The Effect of Fatigue on the Timing of Electrical Stimulation-Evoked Muscle Contractions in People with Spinal Cord Injury

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∎ ABSTRACT

This study investigated the activation dynamics of electrical stimulation-evoked muscle contractions performed by individuals with spinal cord injury (SCI). The purpose was to determine whether electrical stimulation (ES) firing patterns during cycling exercise should be altered in response to fatigue-induced changes in the time taken for force to rise and fall with ES. Seven individuals with SCI performed isometric contractions and pedaled a motorized cycle ergometer with stimulation applied to the quadriceps muscles. Both exercise conditions were performed for five minutes while the patterns of torque production were recorded. ES-evoked knee extension torque fell by 75% under isometric conditions, and the rate of force rise and decline decreased in proportion to torque ($r = 0.91$, $r = 0.94$, respectively). There was no change in the time for torque to rise to 50% of maximum levels. The time for torque to decline did increase slightly, but only during the first minute of exercise. Cycling power output fell approximately 50% during the five minutes of exercise, however, there was no change in the time taken for torque to rise or fall. The magnitude of ES-evoked muscle torques decline substantially with fatigue, however, the overall pattern of torque production remained relatively unchanged. These results suggest there is no need to alter stimulation firing patterns to accommodate fatigue during ES-evoked exercise. ∎

KEY WORDS: cycling exercise, electrical stimulation, FES, muscle activation, paraplegia.

INTRODUCTION

Electrical Stimulation (ES) provides a means to evoke muscle contractions in the legs of people

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with spinal cord injury (SCI) to provide exercise for the paralyzed muscle. Cycling is a form of ES-evoked exercise that can be readily performed by people with SCI and has been utilized in a number of rehabilitation programs over the past 20 years (1–3). The exercise benefits for SCI individuals are limited, however, by the low power outputs able to be achieved during ES-evoked cycling (5–10 W, Ref. 4; or 17 W, Ref. 5). Fatigue of the muscles is more rapid than for voluntary cycling due to the

preferential hypotrophy of slow twitch fibers in the muscles of SCI individuals (6) and/or the non-physiologic nature of fiber recruitment during ES-evoked contractions (7).

Coordinating the timing of muscle contractions for cycling exercise is important in order to produce contractions that provide forward propulsion, rather than resist the cycling motion (2). After stimulation commences, there is a delay before muscle force rises enough to apply force against the pedal. This delay must be considered when designing stimulation patterns for effective cycling. Fatigue has been shown to induce large changes in the rate of force development for individuals with SCI performing isometric contractions (8). It is possible that these changes in force development may affect the stimulation firing patterns required to generate effective cycling.

Beelen and colleagues (9) examined the torque applied to pedals by able-bodied individuals cycling using ES-evoked contractions. They found that after fatigue, the rate of rise in pedal torque declined in proportion to the loss of peak torque. While they didn't directly report the time taken for torque to reach a maximum, the proportional decline in peak torque and rise rate suggests that the time to peak torque would have remained relatively unchanged, despite the onset of fatigue. The reduction in muscle force rise rate has been found to be more pronounced in SCI individuals than for able-bodied persons (8). Also, while Beelen et al. (9) measured changes in electrically stimulated contractions, the fatigue was induced using a voluntary exercise protocol. It is therefore unclear whether the amount of time taken for torque to rise would change for SCI individuals performing ES-evoked cycling.

Therefore, the purpose of this study was to investigate the effect of fatigue on the timing of muscle contractions elicited in individuals with SCI. This was tested under isometric conditions in order to confirm the results of Gerrits et al. (8), particularly as they only reported the rate of force development, but not the actual time taken for force to rise. The second component of this study examined the effect of fatigue on torque development during ES cycling for individuals with SCI. If fatigue alters the time required for torque to be applied to the pedals in response to stimulation, then this would change the optimal stimulation patterns required for effective cycling. It was anticipated that studying changes in rise and fall times with fatigue might provide insights into what changes in stimulation timing, if any, would be required to maximize power output under fatigued conditions.

MATERIALS AND METHODS

Subjects

SCI individuals with complete motor lesions between T4 and T9 were recruited for each component of this study. One female and six males completed the isometric tests (6 classified ASIA—A, 1 ASIA—B), while two females and four males participated in the cycling experiments (6 ASIA—A, 1 ASIA—B). All participants underwent informed consent procedures according to the guidelines of the University of Sydney Human Ethics Committee and received medical screening for pre-existing musculo-skeletal or cardiorespiratory disorders before participating in the study. The subjects had previously been training regularly using ES, however, not all subjects were in regular training at the time of the study. Details of subjects are summarized in Table 1.

Isometric Contractions

Isometric contractions were performed on a Biodex 2000 Isokinetic Dynamometer (Biodex Medical Systems, Shirley, NY). Contractions were elicited using a laboratory-designed stimulator delivering monophasic square wave pulses at 35 Hz with a pulse width of 250 μs and enough current (between 60 and 120 mA) to produce stable tetanic contractions. Stimulation was delivered via 8×10 cm self-adhesive electrodes (Medtronic Cat no. 86906350, Medtronic, Inc., Minneapolis, MN) placed over the belly of the quadriceps muscles; with the anode located proximal to the superior surface of the patella, 2/3 medial to the midline of the thigh, and the cathode distal to the perineum, 2/3 lateral to the thigh's midline (Fig. 1). A personal computer, sampling at a frequency of 1000 Hz, was used to monitor torque from the dynamometer and current generated by the muscle stimulator. The stimulator produced a constant voltage output, and therefore small variations in current

Table 1. Subject Characteristics

Subject	Injury level	Age	Weight	Years since injury	Training Frequency[a]
1[b]	T4	31	70	12	3/week for 1 years
2[b]	T5	31	49	5	> 3/week for 4 years
3[b]	T5–6	56	82	41	Not current
4[b]	T4–6	36	55	22	Not current
5[c]	T4–6	30	76	8	Not current
6[c]	T8	35	70	14	3/week for 1 years
7[c]	T7–8	45	72	5	Not current
8[d]	T4	34	53	3	2/week for 6 months
9[d]	T4–5	25	60	1.5	2/week for 6 months

[a]"Not current" indicates that subjects had not used regular NMES training within the previous year. These subjects had previously trained for at least six months, twice per week, however, detraining would be expected to negate this.
[b]Subject completed both Isometric and Cycling components.
[c]Subject completed just the Isometric component.
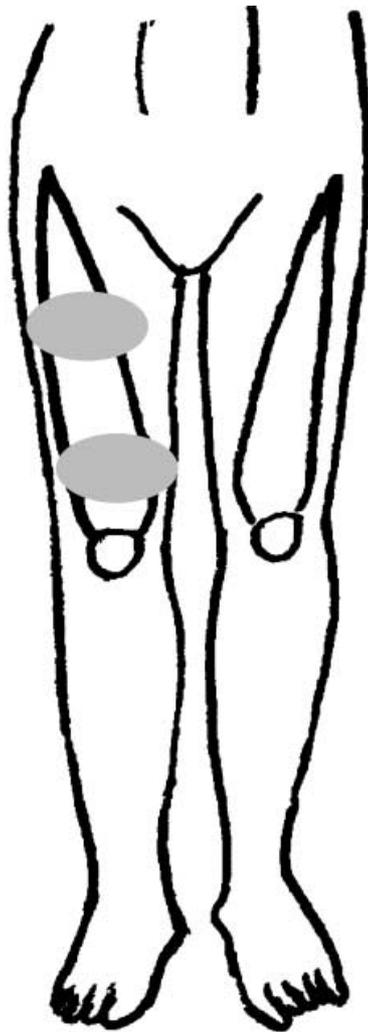[d]Subject completed just the Cycling component.

Figure 1. Electrode placement for both experimental procedures.

were possible when impedance between the stimulation electrodes changed during the experiment. In this experiment, data from the final minute of one subject was eliminated after current increased and resulted in an uncharacteristic rise in torque production for this single point in time. The original data have been retained for one other subject where current fell by less than 5% over during the test, and current remained with 1% of original values for all other subjects.

Stimulation was delivered as alternating 2 s contraction with 2 s recovery over a continuous period of five minutes. Fifteen-second samples were recorded at the beginning and at one-minute intervals throughout this period of five minutes. A knee angle of 60 deg was used for all contractions. Prior to the fatigue protocol, subjects performed eight sets of three isometric contractions at different knee angles with five minutes rest between sets (10). Results for the present study are therefore presented with a rested condition conducted prior to the contractions at different knee angles, and a time zero at the commencement of the five minutes fatigue protocol. Table 2 describes all variables that were derived from these data.

Changes in muscle performance with fatigue were analyzed using repeated measures ANOVAs. Given the large number of variables and relatively few subjects, there were insufficient residual degrees of freedom to perform a multivariate ANOVA. Univariate results are therefore presented cautiously, mindful of the risk of Type 1 errors being increased by the number of comparisons

Table 2. Experimental Variables Derived from Measures of Isometric Knee Extension Torque and Stimulation Timing

Torque:	Net Torque averaged from 500 ms after stimulation onset to cessation.
Rise Delay:	Time from stimulation onset to when torque was continuously greater than 0.1 N m.
Rise Time:	The time taken for torque to rise from 0.1 N m up to 50% of Torque.
Rise Rate:	$\dfrac{50\% \text{ of Torque} - 0.1\text{N m}}{\text{Rise Time}}$
Fall Delay:	The time from stimulation cessation to when torque was continuously more than 0.1 N m below the torque at cessation.
Fall Time:	Time for torque to fall from 0.1 N m below torque at cessation to 50%.
Fall Rate:	$\dfrac{50\% \text{ of Torque at cessation} - 0.1\text{N m}}{\text{Fall Time}}$

performed. Although 5% was chosen as the significance level for statistical comparisons, all variables subsequently deemed significant were found to have univariate *p*-values less than or equal to 0.002. The risk of Type 1 error therefore seems acceptably small, even considering the number of comparisons being performed.

Cycling

Cycling was performed using a MOTOmed Viva cycle ergometer (Reck Medizintechnik, Betzenweiler, Germany) designed specifically for rehabilitation of mobility-impaired patients (11). The ergometer utilized a motor to provide passive leg movement for those patients without the capacity to cycle unaided. For subjects strong enough to pedal against some force, the motor provided resistance by acting as a DC generator, rather than drawing electrical current. Computer monitoring of the crank velocity aimed to achieve constant cycling velocity by regulation of the motor current. The ergometer was adapted to provide output of crank angle, and motor current via an RS232 interface to an IBM compatible personal computer (Celeron 333 MHz, Intel, Inc., Santa Clara, CA). Labview software (Version 4.01, National Instruments Corp, Austin, TX) sampled crank angle and used this to control the same muscle stimulator used for isometric experiments. Stimulation parameters (frequency, pulse width, etc.) were identical to those used for isometric trials.

Force transducer pedals (12) were used to record force applied to the pedals and the angle of the pedals. Voltages proportional to the pedal force and angle were low pass filtered at 25 Hz, then sampled at a frequency of 250 Hz using an IBM compatible personal computer (Intel 80386) and 12 bit analog to digital converter (DT2801, Data Translation, Marlboro, MA). Pedal forces, crank, and pedal angles were subsequently used to calculate the torque applied to the cranks.

The ergometer chair was positioned so that the subjects' knees were approximately 45 deg at their most extended position. The ergometer motor was used for 5 min of passive cycling, after which stimulation current was adjusted until strong contractions were recorded by the pedals. Subjects then cycled continuously for five minutes with stimulation applied to the right quadriceps muscles when the right crank was positioned between 60 deg before top dead center to 20 deg after top dead center. Data were collected for 20-s periods at the beginning of the cycling period and at one-minute intervals thereafter.

For each trial, net pedal torque was calculated by subtracting the torque measured at each crank angle during passive cycling from the active pedal torque. Instantaneous power output was calculated as the product of nett crank torque and angular velocity of the crank. Average power output was calculated for each trial by averaging instantaneous power across six complete revolutions. To test the general pattern of torque production, the average power output, crank angle where torque was maximum (Maxθ), and angles where 50% peak torque was reached in both the ascending (Upθ) and descending (Downθ) phases were analyzed for each minute of the experiment. Changes to these variables were assessed by means of a multivariate, one way, repeated measures ANOVA, with six levels used for time throughout the fatigue protocol.

RESULTS

Isometric Contractions

There were variables missing for one subject at the final time period; caused by stimulator current drifting away from initial levels. Two options were considered for replacing these missing values. The

Table 3. Summary of all Experimental Results[a]

Time[b]	Rested	0	1	2	3	4	5	Significance
Isometric								
Torque	14.9	10.7	8.2	5.6	4.7	4.6	3.8	0.000[c]
(Nm)	(3.5)	(2.5)	(2.0)	(1.4)	(1.2)	(1.2)	(1.0)	
Rise Delay	33	34	34	33	34	35	37	0.269
(ms)	(3)	(3)	(3)	(6)	(4)	(4)	(4)	
Rise Time	86	86	83	96	88	92	84	0.724
(ms)	(16)	(21)	(30)	(59)	(51)	(72)	(55)	
Rise Rate	87.7	65.2	50.9	34.0	30.3	31.4	28.8	0.000[c]
(Nm/s)	(18.5)	(18.5)	(13.1)	(10.8)	(9.5)	(11.1)	(10.3)	
Fall Delay	58	59	63	66	65	67	68	0.433
(ms)	(5)	(7)	(14)	(9)	(6)	(9)	(19)	
Fall Time	71	60	87	85	82	76	72	0.001[c]
(ms)	(11)	(7)	(18)	(17)	(12)	(16)	(14)	
Fall Rate	106.1	93.1	47.9	32.2	28.4	29.1	24.4	0.000[c]
(Nm/s)	(29.5)	(20.5)	(8.7)	(11.2)	(9.8)	(9.6)	(8.2)	
Cycling								
Power		2.6	2.4	1.6	1.4	1.3	1.3	0.001[c]
		(1.0)	(0.9)	(0.7)	(0.6)	(0.6)	(0.6)	
Upθ		345.3	345.7	347.0	348.3	346.8	345.3	0.770
		(8.4)	(6.1)	(8.5)	(10.5)	(8.4)	(7.6)	
Maxθ		19.3	19.3	21.7	21.0	23.3	18.7	0.686
		(8.8)	(6.2)	(5.3)	(5.9)	(7.3)	(13.2)	
Downθ		50.7	53.0	54.0	53.3	52.2	51.0	0.246
		(7.8)	(7.0)	(6.1)	(7.2)	(6.7)	(7.1)	

[a]Data represent mean and standard deviation
[b]The rested values came from the first isometric trial from each session. The number of all other times refers to the time (in minutes) during the fatigue protocol.
[c]ANOVA displayed significant effect for time ($p < 0.05$).

missing values could have been replaced by an exponential fit from the individual's available data. Alternatively, the missing values could be replaced by the mean of all other subjects' data at that time. In practice, no differences were found in the statistical significance of whole group trends between the two methods. The exponential fit method was selected after visual inspection of the data because it produced a more consistent looking pattern for the individual subject concerned.

All results are summarized in Table 3. Isometric torque declined significantly with fatigue with final values averaging less than 25% of rested levels (Fig. 2, $p = 0.000$). Rise Rate fell in proportion to Torque ($r^2 = 0.996$) so that the time taken to generate torque remained constant with fatigue. There was no significant change in mean Rise Delay (mean = 34 ms, $p = 0.269$) or Rise Time (mean = 88 ms, $p = 0.724$) with fatigue, however, Rise Time became more variable as time progressed. Fall Delay did not change as the muscles fatigued (mean = 64 ms, $p = 0.433$) and Fall Rate
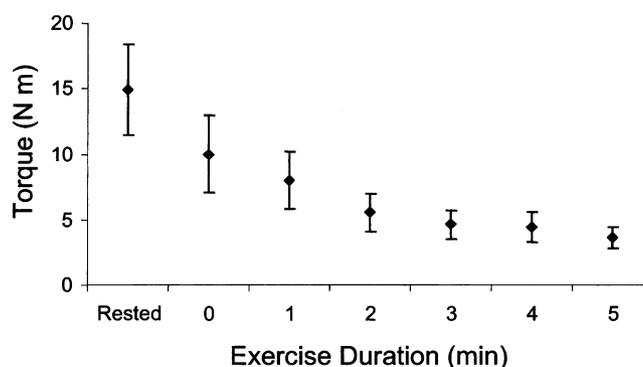

Figure 2. Changes in isometric torque with fatigue during repeated contractions. Data represent mean and standard deviation. The rested values came from the first isometric trial from each session. The number of all other times refers to the time in minutes during the fatigue protocol. $n = 7$ for all time periods except 5 min, where $n = 6$.

fell in proportion to Torque ($r = 0.945$). There was a significant increase in Fall Time (Fig. 3, $p = 0.001$), however, tests of within-subjects contrasts indicated that only times zero and one
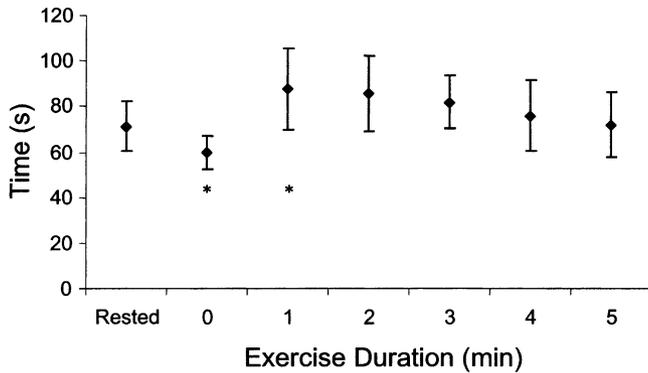
Figure 3. Changes in Fall Time with fatigue during repeated isometric contractions. Data represent mean and standard deviation. $n = 7$ for all time periods except 5 min, where $n = 6$. *indicates a value significantly different to the rested condition ($p < 0.05$).
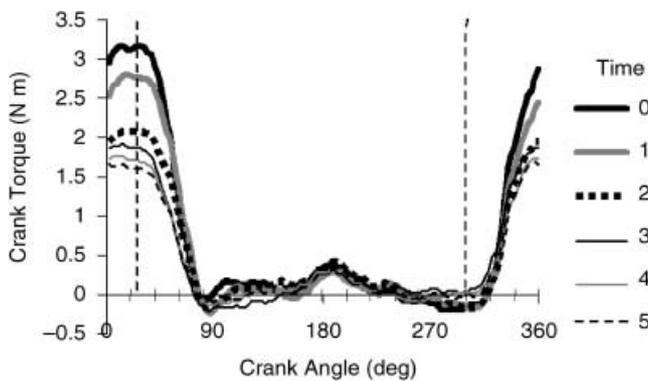

Figure 4. Typical crank torque-angle curve for a single subject with stimulation firing angles between 300 and 20 deg. Vertical dotted lines represent the timing of stimulation onset and cessation. Numbers for each curve represent the time of data collection (in minutes) within the five minutes continuous cycling.

minute differed significantly from the nonfatigued Fall Time. After this, the decline in Fall Rate was greater than that of Torque, resulting in Fall Time returning to near initial levels.

Cycling

Figure 4 illustrates how a typical net crank torque-angle curve changed during the five minutes of this experiment. Over the course of five minutes, muscle fatigue caused average power output to drop nearly 50% from an average of 2.6 W down to 1.3 W (Fig. 5). The drop in power output was most evident during the first two minutes of cycling and tended to plateau thereafter.
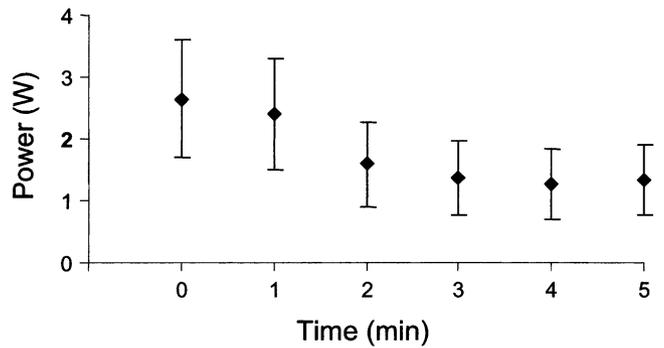

Figure 5. Change in power output during the course of five minutes continuous cycling using stimulation of the right quadriceps muscles.
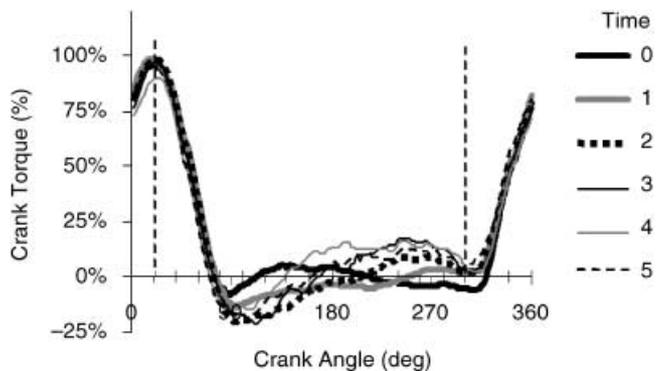

Figure 6. Torque patterns averaged for all subjects and normalized against peak torque at time zero. Vertical dotted lines represent the timing of stimulation onset and cessation. Numbers for each curve represent the time of data collection (in minutes) within the five minutes continuous cycling.

Although peak torque and hence power output declined throughout the cycling period, there was little change in the overall shape of the torque-angle curves (Fig. 6). Time 4 is the only curve that differs from the others on Figure 6 and this was affected by a single subject who fatigued relatively more than the others, with a subsequent decrease in signal to error ratio. If this subject were removed from calculations of the time 4 average, then this curve would have then been superimposed over the others.

The pattern of curves illustrated by Figure 4 were analyzed by a multivariate, repeated measures ANOVA. Only the average power output generated a significant change ($p = 0.001$). All other variables representing the rise and fall times of the curve showed no significant change (Table 3).

DISCUSSION

Isometric Contractions

The decline in torque levels with fatigue was similar in timing to values reported for isometric quadriceps contractions performed by SCI subjects (8). While data from Gerrits et al. (8) demonstrated a similar plateau in fatigue occurring after approximately two minutes of exercise, their subjects stabilized at approximately 40% of maximum torque values, rather than the 25% found for the present study (Fig. 2). A number of factors are known to affect the amount of fatigue for SCI individuals exercising with ES and may account for the different fatigue rates between studies. Gerrits et al. (8) used a shorter contraction duration (1 s on, 1 s rest), shorter pulse width (200 ms), and a higher stimulation intensity (142 mAmp). These stimulation parameters, however, cannot explain the higher plateau level they found because all parameters were more likely to increase the amount of fatigue (13). It is possible that the subjects used by (8) had a higher level of training prior to the experiment, with a higher percentage of fatigue-resistant fibers (14) and correspondingly higher plateau level. The training status was not reported, however, and therefore cannot be compared with the present study. The fatigue protocol for the present study was performed after a number of isometric contractions had been performed at differing knee angles (eight sets of three contractions, with five minutes rest between sets). While the rest periods between sets were chosen to minimize fatigue, Figure 2 demonstrates that torque was already reduced at the beginning of the fatigue protocol. This may have affected the resulting plateau level for the present study. Gerrits et al. (8) used a 20 Hz stimulation frequency while the present study used 35 Hz. ES-evoked cycling exercise commonly utilizes a frequency near 35 Hz in order to generate enough stimulation pulses during the brief activation period of each revolution (1,5,11). A lower stimulation frequency would be expected to reduce the rate of fatigue (15) and hence is the most likely explanation for the higher plateau found by (8).

The increase in relaxation time with fatigue for the present study (Fig. 3) was considerably smaller than the 200% changes reported for quadriceps contractions (8), and for isometric contractions of the wrist muscles of quadriplegic subjects (16). It is not clear why the present study found less change, particularly given that the magnitude of fatigue-induced torque decline was greater for the present study. Direct comparisons are difficult to draw because of the different methods used to determine Fall Time. Gerrits et al. (8) measured time for force to decline from 50% to 25% of peak value, while Cameron and Calancie (16) reported the time from the end of stimulation to when force reached 30% of its value at stimulation cessation.

Previous findings regarding the change in force rise time with fatigue have been equivocal. Changes in the time of force rise with fatigue were not reported by Gerrits et al. (8) as they examined only maximum rise rate. Cameron and Calancie (16) found statistically significant increases in force rise time after four minutes of isometric, ES-evoked wrist extension contractions performed by quadriplegic individuals that were similar in magnitude to the present study. The difference in significance may possibly be explained by their use of a simple *T*-test between the first and last time period, perhaps making their analysis less conservative. Like the present study, Sahlin and Seger (17) found no change in the rise time for able-bodied subjects performing isometric contractions in response to electrical stimulation. It therefore appears that, if rise time does increase with fatigue, the effects are relatively small.

Cycling

The cycling power outputs achieved in this study (2.6 W) are very low compared to most previously reported studies on ES-evoked cycling for SCI individuals (17 W, Ref. 5). The present data, however, represent the stimulation of only one isolated quadriceps muscle, rather than bilateral stimulation of the quadriceps, hamstrings, and gluteal muscles. SCI individuals within our laboratory typically exercise at power outputs of 8–12 W when ES is applied to all six muscle groups.

Our finding that patterns of torque production do not change with fatigue (Fig. 6) is consistent with measurements from able-bodied individuals cycling an isokinetic ergometer using ES-evoked contractions (9). The amount of torque decline for the present study was greater than that

experienced by able-bodied subjects (9), as was expected from the isometric experiments (8). The peak pedal forces measured by Beelen et al. (9) decreased by 30%, and the rate of force development declined in proportion to peak force ($r = 0.94$). The constant time to peak torque of the present study is consistent with this proportionality. Although the number of subjects was small ($n = 6$), the high *p*-values (0.770, 0.686, 0.246) increase our confidence that there really was no demonstrable change in the timing of torque responses with fatigue.

The initial rationale for this study was that the effect of fatigue on the rate of force rise in response to stimulation might alter the selection of effective stimulation timing patterns. It was thought that stimulation patterns might need to be advanced as a muscle fatigued in order to maintain the production of torque at constant crank angles. Cycle ergometers for individuals with SCI typically incorporate a fixed ankle orthosis to limit the degrees of freedom of movement to one (2). Therefore, the range of crank angles through which muscle force provides forward propulsion always remains constant, and stimulation must commence in advance of force being needed in order to accommodate the delay in generating force. The findings of this study that force rise times remain constant with fatigue suggest that there is no need to adjust the timing of stimulation during a session of cycling. If the time for muscles to generate force remains constant, then the optimum range of stimulation firing angles would also remain unchanged.

The present findings have only been made with respect to a five-minute period of cycling. This duration was chosen because previous studies have shown fatigue to be greatest within the first two minutes, with force levels reaching a plateau after this time (8,13). It is possible that, over a typical exercise session of 30 or 60 min of cycling, further physiologic changes within the muscles may provoke alterations in the rise or fall times of the muscles that were not present after five minutes of exercise. Theisen and colleagues (4) demonstrated that the pattern of power output declines after 2–5 min, and then recovers to higher levels during 45 min of ES-evoked cycling exercise. The physiologic adaptations underpinning these fluctuations in power output remain

unclear. There are, at present, no studies known to the present authors that have investigated changes in activation dynamics for ES-evoked contractions over exercise durations of longer than five minutes.

CONCLUSIONS

Progressive fatigue throughout the series of experiments at each knee angle, followed by a five-minute period of repeated stimulation, caused isometric torque to decline by approximately 75% of its rested value. Despite such large changes in muscle force, there were only relatively small changes in the dynamics of each contraction. The time for torque to fall to 50% of active torque following the cessation of stimulation increased by 25% from resting values, however, the pattern of change was not consistent. The increase in Fall Time occurred during the first minute of the fatigue trial before declining back to nonfatigued levels. Rise Time, Rise Delay and Fall Delay were all unaffected by fatigue. Therefore, while the magnitude of ES-evoked torques decline substantially with fatigue, the overall pattern of torque production remains relatively unchanged.

Over a period of five minutes of continuous cycling, there was a reduction in power output by the quadriceps muscles of approximately 50%. Consistent with isometric results, however, there was little change in the shape of crank torque curves as power declined. When normalized to 100% peak torque, there was no apparent difference between trials collected when the muscles were fresh and when the muscle had fatigued. Muscles took the same time to generate and reduce torque in response to stimulation onset and cessation. Stimulation patterns developed for nonfatigued muscle would be equally suitable as the muscle fatigues, with no need for adjustment over time.

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