

Effects of stimulation pattern on electrical stimulation-induced leg cycling performance

Thomas W. J. Janssen, PhD, FACSM; Maaïke Bakker, MSc; Annick Wyngaert, MSc; Karin (H. L.) Gerrits, PhD; Arnold de Haan, PhD

Institute for Fundamental and Clinical Human Movement Sciences and Faculty of Human Movement Sciences, Vrije Universiteit, Amsterdam, The Netherlands; Rehabilitation Center Amsterdam, Amsterdam, The Netherlands; Institute for Biophysical and Clinical Research into Human Movement, Manchester Metropolitan University, Alsager Campus, United Kingdom

Abstract—Electrical stimulation-induced leg cycling (ES-LC) is beneficial for individuals with spinal cord injury (SCI), but cycling performance is often limited because of rapid fatigue of the stimulated muscles. This study evaluated whether a stimulation pattern with a catchlike-inducing pulse train increased force production and hence cycling performance. Five men with SCI performed ES-LC using different stimulation patterns: (1) the standard pattern with ramp modulation, (2) a pattern with no ramp modulation, (3) a pattern with no ramp modulation but with an initial doublet, and (4) a pattern with a middle doublet. None of the experimental patterns resulted in significantly improved cycling performance compared with the standard pattern. However, during the first 3 min of cycling, the current amplitude was significantly higher with the standard stimulation, suggesting that stimulation with no ramp modulation produces more force at the same submaximal current amplitude. The results do not indicate that stimulation with catchlike-inducing trains with the current parameter settings improves ES-LC performance.

Key words: catchlike property, electrical stimulation, exercise, fatigue, paraplegia, spinal cord injury, tetraplegia.

INTRODUCTION

A spinal cord injury (SCI) leads to loss of motor, sensory, and autonomic functions in those parts of the body

innervated by neural pathways below the level of the lesion. The lower-limb paralysis following SCI leads to a number of adaptations in the musculoskeletal system [1–2], as well as in blood circulation [3] and physical capacity [4]. The problems that arise from the injury may be counteracted by exercise (or training) of the muscles of the paralyzed lower limbs. Electrical stimulation-induced leg cycling (ES-LC) can induce exercise of these muscles. ES-LC has been shown to increase muscle mass and to activate the muscle pump, which enhances blood circulation during cycling. If the amount of activated muscle mass is sufficient, an increased level of cardiovascular fitness may even result (for a review, see Janssen et al [5]).

Abbreviations: ES-LC = electrical stimulation-induced leg cycling, ID = initial doublet, NR = no ramp (modulation), R = ramp (modulation), SCI = spinal cord injury.

This material was based on work partially supported by the Duyvensz Nagel Stichting and Rehabilitation Center Amsterdam, both of Amsterdam, The Netherlands.

Address all correspondence to Thomas W.J. Janssen, PhD, FACSM; Faculty of Human Movement Sciences, Vrije Universiteit, Van der Boechorststraat 9, 1081 BT Amsterdam, The Netherlands; +31-20-444-8586; fax: +31-20-444-8529; email: t.janssen@fbw.vu.nl.

DOI: 10.1682/JRRD.2004.03.0030

One of the major problems with applying ES-LC is a rapid onset of fatigue in the paralyzed muscles. Muscle fatigue is a transient decrease in the force-generating ability of a muscle as a result of recent activation [6–7]. A current method used to compensate for this fatigue during ES-LC is increasing the current amplitude, which results in the recruitment of additional nonfatigued muscle fibers. However, the amplitude cannot be increased indefinitely. Hence, a maximum in the compensation for fatigue exists, after which power output will decrease. The duration that a subject with SCI is able to cycle at a constant power output depends, therefore, on the duration that current amplitude is submaximal. If increasing the duration of submaximal stimulation were possible, cycling performance could be increased, potentially resulting in a greater training effect and hence greater muscular adaptations.

The duration of submaximal stimulation might be increased if one augments the force produced at a given current amplitude, enabling compensation for a greater amount of fatigue at the previously set maximal current amplitude. Force production might be augmented if one changes the stimulation pattern applied to the muscles. The stimulation pattern currently applied with ES-LC is a constant-frequency pulse train. Others have reported that in humans, catchlike-inducing pulse trains can generate higher forces and performance compared to constant-frequency stimulation [8–14]. Catchlike-inducing trains begin with two to four closely spaced pulses followed by a constant-frequency train of pulses. Furthermore, one study showed that doublets (two fast initial pulses) resulted in a higher isometric force per pulse compared to single pulses in both individuals with SCI and able-bodied individuals [14]. On the other hand, Bickel et al. found that a doublet given to the quadriceps muscle had more effect (enhanced isometric torque-time integral) in able-bodied individuals than in individuals with SCI [13]. The augmentation in force and performance generated by these catchlike-inducing trains has been shown to be most prominent in fatigued muscle [9]. Because muscle fatigue is a frequent feature in ES-LC, catchlike-inducing trains may be especially effective in augmenting force and performance during ES-LC compared to stimulation with a constant frequency. However, until now, no study has investigated the effects of catchlike-inducing trains during ES-LC. Therefore, the first purpose of this study was to evaluate if stimulation with a catchlike-inducing train at the beginning of the pulse train can improve cycling performance compared to stimulation with a constant frequency.

Force augmentation induced by catchlike-inducing trains appears to depend on the type of contraction. Although catchlike-inducing trains can be effective in augmenting force of the human quadriceps muscle during both isotonic [8–9] and isovelocity contractions [10], the extent of force augmentation is reported to be less during isovelocity movements than during isometric contractions in cat soleus muscle and human quadriceps muscle [10,15].

Both the number of closely spaced pulses at the beginning of a catchlike-inducing train and the interpulse interval can influence the induced force augmentation. For the human quadriceps muscle, a doublet with an interpulse interval of 5 ms has been shown to produce the highest force per pulse during isometric contractions [14], as well as for isovelocity [10] and isotonic contractions [8]. The present study, therefore, examines a catchlike-inducing train with two closely spaced pulses (doublet) with an interpulse interval of approximately 5 ms.

In the stimulation protocol currently applied with ES-LC, ramp modulation is applied at the beginning and end of each train of pulses. With ramp modulation, the current amplitude gradually increases at the beginning of a train of pulses and gradually decreases at the end of the train. This increase allows for a gradual recruitment of motor nerve fibers, resulting in a gradual increase in muscle force output and a more comfortable contraction. Applying ramp modulation at the onset of catchlike-inducing trains might, however, diminish the effect of the doublet because it would have very low amplitude.

Therefore, the second purpose of this study was to examine whether stimulation without ramp modulation induces changes in cycling performance compared to stimulation with ramp modulation. The third purpose was to evaluate if stimulation with ramp modulation and a doublet placed after the ramp can improve cycling performance.

METHODS

Subjects

After giving written informed consent, five men with complete SCI participated in this study, approved by the institutional ethical committee. All subjects were experienced in ES-LC exercise, because they had participated in previous experiments and had already reached a plateau level in performance at the onset of the present experiments. **Table 1** shows relevant subject characteristics.

Table 1.
Subject characteristics.

Subject	Age (yr)	Lesion Level	Body Mass (kg)	Time Since Injury (mo)
1	34	T4	60	33
2	27	T5–6	67	134
3	64	T8	81	48
4	18	T11	70	8
5	16	C5–6	71	14
Mean \pm SD	32 \pm 19	—	69 \pm 2	47 \pm 51

SD = standard deviation

Not all subjects participated in both experiments of this study: subjects 1 to 4 participated in experiment 1 (comparison of standard stimulation pattern vs. pattern with an initial doublet) and subjects 2 to 5 participated in experiment 2 (comparison of standard stimulation pattern vs. pattern with a middle doublet).

Electrical Stimulation-Induced Leg Cycling

Cycling was performed on a computer-controlled leg cycle ergometer (ERGYS 2, Therapeutic Alliances, Inc., Dayton, Ohio, USA). Electrical stimulation is used to induce contractions of the paralyzed leg muscles to produce a cycling movement on the ergometer. Twelve self-adhesive electrodes were placed over the quadriceps, hamstrings, and gluteal muscle groups. To ensure that the electrodes were placed at the same location during each session, we determined the electrode position using anatomical landmarks and birthmarks. The computer of the cycle ergometer receives feedback from sensors about pedal position and velocity to control the cyclic stimulation pattern and current amplitude. As muscle fatigue progresses during the test, current amplitude automatically increases to a maximum of 140 mA to recruit extra nonfatigued muscle fibers in an attempt to maintain the target velocity. When maximal current is reached and additional muscle fiber recruitment is no longer possible, pedaling rate declines. When pedaling rate falls below 35 rpm, the

test is terminated. Stimulation parameters were biphasic rectangular waveform, pulse duration of 450 μ s, and a frequency of 30 Hz.

With the standard software of the ERGYS, each pulse train consists of a period with increasing current amplitude (ramp up), a period with constant amplitude, and a period with decreasing amplitude (ramp down). During ramp up and down, the amplitude increases or decreases in a straight line. For each muscle the ramp up and down is realized within 21° of the crank angle, but the period of constant current amplitude is different for each muscle (**Table 2**).

A computer connected to the ERGYS sampled (60 Hz) current amplitude, crank position, and resistance. With the aid of custom-written MATLAB software, we calculated crank velocity, current amplitude, and power output. Before the beginning of the experiment, the software of the ERGYS was adapted to allow the ramp modulation to be turned off and a doublet to be applied either at the beginning of the train of pulses or after the ramp up.

Protocol

General

To allow comparison of cycling performance among the different stimulation patterns, we performed ES-LC endurance tests at a constant target velocity and resistance. Exercise time was limited to a maximum of 30 min. Before the actual experiments, we performed a number of test sessions to find an individual resistance level at which the muscles of the subject fatigued within 30 min. This resistance level was subsequently applied during the experimental sessions.

For both experiments performed in this study, each session began with 5 min of ES-LC at a velocity of 49 rpm and submaximal resistance. A 2 min cooldown and a 3 min rest period followed the warm-up. Subsequently, the subjects started ES-LC at an average velocity of 49 rpm (**Figure 1**). No external resistance was present during the first minute of the session. During the second minute, the resistance

Table 2.
Stimulation characteristics for each muscle group.

Muscle	Duration of Pulse Train (ms)	Firing Angle (°)	Ramp Up (°)	Constant Amplitude (°)	Ramp Down (°)
Gluteus	231	4–72	21	27	21
Hamstrings	201	111–170	21	18	21
Quadriceps	255	308–323	21	35	21

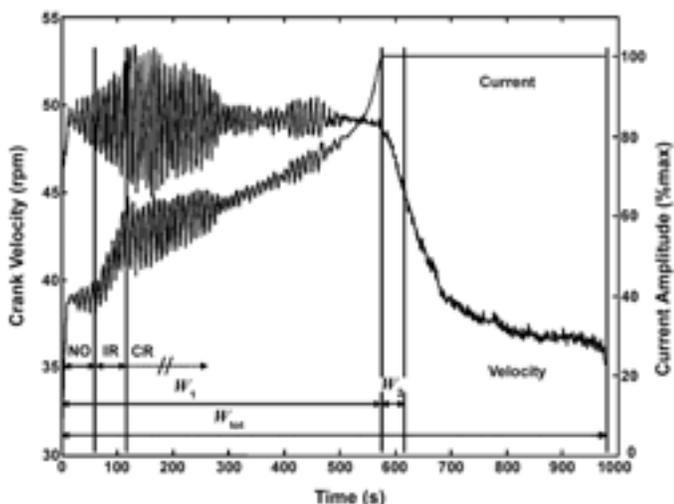


Figure 1.

Example of velocity and current amplitude data collected during cycling session of one subject. Determination of three cycling performance parameters is also illustrated: (1) total work performed during session (W_{tot}), (2) work performed from beginning of session until current amplitude became maximal (W_1) with subjects cycling at target velocity (on average), and (3) work performed while current amplitude was maximal and cycling velocity declined to 45 rpm (W_2). NO = no resistance, IR = increasing resistance, and CR = constant resistance.

was gradually increased, such that the predetermined level was reached at the end of the second minute, after which the resistance remained constant. For each subject, the resistance level was kept the same for each session. During the test, when the maximal current amplitude of 140 mA was reached, cycling velocity started to decline. The session was automatically stopped when cycling velocity dropped below 35 rpm (**Figure 1**).

Experiment 1

In the first experiment, three stimulation patterns were compared. The first was the standard constant-frequency (30 Hz) stimulation pattern with ramp modulation (R). The second pattern was similar to the first but with no ramp modulation (NR), and the third pattern was a pattern with no ramp modulation, but with an initial doublet (ID) at the beginning of the train with an inter-pulse interval of 5.56 ms. The number of pulses delivered to the muscles varied among these stimulation patterns. At the target velocity of 49 rpm, the stimulation patterns without the doublet delivered seven pulses to the gluteus, six to the hamstrings, and eight to the quadriceps, while pattern ID delivered one pulse more to each muscle

group. The number of pulses during ramp up ($n = 2$) and down ($n = 2$) was the same for each muscle, while the number of pulses at constant amplitude stimulation during the standard pattern was two for the hamstrings, three for the gluteal, and four for the quadriceps muscle groups. Each subject performed six cycling sessions; each pattern was used twice, with at least 48 h in between, while the testing order was counterbalanced.

Experiment 2

In the second experiment, the standard stimulation pattern (R) was compared with a similar pattern, with the only difference being a middle doublet after the end of the ramp up, hence at the start of the constant-amplitude range (MD). The inter-pulse interval of the doublet was 5.56 ms. Consequently, the pattern with the doublet (MD) had one pulse more than with the standard pattern (R). Each subject performed four cycling sessions; each pattern was used twice, with at least 48 h in between, while the testing order was counterbalanced.

Cycling Performance

Figure 1 shows an example of velocity and current amplitude data collected during a cycling session of one subject. It also indicates how cycling performance was determined. Cycling performance was defined in three ways: (1) the total work performed during a session (W_{tot}), (2) the work performed from the beginning of a session until the current amplitude became maximal (W_1) with the subjects cycling at the target velocity (on average) (**Figure 2**), and (3) the work performed while current amplitude was maximal and cycling velocity declined to 45 rpm (W_2). The reason for calculating W_2 until 45 rpm instead of 35 rpm was that responses after 45 rpm varied substantially. Some subjects could cycle for extended periods just above 35 rpm, whereas for others, the velocity dropped below 35 rpm immediately. Hence, calculating until 45 rpm gave more consistent and valid results.

Submaximal Current Amplitude

To evaluate the effect of the different stimulation patterns on the amount of stimulation needed at a given workload, we averaged the recorded current amplitude for the first, second, and third minutes. Because the subject takes approximately 15 s to cycle completely without assistance, the average for the first minute was calculated from 30 to 60 s.

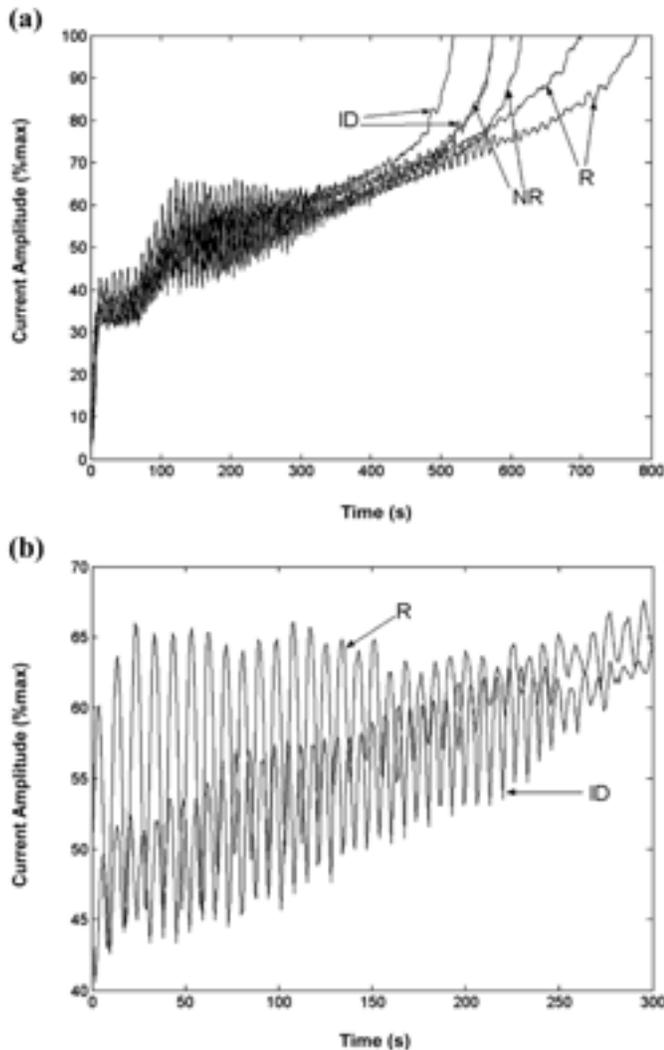


Figure 2. Example of current amplitude data from one subject for three different stimulation patterns used twice in experiment 1, standard with ramp (R), with no ramp (NR), and with initial doublet (ID): (a) data from all six sessions with current increasing to maximal amplitude and (b) part of same graph (from 100 s to 400 s), but for only two sessions, R and ID.

Data Analysis

The values for the stimulation patterns NR and ID were expressed relative to the values for the standard pattern R (set at 100%). A one-way analysis of variance with repeated measures detected significant differences in cycling performance among the different stimulation patterns. When significant differences were detected, a Student's paired *t*-test revealed which stimulation patterns led to these significant differences. Levels of significance were set at $p < 0.05$.

RESULTS

Figure 2 shows an example of current amplitude data from one subject for the three different stimulation patterns used twice in experiment 1. Because there was substantial variability in the responses for each pattern used, the cycling performance and current amplitude values for the two tests for each stimulation pattern were averaged and used for further data analysis.

Experiment 1

The different stimulation patterns did not result in significant differences in W_{tot} (**Table 3**, $p = 0.324$) or W_1 ($p = 0.695$). A trend emerged only for a lower W_{tot} and W_1 in ID compared with NR ($p = 0.061$ and $p = 0.077$, respectively). Only one subject performed better with NR and ID, which was especially because of the higher W_1 . In contrast, W_2 was significantly different among the three patterns (**Table 3**, $p = 0.006$), with R resulting in significantly higher W_2 values than NR ($p = 0.048$) and ID ($p = 0.020$).

The different stimulation patterns resulted in significant ($p = 0.000$) differences in the current amplitude during the first 3 min (**Figure 3**). The current was significantly higher in R than in NR ($p = 0.003$) and in ID ($p = 0.005$). The latter two patterns were not significantly different.

Experiment 2

The pattern with the doublet included after the ramp (MD) did not result in a significantly different W_{tot} ($p = 0.217$), W_1 ($p = 0.472$), or W_2 ($p = 0.348$) compared with pattern R (**Table 3**).

DISCUSSION

With the present experiments, given the large variations in responses and the small number of subjects, we are not able to exclude an effect of doublets. However, in contrast to our expectations, none of the experimental stimulation patterns resulted in a significantly improved cycling performance compared with the previously used standard stimulation pattern that uses ramp modulation. The only advantageous effect was observed in the first experiment: we demonstrated that during the first 3 min of cycling, the current amplitude was significantly higher with ramp modulation than without (**Figure 3**), suggesting

Table 3.

Cycling performance for each experimental stimulation pattern, expressed as percentage of standard pattern.

Variable	Subject	Stimulation Pattern		
		NR	ID	MD
W_{tot} (% of R)	1	72	52	—
	2	48	44	112
	3	89	75	96
	4	152	120	52
	5	—	—	57
	Mean \pm SD	90 \pm 44	73 \pm 34	80 \pm 29
W_1 (% of R)	1	112	89	—
	2	77	68	113
	3	78	75	137
	4	172	154	53
	5	—	—	74
	Mean \pm SD	110 \pm 45	96 \pm 39	94 \pm 37
W_2 (% of R)	1	54	42	—
	2	25	26	97
	3	16	18	225
	4	90	76	16
	5	—	—	48
	Mean \pm SD	46 \pm 33	40 \pm 26	96 \pm 92

 W_{tot} = total work W_1 = work until 100 percent stimulation W_2 = work after reaching 100 percent stimulation until 45 rpm

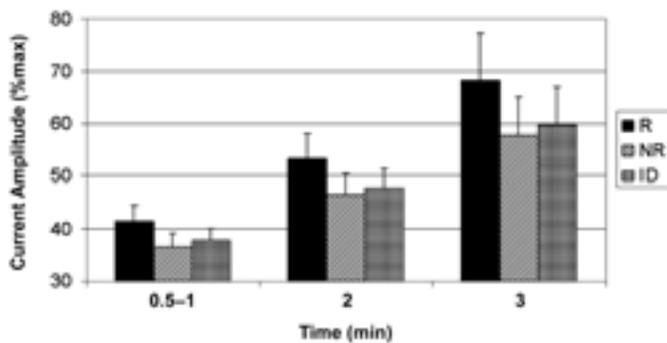
R = standard pattern

SD = standard deviation

NR = no ramp modulation

ID = initial doublet at beginning of train with an interpulse interval of 5.56 ms; no ramp modulation

MD = middle doublet after end of ramp up, hence at start of constant-amplitude range

**Figure 3.**

Current amplitude during first 3 min of electrical stimulation-induced leg cycling with use of three different stimulation patterns in experiment 1: standard ramp (R), with no ramp (NR), and with initial doublet (ID). R is significantly higher than NR and ID.

that stimulation without ramp modulation, either with or without a doublet, produces more force at the same sub-maximal current amplitude.

This difference in force production was probably due to a difference in muscle fiber recruitment. During stimulation without ramp modulation, all muscle fibers that could be recruited at the given highest current amplitude within the pulse train were recruited directly at the beginning of each pulse train, whereas with ramp modulation, the muscle fibers were recruited more gradually. Thus, a longer maximal force production resulted when ramp modulation was not applied. Despite this increased force production, stimulation without ramp modulation did not increase the work performed before reaching maximal stimulation, indicating that this force augmentation was not maintained. This might be due to a difference in resistance level, for the resistance level was lower during the first and second minutes of the session compared to the rest of the session. It could be that stimulation without ramp modulation only resulted in an augmentation of force when the subjects cycled at a low resistance level. When the resistance level increased, fatigue developed

more rapidly during stimulation without ramp modulation than during stimulation with ramp modulation. This rate of fatigue development increased probably because the maximum number of muscle fibers was recruited for a longer duration during stimulation without ramp modulation.

The observed trend of lower W_1 during stimulation with a doublet (ID) compared to stimulation without a doublet (NR) (**Table 3**) suggests that the doublet increased the rate of fatigue development, possibly due to the extra pulse delivered to the muscles. For constant-frequency trains, the number of pulses has been shown to influence the rate at which fatigue develops, with more pulses resulting in more fatigue [16]. The greater number of pulses (1 more than the 6–8 in the standard pattern, an increase of 13%–17%) with the doublet may therefore have resulted in greater fatigue. A second factor that may have influenced faster fatigue development was the doublet itself. A study by Binder-Macleod et al. indicated that although stimulation with a catchlike-inducing train produced more force in fatigued muscles, it also produced greater fatigue than comparable constant-frequency trains [12]. This finding was true despite the use of the same number of pulses, average frequency, and train duration as with the constant-frequency train. The authors suggested that this variation in fatigability might be due to differences in the force-time integral of the responses to the trains. The higher frequency of the doublet also gives an augmented calcium ($[Ca]^{2+}$) release that is more than the summation of two pulses at a lower frequency [17–18]. This larger amount of $[Ca]^{2+}$ influences the cross-bridge formation and increases the phosphorylation of the myosin light chain. As a result, the number of cross-bridges in the force-generating state increases and/or the force-generating state of each cross-bridge is prolonged, which could have improved performance. On the other hand, this augmented $[Ca]^{2+}$ release leads to more free $[Ca]^{2+}$ that needs to be actively reaccumulated by the sarcoplasmic reticulum $[Ca]^{2+}$ -ATP-ase, therewith increasing the energy cost and hence potentially leading to earlier fatigue with the use of a doublet in fresh muscles [17–18].

Stimulation with an ID resulted in lower current amplitude compared to the standard stimulation with ramp modulation (R) (**Figure 3**). However, no differences between ID and NR were found (**Figure 3**), suggesting that an initial doublet did not result in an additional force augmentation that could be used for propulsion. Until now, no study had examined the effects of

catchlike-inducing trains during ES-LC. Studies, however, have demonstrated that catchlike-inducing trains can be effective in augmenting force in the fatigued quadriceps muscles during dynamic [8–10] and isometric [14] contractions in individuals with SCI. These data indicate that catchlike-inducing trains might have been effective in augmenting force in the quadriceps femoris muscles during ES-LC in the present experiments. The doublet in our first experiment could indeed have resulted in an augmentation of force. However, the doublet was possibly not delivered at the right moment of the cycle to exert a positive contribution to the cycling performance. During ES-LC, each muscle is stimulated during a preset angle range in the cycle. Previous studies have shown that the extra force produced by a doublet results from an increase in the rate of rise of force at the beginning of the stimulation [11]. Since no ramp modulation was applied during stimulation (in both NR and ID) the muscles probably produced force earlier during the cycle than with ramp modulation. As a result, the legs might not have been in the right position to exert the force effectively (tangential to the crank) and use the extra force for propulsion.

Since in experiment 2 the doublet was placed after the ramp up, we hypothesized that the increased force production just mentioned would occur at a better time, which would result in improved cycle performance. However, the stimulation pattern with this middle doublet (MD) did not prove significantly better than the standard pattern; not before reaching maximal current amplitude (W_1) or after reaching maximal stimulation (W_2) (**Table 3**). Still, the possibility exists that the doublet still appears too early in the pulse train, because a doublet usually induces a faster contraction. Placing the doublet even later during the pulse train might result in better timing for force enhancement during the cycling movement.

The strategy we used in this study to attempt to increase cycling performance was by augmenting force production with the aid of catchlike-inducing trains. There might, however, be another strategy by which catchlike-inducing trains could be effective in increasing cycling performance. Research has demonstrated that the stimulation frequency at which catchlike-inducing trains produce maximal performance is lower compared to the frequency at which constant frequency trains produce maximal performance [9]. Thus, catchlike-inducing trains may be able to produce the same amount of force at

a lower frequency. Lower stimulation frequencies have been associated with less fatigue [19]. If the rate at which fatigue develops during ES-LC is reduced, the subjects will be able to cycle longer and cycling performance will be improved. A study by Bigland-Ritchie et al. did indeed show that stimulation with catchlike-inducing trains provides a strategy to reduce fatigue [20]. The authors showed that when the initial force time integrals of a catchlike-inducing train and a constant-frequency train were matched, the stimulation frequency of the catchlike-inducing train was lower and less fatigue occurred compared to the constant-frequency train. Thus, an alternative strategy to improve cycling performance during ES-LC may be by using catchlike trains with lower stimulation frequencies, leading to similar force production as in the constant frequency trains.

One reason for finding a reduced cycling performance in ID may be the induction of more fatigue by the use of the doublet on fresh muscles. In fatigued muscles, the doublet may have a more positive effect [9]. It might, therefore, be better to start with a normal stimulation pattern and to include a doublet after maximal current amplitude is reached. Since $[Ca]^{2+}$ release is reduced in the fatigued muscle [21], the doublet may produce more free $[Ca]^{2+}$ and be more effective in improving cycle performance. Kudina and Alexeeva found, in human motor neurons during weak voluntary contractions, cases in which a doublet was followed by a lower stimulation frequency, which allowed the muscle more time to reuptake the free $[Ca]^{2+}$, reduce the residual free $[Ca]^{2+}$, and restore the extra adenosine tri-phosphate used for the reuptake of $[Ca]^{2+}$ [22].

CONCLUSION

The results from this study do not indicate that stimulation with catchlike-inducing trains with the current parameter settings can improve ES-LC performance. However, the combination of the large variability among subjects with the relatively low number of subjects and the positive finding that a lower current amplitude was required during the first few minutes of exercise suggest that further research may be more successful in finding stimulation patterns that can improve cycling performance.

REFERENCES

1. Burnham R, Martin T, Stein R, Bell G, MacLean I, Steadward R. Skeletal muscle fibre type transformation following spinal cord injury. *Spinal Cord*. 1997;35(2):86–91.
2. Thomas CK, Zaidner EY, Calancie B, Broton JG, Bigland-Ritchie BR. Muscle weakness, paralysis, and atrophy after human cervical spinal cord injury. *Exp Neurol*. 1997;148(2):414–23.
3. Taylor PN, Ewins DJ, Fox B, Grundy D, Swain ID. Limb blood flow, cardiac output and quadriceps muscle bulk following spinal cord injury and the effect of training for the Odstock functional electrical stimulation standing system. *Paraplegia*. 1993;31(5):303–10.
4. Hoffman MD. Cardiorespiratory fitness and training in quadriplegics and paraplegics. *Sports Med*. 1986;3(5):312–30.
5. Janssen TWJ, Glaser RM, Shuster DB. Clinical efficacy of electrical stimulation exercise training: effects on health, fitness, and function. *Topics in Spinal Cord Injury Rehabilitation*. 1998;3(3):33–49.
6. Burke RE, Rudomin P, Zajac FE 3rd. The effect of activation history on tension production by individual muscle units. *Brain Res*. 1976;109(3):515–29.
7. Williams JH. Contractile apparatus and sarcoplasmic reticulum function: effects of fatigue, recovery, and elevated Ca^{2+} . *J Appl Physiol*. 1997;83(2):444–50.
8. Lee SC, Becker CN, Binder-Macleod SA. Catchlike-inducing train activation of human muscle during isotonic contractions: burst modulation. *J Appl Physiol*. 1999;87(5):1758–67.
9. Lee SC, Binder-Macleod SA. Effects of activation frequency on dynamic performance of human fresh and fatigued muscles. *J Appl Physiol*. 2000;88(6):2166–75.
10. Binder-Macleod SA, Lee SC. Catchlike property of human muscle during isovelocity movements. *J Appl Physiol*. 1996;80(6):2051–59.
11. Binder-Macleod SA, Barker CB 3rd. Use of a catchlike property of human skeletal muscle to reduce fatigue. *Muscle Nerve*. 1991;14(9):850–57.
12. Binder-Macleod SA, Lee SC, Russ DW, Kucharski LJ. Effects of activation pattern on human skeletal muscle fatigue. *Muscle Nerve*. 1998;21(9):1145–52.
13. Bickel CS, Slade JM, Dudley GA. Long-term spinal cord injury increases susceptibility to isometric contraction-induced muscle injury. *Eur J Appl Physiol*. 2004;91(2–3):308–13.
14. Karu ZZ, Durfee WK, Barzilai AM. Reducing muscle fatigue in FES applications by stimulating with N-let pulse trains. *IEEE Trans Biomed Eng*. 1995;42(8):809–17.
15. Sandercock TG, Heckman CJ. Doublet potentiation during eccentric and concentric contractions of cat soleus muscle. *J Appl Physiol*. 1997;82(4):1219–28.

16. Garland SJ, Garner SH, McComas AJ. Relationship between numbers and frequencies of stimuli in human muscle fatigue. *J Appl Physiol.* 1988;65(1):89–93.
17. Abbate F, Sargeant AJ, Verdijk PW, de Haan A. Effects of high-frequency initial pulses and posttetanic potentiation on power output of skeletal muscle. *J Appl Physiol.* 2000;88(1):35–40.
18. Binder-Macleod SA, Russ DW. Effects of activation frequency and force on low-frequency fatigue in human skeletal muscle. *J Appl Physiol.* 1999;86(4):1337–46.
19. Carroll SG, Triolo RJ, Chizeck HJ, Kobetic R, Marsolais EB. Tetanic responses of electrically stimulated paralyzed muscle at varying interpulse intervals. *IEEE Trans Biomed Eng.* 1989;36(7):644–53.
20. Bigland-Ritchie B, Zijdwind I, Thomas CK. Muscle fatigue induced by stimulation with and without doublets. *Muscle Nerve.* 2000;23(9):1348–55.
21. Westerblad H, Bruton JD, Allen DG, Lannergren J. Functional significance of Ca^{2+} in long-lasting fatigue of skeletal muscle. *Eur J Appl Physiol.* 2000;83(2-3):166–74.
22. Kudina LP, Alexeeva NL. Repetitive doublets of human motoneurons: analysis of interspike intervals and recruitment pattern. *Electroencephalogr Clin Neurophysiol.* 1992;85(4):243–47.

Submitted for publication on March 1, 2004. Accepted in revised form May 4, 2004.