Furthermore, 15 Tenenbaum and colleagues discuss this questionnaire as being 16 suitable for measuring discomfort in a population performing 17 aerobic exercise and therefore it was felt that this tool would 18 be able to detect levels of discomfort in our version of aerobic 19 training with NMES.²⁷ The questionnaire was modified slightly 20 by removing any reference to the activity of running. In place 21 of such references, the word, "task" was used instead. The 22 participant was also asked a number of open ended questions 23 regarding his overall training with the NMES unit to gain 24 further insight into his experience with this type of stimulation. 25

26 NMES training protocol

30 31 32

43

53

54 55

56

57

58

59

60

27 The participant undertook a familiarisation session where he 28 learnt how to apply the system independently. He had no 29 previous experience with NMES or FES modalities. Four

Figure 1. Setup of the NMES electrodes

adhesive electrodes each 175 cm², in size were applied bilaterally to the proximal and distal quadriceps and hamstrings. The electrodes were applied to the body using a neoprene garment that was wrapped around the leg and secured to the thigh with a velcro strap (Figure 1). A specially designed hand held NMES stimulator (NT2010, BioMedical Research Ltd, Galway, Ireland) delivered a series of four complex pulses at an overall series frequency of 5 Hz was used to deliver the stimulation. The participant trained at home with the system for one hour five times a week for 6 weeks at his maximum tolerable NMES intensity (120 milliamps (mA)) in his position of choice (long sitting). He received weekly phone calls from the lead investigator to monitor his training response and compliance.

RESULTS

Aerobic capacity, bone mineral density and body composition The participant completed the 6 week training intervention completing a total of 30 sessions. Pre and post test measures revealed improvement in peak VO₂, HR and exercise tolerance (Table 1). The test duration and speed in the post test also increased. Furthermore, minor decreases in TBFM were detected, as well as increases in LBM post intervention (Table 2)

Table 1. Differences in peak VO2, HR, maximum propulsion	
speed and duration of exercise pre and post intervention.	

	Pre	Post
Peak VO2 (ml/min/kg)	16.88	27.94
Peak HR (bpm)	161	173
Max propulsion speed (kmh-1)	7.3	7.8
Duration of exercise (min:sec)	15:08	16:30

Table 2. Differences in BMD, BMI, total % BF, total BFM and total LBM pre and post intervention.

		BMD	BMI	Total BF %	Total BFM (kg)	Total LBM (kg)
F	Pre	1.20	24.7	28.6	23.96	56.83
F	Post	1.28	24.7	27.7	23.07	57.26

BMD = Bone Mineral Density, BMI = Body Mass Index, BF = Body Fat, BFM = Body fat Mass, LBM = Lean Body Tissue Mass

Subjective feedback

Based upon the subjective feedback given by the participant, he had a positive experience with this version of NMES training. He reported that training with the unit 5 times a week was achievable and that he preferred to do so just before going to sleep at night as the training would normally leave

Table 3: Results of the eight dimensions of the modified perceived discomfort in running scale.

ว			
3	Dimensions	Score	Total Possible Score
4 5	Proprioceptive symptoms	12	50
6			
7 8	Leg symptoms	11	30
9	Respiratory difficulties	8	20
10			10
11	Dissorientation	2	10
13	Dryness and heat	4	10
14			
15	Task completion	6	15
16	—		
1/	Mental toughness	5	10
18	Hend and determined a markened	2	15
20	neda ana siomach symptoms	3	15
21	How demanding was the task?	2	5
22			5
23	How much suffering did you experience?	1	5
24			
25	Overall score	54	170
26			
27			

28 him feeling extremely fatigued. The participant reported 29 feeling an increase in HR and shortness of breath whilst 30 31 training at his maximal tolerable intensity of 120 mA. 32 Furthermore, the participant was impressed with the increase in lower limb circulation and temperature which occurred 33 immediately post a bout of NMES training. Results of the 34 modified perceived running discomfort questionnaire are 35 outlined in Table 3. 36 37

38 DISCUSSION

39 The primary finding of this pilot case study demonstrates that a
40 6 week NMES training intervention can improve aerobic
41 capacity in a SCI male. Secondary findings included

42 alterations in BC. Subjective feedback from the participant

43 indicated that this form of training is acceptable to people with
44 SCI as an exercise tool.
45

46 Aerobic capacity

47 Peak VO₂ is an index of exercise capacity and its increase 48 illustrates that the participant's exercise tolerance following the 49 NMES training intervention improved.²⁸ This result is further 50 supported by the increase in test time duration and propulsion 51 speed which was observed in the post intervention peak VO2 52 test. In agreement with other studies which have previously 53 examined the effects of lower limb FES, improvements in 54 aerobic capacity have ranged from 10% to 70% 55 improvements in peak VO2.¹⁵⁻¹⁷ Reasons for the improvements

in VO₂ peak are of a multiple nature. De Carvahlo et al
 (2006) propose that the increased muscle contractions

57 (2006) propose that the increased muscle contractions
 58 guament oxygen delivery rate to the musculature by increasing

58 augment oxygen delivery rate to the musculature by increasing 59 stroke volume, blood pressure and cardiac output ¹⁹

59 stroke volume, blood pressure and cardiac output.¹⁹

60 Furthermore, researchers suggest that the paralysed muscles

which are externally contracted will extort more oxygen, thus enhancing VO₂ peak.^{19, 28} Additional peripheral mechanisms have been discussed such as those by Krauss and colleagues whereby increased VO₂ peak post FES-LCE was proposed to be due to increased muscle metabolism.²⁹ Research by Martin and colleagues complements this theory whereby the group found that after 24 weeks of NMES, muscle oxidative capacity increased in alliance with an escalation in type 1 fibres and capillarisation.³⁰ Krauss et al also discuss central adaptations following bouts of NMES training as being responsible for improvements in VO₂ peak due to the resultant increased oxygen consumption for a given HR which was observed after a period of FES- LCE training.²⁹ The reason for this effect was placed on the increased venous return elicited by LCE which caused an increased cardiac output and blood flow to the exercising muscle.

Although physiological changes following the use of FES-LCE are encouraging, it is important to note that studies incorporating this exercise technique have many limitations including the requirement to engage the lower limbs in external work, the need to improve the biomechanics of the limbs whilst engaging in this type of exercise, its need for cumbersome and expensive equipment and the need for training in the system's operation.¹⁹ Conversely, this NMES system, which achieved a 65% improvement in VO₂ peak in a participant similar to those in the previously discussed FES studies, overcomes these issues as it is a relatively smaller and cheaper unit to that of FES-LCE, thus aiding its ease in introducing it into a person's home exercise regime. Furthermore, it does not require extensive training in its operation, can be easily applied by the individual and can be used in a position of comfort at any time of the day. Added to

the improved aerobic fitness of our participant, these features
 highlight the potential value of this enhanced version of
 NMES training and allude to its potential use over current
 methods.
 Further acute measurements on this participant using the

same parameters as the intervention period revealed that 6 when training at maximal current amplitude (200 mA), he 7 achieved a VO2 peak of 12.88 ml/min/kg and a HR peak of 8 97 bpm and at his training current amplitude of 120 mA a 9 10 V02 peak of 10.32 ml/min/kg and a HR peak of 83 bpm 11 was achieved. These values are akin to those experienced 12 during arm cranking, basketball shooting and vigorous 13 household chores,³¹ and indicate the capacity of the stimulator 14 to induce training at high levels of aerobic intensity despite 15 only stimulating the lower limb. Higher VO₂ and HR values 16 during the incremental treadmill test were due to the additional 17 energy demand required with upper body movement to 18 propel the wheelchair and greater levels of required venous 19 return.

21 Bone mineral density and body composition

20

22 Body composition measurements of increased LBM and 23 concurrent decreased BF post NMES training are encouraging 24 and suggest that our NMES system can have a positive effect 25 on the body composition of people with SCI who are often 26 subject to increases in BF and the development of muscle 27 atrophy.^{32, 33} Maintaining LBM is difficult for people with SCI 28 and the loss of muscle function can have a detrimental effect 29 on BMD as muscle contraction and loading are required to 30 stimulate bone formation.¹³ Research has stated that paralysed 31 muscle is still capable of adapting and this has been exhibited 32 where NMES has improved torque output and fatigue 33 resistance in paralysed muscle via overloading the muscle.¹³ 34 Similar to our study, reports based on MRI imaging have 35 shown 12% increases in LBM and relative decreases in BF 36 following one year of FES-LCE training.^{35, 36} Furthermore, 37 Pacy et al demonstrated large improvements in quadriceps 38 muscle mass following resistance training. Although the 39 changes in muscle composition are relatively small, it is 40 noteworthy that in spite of not including resistance training, 41 this NMES system still accomplished increases in muscle mass 42 over a reasonably short duration of training.³⁶ Our 6 week 43 NMES training programme resulted in no changes in BMD and 44 we propose that the short intervention period may be reason 45 for this. Earlier research by Dudley-Javoroski and Shields 46 which resulted in 31% increases in distal tibial trabecular 47 BMD of trained limbs in people with SCI included participants 48 training with NMES for 3 years.¹³ Similarly, nearly 30% of 49 bone lost following SCI was recovered after 24 weeks of 50 quadriceps stimulation.³⁸ Bloomfield and colleagues detected 51 an 18% increase in distal BMD following 3 months of FES-LCE 52 in a subset of individuals with SCI who trained at a high power 53 output of 18 watts.⁸ This research group's total training group 54 of participants with SCI however did exhibit a statistically 55 significant improvement in their lumbar spine BMD following 9 56 months of training with a corresponding 78% increase in 57 serum osteocalcin (a marker of bone formation).⁸ To assess if 58 comparable results can be achieved with our NMES system, it 59 is suggested that future studies should include a longer 60 intervention training period.

Subjective feedback

The total score from the modified version of the Perceived Discomfort in Running Scale equated to 54/170 indicating that the participant did not feel a significant level of discomfort with the NMES training. The participant reported that the training task was slightly demanding and that he felt an increased HR and a slight shortness of breath whilst using the NMES unit. He also reported feeling moderately fatigued after training. These reports are thought to be due to the effect of the exercise itself. In response to all the other symptoms, the participant did not experience them at all during episodes of training. This result encourages us that this NMES training device is one which people with SCI will be satisfied with in terms of comfort of training and that adverse effects of such training are minimal. During the open-ended questioning, our participant also reported that he would recommend this type of training to other people with SCI and that he found the training to be feasible and worthwhile.

CONCLUSION

This pilot case study has indicated that this type of NMES system is capable of eliciting an aerobic training effect in people with SCI which could potentially improve their overall CV fitness and strength. This could prove to be a beneficial method of offsetting a range of comorbidities of SCI such as CV disease and diabetes, whilst also advancing on existing NMES technology. The novelty of this NMES system is that it creates an exercise response without loading the limbs or joints or requiring external work, coupled with the ease of its application. It could provide people with SCI with a much needed exercise tool incorporating exercise of the lower limb musculature. This work is only a single case study, which limits the extent to which conclusions can be drawn, however it is suggested that the system used in this case study should be evaluated in a study with a larger number of participants to establish its efficacy in a broader SCI population.

ACKNOWLEDGEMENTS

This research is supported by Enterprise Ireland and BioMedical Research Ltd under an Enterprise Ireland Innovation Partnership Project. The authors would like to thank the participant for his involvement with this study.

REFERENCES:

- 1. Fox S. Human Physiology: 10th ed. London: McGraw Hill; 2008.
- Maynard JFM, Bracken MB, Creasey G, Ditunno JJF, Donovan WH, Ducker TB, et al. International standards for neurological and functional classification of spinal cord injury. Spinal Cord. 1997;35: 266-74.
- Paddison S, Middleton F. Physical Management in Neurological Rehabilitation. 2nd ed. Elsevier: Netherlands; 2004.
- 4. Alabama TNSSCBUO. Facts and figures at a glance. 1999.
- O'Connor R, Murray P. Review of Spinal Cord Injuries in Ireland. Spinal Cord. 2006;44: 445-8.
- de Carvalho DC, de Cassia Zanchetta M, Sereni JM, Cliquet A. Metabolic and cardiorespiratory responses of tetraplegic subjects during treadmill walking using neuromuscular electrical stimulation and partial body weight support. Spinal Cord. 2005;43: 400-5.
- 7. Hjletnes N, Janssen TW. Physical endurance capacity, functional status and medical complications in spinal cord subjects with

1	lonastandina lesions Paraplegia 1990-28: 428-32	exercise canacity in natients with stable chronic heart failure
2	8. Bloomfield S. Mysiw M. Jackson R. Bone mass and endocrine	Card Fail, 2009:15: 319-26.
3	adaptations to training in spinal cord injured individuals. Bone.	24. Hodgson S, Johnston C, Avioli L, Heath H, Khosla S, Kleerekoper
4	1996;19: 61-8.	M, et al. AACE Clinical practise guidelines for the prevention and
5	9. Bostom A, Toner M, McArdle W, al e. Lipid and lipoprotein	treatment of postmenopausal osteoporosis. AACE. 2001.
6	profiles relate to peak aerobic power in spinal cord injured men.	25. Kohrt WM. Preliminary evidence that DEXA provides an accurate
7	Med Sci sports and Exerc. 1991;23: 409-14.	assessment of body composition. J Appl Physiol. 1998;84: 372-7.
8	10. Jacobs P, Nash MS. Exercise recommendations for individuals	26. Mazess R, Barden H, Bisek J, Hanson J. Dual-energy x-ray
9	with spinal cord injury. Sports Med. 2004;34: 727-51.	absorptiometry for total-body and regional bone- mineral and soft-
10	11. Durstine JL, Moore GE. ACSM's Exercise Management for	tissue composition. Am J Clinical Nutrition. 1990;51: 1106-12.
10	Persons with Chronic Diseases and Disabilities. 3rd. Human	27. Tenenbaum G, Fogarty G, Stewart E, Calcagnini N, Kirker B,
12	Kinetics; 2009.	Ihorn G, Christensen S.
14	12. van den Berg-Emons RJ, Bussmann JB, Haisma JA, Sluis IA, van	Percieved discomfort in running: Scale development and theoretical
15	der vvoude Ln, Bergen Mr, et al. A prospective study on physical	considerations. Journal of Sports Sciences. 1999;17: 183-90.
16	rehabilitation and the year after discharge. Arch Phys Med	Levine T, et al. Cardiac transplantation, Task force 3, Recipient
17	Rehabil 2008-89: 2094-101	auidelines/prioritisation 24th Bethesda Conference: Cardiac
18	13. Dudlev-lavoroski S. Shields R. Muscle and bone plasticity after	transplantation: I AM Coll Cardiol: 1993, 21-31.
19	spinal cord injury: Review of adaptations to disuse and electrical	29. Krauss JC, Robergs RA, Depaepe JL, Kopriva LM, Aisenbury JA,
20	muscle stimulation. Journal of Rehabil Res Dev. 2008;45: 283-96.	Anderson MA et al. Effects of electrical stimulation and upper
21	14. Davis GM, Hamzaid NA, Fornusek C. Cardiorespiratory,	body training after spinal cord injury. Med Sci Sports Exerc.
22	metabolic, and biomechanical responses during functional	1993;25: 1054-61.
23	electrical stimulation leg exercise: health and fitness benefits. Artif	30. Martin D, Al E. Muscle and bone in paraplegic patients and the
24	Organs. 2008;32: 625-9.	effects of functional electrical stimulation. Clinical Science,
25	15. Hooker SP, Figoni SF, Rodgers MM, Glaser RM, Mathews T,	1988;75: 481-7.
26	Suryaprasad AG, et al. Metabolic and hemodynamic responses	31. Collins E.G, Gater D, Kiratli J, Butler J, Hanson K, Edwin
2/	to concurrent voluntary arm crank and electrical stimulation leg	Langbein W (2010) Energy cost of physical activities in persons
20	cycle exercise in quadriplegics. J Rehabil Res Dev. 1992;29: 1-	with spinal cord injury. MSSE. Epub ahead of print.
27		32. Wheeler GD, Andrews B, Lederer R, Davoodi R, Natho K, Weiss
31	10. There is in the second sec	C, et al. Functional electric stimulation-assisted rowing: increasing
32	valiberg-herrically stimulated log cycling in totraplacic patients. Am I	rowing training in persons with spingl cord injury. Arch Phys Med
33	Physiol Regul Integr Comp Physiol 1997-273: 1072-9	Rebabil 2002:83: 1093-9
34	17. Janssen TW. Pringle DD. Effects of modified electrical stimulation	33. Scelsi R. Marchetti C. Pogai P. Lotta S. Lommi G. Muscle fiber
35	induced leg cycle ergometer training for individuals with spinal	type morphology and distribution in paraplegic patients with
36	cord injury. Journal of Rehabil Res Dev. 2008;45: 819-25.	traumatic cord lesion. Histochemical and ultrastructural aspects of
37	18.Johnston TE, Smith BT, Mulcahey MJ, Betz RR, Lauer RT. A	rectus femoris muscle. Acta Neuropathol. 1982;57: 243-8.
38	randomized controlled trial on the effects of cycling with and	34. Castro M, Apple DJ, Staron R, Campos G, Dudley G. Influence of
39	without electrical stimulation on cardiorespiratory and vascular	complete spinal cord injury on skeletal muscle within 6 months of
40	health in children with spinal cord injury. Arch Phys Med Rehabil.	injury. J Appl Physiol. 1999;86:8.
41	2009;90: 1379-88.	35. Mohr T, Anderson J, Biering-Sorensen F, Galbo H, Bangsbo J,
42	19. DeCarvalho DC, Martins CL, Cardoso SD, Cliquet A.	Wagner A. Long-term adaptation to electrically induced cycle
43 11	Improvement of metabolic and cardiorespiratory responses	fraining in sever spinal cord injured individuals. Spinal Cord.
45	through fredamili gait fraining with neuromuscular electrical	26 Anderson L Mahr T Bigging Serenson E Galha H Kigar M
46	simulation in quadriplegic subjects. Artif Organs. 2000;30: 30-	Muosin heavy chain isoform transformation in single fibers from
47	20 Baneries P. Caulfield B. Crowe I. Clark A. Prolonged electrical	m vastus lateralis in spingl cord injured individuals: effects of
48	muscle stimulation exercise improves strength and gerobic	long-term functional electrical stimulation. Pflugers Arch
49	capacity in healthy sedentary adults. I Appl Physiol. 2005:99:	1996:431:5.
50	2307-11.	37. Pacy PJ, Hesp R, Halliday DA, Katz D, Cameron G, Reeve J.
51	21. Caulfield B, Crowe L, Minogue C, Banerjee P, Clark A. The use of	Muscle and bone in paraplegic patients and the effect of functional
52	electrical muscle stimulation to elicit a cardiovascular exercise	electrical stimulation. Clinical Science. 1988;75: 481-7.
53	response without joing loading: a case study. J Exercise Physiol	
54	Online. 2004;7:4.	
55	22. Banerjee P, Caulfield B, Crowe L, Witte K, Clark A. Electrical	
56	stimulation of unloaded muscles causes cardiovascular exercise	
57	by increasing oxygen demand. Eur J Cardiovasc Prevention	
58	Rehab. 2005;12: 503-8.	
27	23. Banerjee P, Caultield B, Crowe L, Clark AL. Prolonged electrical	
00	muscle stimulation exercise improves strength, peak VO ₂ , and	