EFFECTS OF STIMULATION PATTERN AND FREQUENCY ON THE ABILITY OF THE HUMAN QUADRICEPS FEMORIS TO PRODUCE REPETITIVE DYNAMIC CONTRACTIONS

by

Amanda E. Turner

A thesis submitted to the Faculty of the University of Delaware in partial fulfillment of the requirements for the degree of Honors Bachelor of Arts in Neuroscience

Spring 2000

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ABSTRACT

This study tested the ability of sixteen different electrical stimulation trains to produce repetitive lower leg movements through a fifty-degree target excursion. Five constant-frequency trains (CFTs), five variable-frequency trains (VFTs), five doubletfrequency trains (DFTs) and a high-frequency (100Hz) burst were tested. The results indicated that the DFT was the most successful train type, and that the high-frequency burst was the most successful train overall. The repetitive doublet activation offered by DFTs may have stimulated force augmentation mechanisms many times within a train, therefore improving performance in fatigued muscle. In addition, the success of the high-frequency burst may have been due to activation of the same mechanisms responsible for force augmentation as those triggered by doublets.

Chapter 1

INTRODUCTION

Functional electrical stimulation (FES) artificially activates muscles to produce functional movement in individuals with central nervous system disorder. FES has been used to aid in functions such as grasping, standing and walking (11,13,20). Typically, FES stimulation patterns use trains of equally-spaced electrical pulses which are known as constant-frequency trains (CFTs). Although FES using CFTs can produce effective muscle contractions, rapid fatigue limits its utility in performing functional tasks (12). For FES to attain widespread clinical use, methods to minimize fatigue while still generating adequate forces must be identified. One method that has been explored in this laboratory varies the inter-pulse interval (IPI) within the trains delivered to the muscle. This, in turn, varies the instantaneous frequency of the stimulation; such trains are referred to as variable-frequency trains (VFTs).

Burke and colleagues showed that a particular type of VFT stimulation enhanced the force output of motor units in cat gastrocnemius (7). By inserting two pulses separated by a 5 to 10ms IPI in the beginning of a low-frequency CFT, these

researchers were able to produce a greater force-time integral (the area under a forcetime curve) than CFTs without the initial closely-spaced pair of pulses. They believed that this force enhancement was a result of the catch-like property of mammalian skeletal muscle. The catch-like property is an inherent property of the muscle and is similar to the true catch property of molluscan muscle in which similar force augmentation is observed, but is sustained without constant activation (6,7).

Binder-Macleod and colleagues have demonstrated that VFTs exploiting the catch-like property produce greater forces than CFTs in both human quadriceps muscle (4,5) and rat soleus muscle (3). In addition, their studies on humans indicate that this augmentation is much greater in fatigued muscle. They found that VFTs similar to those described by Burke (trains with an initial brief IPI followed by a constant, longer series of IPIs) provide greater peak forces and force-time integrals than comparable CFTs when stimulating fatigued muscle (5). This phenomenon was observed for isometric contractions both with the leg at 90° and at 15° of flexion, as well as in isovelocity movements (4,5,16).

Lee and colleagues demonstrated that similar catch-like inducing VFTs augmented muscle performance (joint excursion, work, peak power and average power) over CFTs in repetitive isotonic contractions elicited from both fresh and fatigued muscle (15). In addition, Lee and colleagues reported that VFTs with an initial pair of pulses separated by 5ms activated the fresh muscle better than other catch-like inducing VFTs (15). Another VFT pattern that has been described involves trains composed only of closely spaced pairs of pulses (doublets) separated

by longer, constant time intervals (inter-doublet intervals) (9,12). The pulses in these doublets are typically separated by 5 to 10ms. We have termed these doublet-frequency trains (DFTs).

Although many different CFTs and VFTs have been tested in the attempt to identify stimulation trains that minimize fatigue and maximize force, few studies have been done using DFTs (9,12). Karu and colleagues and Maxwell and colleagues, however, both reported that DFTs were able to augment the force-time integral produced by comparable CFTs and that 5ms doublets were optimal (12,19). In addition, recent modeling work in this laboratory suggested that DFTs were the optimal stimulation pattern for force production in fatigued muscle (9).

Another recent study in this laboratory examined the ability of different stimulation patterns to produce knee angle excursions, comparing the responses of a CFT with an IPI of 50ms (C50), a VFT consisting of an initial doublet separated by 5ms followed by constant pulses with 50ms IPIs (V50) and a DFT with 5ms doublets and an inter-doublet interval of 50ms (D50). The results demonstrated that the DFT was more successful than the VFT and CFT in moving the lower leg through a fiftydegree range of motion to a fixed target (unpublished observations). However, an ordering effect was noted in which the CFTs and VFTs performed better when they were not preceded by a DFT. Despite this ordering effect, the experiment did indicate that there was a difference in performance among the three train types tested.

The purpose of the present study was to determine the effect of varying the train frequencies on the ability of the different train types to repeatedly move the

lower leg through the target excursion. Repetitive, dynamic contractions were examined because they are similar to certain movements produced during FES (15). Due to the ordering effect observed when different train types were tested within the same session, only one train type (either DFTs, CFTs, or VFTs) was tested in an individual session.

A wide range of frequencies was tested because it has been shown that highfrequency stimulation produces high forces, but low-frequency stimulation is better at minimizing fatigue (2). In addition, Lee and colleagues demonstrated that when the human quadriceps was tested in the fresh and fatigued state with different 6-pulse trains, VFTs with an initial triplet of pulses (the first two IPIs were 5ms) were more successful than other VFTs and all CFTs in activating fatigued muscle (15). The VFTs tested in this study were therefore all initiated with a triplet of pulses with 5ms between each pulse in an attempt to maximize force output as the muscle fatigued.

Chapter 2 METHODS

2.1 Subjects

Data was collected from twelve healthy volunteer subjects (6 male) ranging in age from 20 to 32 years old (mean 24.25, S.D. 4.37 years). None had a history of neurological or cardio-vascular problems or any orthopedic problems in the leg being tested. Ten subjects were tested on their right leg and two subjects were tested on their left. The study was approved by the University of Delaware Human Subjects Review Board and all subjects signed informed consent forms.

2.2 Experimental Set-Up

Subjects were seated on a computer-controlled dynamometer (KinCom II 500-11, Chattecx Corporation, Chattanooga, TN) with hips flexed to about 75° and knees flexed to 90°. The dynamometer axis was aligned with the knee joint axis and the force transducer pad was positioned anteriorly against the tibia, about 3cm proximal to the lateral malleolus. Two 3" x 5" self-adhesive electrodes were used to stimulate the muscle. With the knee positioned at 90°, the anode was placed proximally over the motor point of the rectus femoris portion of the quadriceps femoris muscle. The cathode was placed distally over the vastus medialis motor point with the knee at 15° of flexion to compensate for skin movement during knee extension. The trunk, pelvis, and thigh of the leg being tested were each stabilized with straps.



Figure 1. Schematic for the experimental set-up used to test the different train types. The subject was stabilized across the trunk, shoulder, hips and thigh.

2.3 Equipment

A Grass S8800 stimulator with a SIU8T stimulus isolation unit (Grass Instruments, West Warwick, RI) was used to administer the stimulation. The stimulator was driven by a personal computer that controlled the timing parameters of each stimulation protocol. Force, angle and velocity data were digitized at 200Hz and stored for subsequent analysis.

2.4 Stimulation Test Trains

Sixteen different pulse trains were tested. Each train was 1s in duration and each individual pulse was 600µs. Constant-frequency trains (CFTs) with IPIs of 30ms (33.3Hz), 50ms (20Hz), 70ms (14.3Hz), 90ms (11.1Hz) and 110ms (9.1Hz) were tested. These five trains are hereafter referred to as C30, C50, C70, C90 and C110, respectively (see Figure 2). Five variable-frequency trains (VFTs) and five doublet-frequency trains (DFTs) were also tested. Each VFT had an initial triplet of pulses (three pulses with a 5ms IPI between each pulse) followed by a series of single pulses with constant IPIs. These IPIs were 30ms, 50ms, 70ms, 90ms and 110ms and the trains were labeled V30, V50, V70, V90, and V110, respectively. The five DFTs used a series of doublets (5ms IPIs) and the inter-doublet intervals were 30ms, 50ms, 70ms, 90ms and 110ms; these five trains were labeled D30, D50, D70, D90 and D110, respectively. In addition, a high-frequency burst with a constant IPI of 10ms was tested; it was labeled as the C10 burst.



Figure 2: Examples of the three stimulation patterns that were tested. The trains could continue for up to 1000ms. Vertical boxes represent each 600 μ s pulse. The D30 consists of 5ms doublets each separated by 30ms, the V30 begins with a 5ms triplet followed by constant 30ms IPIs, and the C30 consists only of constant 30ms IPIs.

2.5 Experimental Sessions

Each subject participated in six testing sessions during which two or three of the sixteen test trains were administered. Subjects were asked to refrain from strenuous exercise for 24 hours prior to each testing session and the sessions were separated by at least 48 hours. At the beginning of every session, subjects performed a maximum voluntary isometric contraction (MVIC) of their quadriceps muscle. A burst superimposition technique was used to make sure that the maximal contraction was being performed (22). If no force augmentation was produced by the superimposed burst, then the muscle was considered fully activated. The peak force evoked from the voluntary contraction was the subject's MVIC. Subjects were included in the study only if their voluntary effort was \geq 95% of their force with the supramaximal stimulation. If this criterion was not met within three attempts, the experimental session was rescheduled for another day.

After successful completion of the MVIC, the subject was asked to relax and the lower leg was weighed for ten seconds with the knee held at 15°, 30°, 45° and 60° of flexion. The weight of the limb was determined at each knee joint angle using a cosine function reflecting the angle of the leg with respect to the ground (17). All four estimates of the limb's weight were averaged and used for gravity correction during data analysis (17). While the knee was held at 90° of flexion, the stimulation intensity was set to produce an isometric force equal to 20% of the subject's MVIC using a 1000ms CFT train with an IPI of 50ms (C50). The C50 was delivered every five seconds to potentiate the muscle (until the force did not increase over three successive trains). The potentiation required ~10 stimulation trains and the intensity was adjusted during potentiation to maintain the force level at 20% of the MVIC. Once the intensity was set, it was not changed for the remainder of the test.

After setting the intensity, the subject was given a five-minute rest before the test trains were administered. Subjects were told to relax during the test and not to assist in the leg movements. The dynamometer settings were adjusted to begin all movements at 90° of knee flexion and to provide an isotonic resistance ("load") of 10% of the MVIC force. Before the KinCom was set to the isotonic protocol to allow

the leg to move during the test trains, the muscle was isometrically re-potentiated with ten, 7-pulse, 100 Hz stimulation trains delivered once every 5 seconds. Within 5 seconds of completion of the last potentiation train, the dynamometer was set to the isotonic mode and the first test train was administered. The dynamometer's velocity was set at the maximum of 250°/second. The rate of speed at which the dynamometer's lever arm accelerated to and from the start position was set at "LOW" for smooth transitions.

The stimulator was controlled by a custom-made circuit and software that terminated stimulation when the knee reached the 40°-flexion target angle. Thus, the subject did not receive the entire 1000ms stimulation train if the leg met the target angle in less than one second. The number of times the leg met the target, the time required for the leg to meet the target, the total number of pulses administered to the muscle (this varied depending on the time needed to reach the target), and the amount of work and power produced during each muscle contraction were calculated. The dynamometer was set so that the weight of the leg returned it to the starting position after the stimulation train was administered. Stimulation trains were delivered every 2 seconds and testing was stopped after the knee failed to reach the target three consecutive times. A maximum of 150 contractions could be performed for each train, as the KinCom automatically stopped running after 5 minutes of testing.

Up to three different trains were tested within one session and each test was separated by at least 10 minutes. Within each session, only one train type (CFT, VFT, or DFT) was tested, but different frequencies were used. Since there were

sixteen test trains, four of the six sessions tested three trains and two sessions tested only two trains each. Within each session, the order of frequencies to be delivered was randomized. The order of sessions to be tested (2 CFT sessions, 2 VFT sessions and 2 DFT sessions) was also randomized.

2.6 Data Management

All force responses were gravity corrected and the dependent variables were calculated for each shortening contraction using custom written software (Lab View 4.0). The variables studied were 1) the number of times the leg reached the 40° target angle (this was the primary outcome measurement) and 2) the time (ms) required for the leg to move from the 90° starting position to the target angle.

The rest time (time without stimulation) for each contraction was calculated by subtracting the time required to reach the target from 2000ms (total time between trains). The time to reach the target was used as a measure of stimulation time because the trains were terminated once the leg met the target. However, there were a few instances in which the subject took longer than 1000ms to reach the target, indicating that the time to target measurement did not equal total stimulation time since the maximum train length is 1000ms. These subjects were still able to reach the target after the stimulation had stopped because of the momentum of the leg. For these contractions, the stimulation time and rest time were both equal to 1000ms.

The number of pulses needed for each train to move the leg to the target was calculated by Lab View using the time to target data and the train frequency.

Excursion was calculated as the maximum lower leg displacement in degrees. As described for the trains that required longer than 1000ms to reach the target, the momentum of the leg caused many excursions to be greater than 50° even though stimulation was stopped at the 40° target angle. Average time to target, rest time and number of pulses were examined for the first and last target meeting contractions. The last target meeting contraction was the final contraction to meet the target before three consecutive failures.

2.7 Data Analysis

A two-way, repeated measures Analysis of Variance (ANOVA) was performed to compare the effect of train type and the effect of frequency on the number of times the leg met the target. The analyses of overall train type and overall frequency did not include the C10 burst data since it did not have a VFT and DFT 10ms IPI match. One-way, repeated measures ANOVAs were performed to analyze each train type (CFT, VFT, DFT) across IPIs (30ms, 50ms, 70ms, 90ms and 110ms) and to analyze each IPI across train type. In addition, one-way, repeated measures ANOVAs were used to compare the optimal CFT, VFT, DFT, and the C10 burst. When significant differences were observed, Bonferroni-corrected, paired t-tests were performed. Statistical significance was set at $p \le .05$ for all tests.

Chapter 3 RESULTS

3.1 Typical Subject Data

Complete data sets were collected for all 12 subjects. General trends for the number of successful excursions ($\geq 50^{\circ}$) and the time to target were observed by looking at CFT (including the C10 burst), VFT, and DFT data from typical subjects. For the CFTs, the C10 burst, the C30, the C50 and the C70 were the only trains to produce target-meeting (successful) contractions and the C10 burst produced the greatest excursions (see Figure 3a). In addition, for the CFTs, the C10 burst was the fastest to reach the target followed by the C30, the C50, and then the C70 (see Figure 3b). A steady increase in time was required to meet the target as the contractions proceeded.



Figure 3. Excursion (a) and time to target (b) CFT and C10 burst data for a typical subject. Figure 3a demonstrates how some trains carried the lower leg far beyond the fifty-degree target excursion. Data points on the x-axis of Figure 3b represent unsuccessful contractions. These six trains were tested in two separate sessions. One session tested C10, 110 & 50, respectively. The other tested C70, 30 & 90, respectively. The number of successful contractions for each train were: C10:37, C30:31, C50:26, C70:12, C90:0, C110:0.

The typical subject VFT data showed that the V30 was superior to the V50 in excursion, number of successful contractions produced and in time required to meet the target (see Figure 4). In addition, for this subject, the V70, V90 and V110 produced no target-meeting excursions. DFT data for a different subject revealed that the D50 met the target more times than the D30, and that the D70, D90 and D110 all produced successful contractions (see Figure 5). Although the D50 was the best DFT for this subject, the D30 produced greater excursions throughout most of the test. The time to target data indicated that the D30 and D50 required less time than the D70, D90 and D110 to meet the target. Interestingly, the D30 and D50 met the target in nearly the same time as each other throughout most of the test and the D70, D90 and D110 also met the target in similar times as each other (see Figure 5b).



a.

b.



Figure 4. Excursion (a) and time to target (b) VFT data for a typical subject. These five trains were tested in two separate sessions. One session tested V70, 90 & 30. The other tested V50 & 110. The number of successful contractions for each train were: V30:34, V50:29, V70:0, V90:0, V110:0.



b.

a.



Figure 5. Excursion (a) and time to target (b) DFT data for a typical subject. These five trains were tested in two separate sessions. One session tested D50 & 110. The other tested D30, 90 & 70. The number of successful contractions for each train were: D30:40, D50:44, D70:21, D90:24, D110:25.

3.2 Group Data

The results of the ANOVAs showed that train type and frequency had an effect on the train's ability to meet the target (see Figure 6). As demonstrated by the typical subjects, the high-frequency trains (IPIs of 30ms and 50ms) were better at producing target-meeting (successful) contractions than the low-frequency trains (IPIs of 70-110ms). There were no differences among the effects of the low-frequency trains themselves. Within the CFTs tested, the C30 and the C50 produced targetmeeting excursions significantly more times than the C70, C90 and C110 ($p \le .05$). As seen in the typical subject data, the C30 was the best CFT (it met the target the most times) when the C10 burst was not considered. Within the five VFTs tested, the V30 was the best train, but the V30 and the V50 both met the target significantly more times than the V70, V90 and V110 ($p \le .05$). Within the DFTs, the D50 was the best train. The D50 was the only train to meet the target significantly more times than the D90 ($p \le .01$), but both the D30 and D50 met the target significantly more times than the D110 ($p \le .05$). On average, the C10 burst produced more successful contractions than any other train that was tested (see Figure 6 and Table 1).

Comparisons of the most successful CFT, VFT, and DFT (C30, V30, and D50) to each other and to the C10 burst indicated that there were no significant differences among the four most successful trains. The results of one-way ANOVAs also showed that for four of the five common IPIs tested (30, 50, 70, 90 and 110ms), train type had an effect. At IPIs of 50, 70 and 90ms, the DFTs were significantly more successful than the CFTs ($p \le .05$). In addition, the D110 was more successful

than both the C110 and the V110 ($p \le .05$). Train type did not have an effect at an IPI of 30ms (see Figure 6).

There was a great deal of variation among individual subjects for the number of times they met the target (see Table 1). For example, only one subject was able to meet the target with the C90 (she met the target once) and only one subject was able to meet the target with the V90 (she met the target 84 times). The subject who did so well with the V90 also met the target 76 times with the V70, a train that was not successful for most other subjects. In addition, the C10 burst was the train that, on average, met the target the most times, but it was only superior to the C30 for six subjects, the V30 for six subjects, and the D50 for five subjects. Thus, the D50 produced more target-meeting excursions than the C10 burst for seven of the twelve subjects. In addition, both the C10 burst and the V30 each met the target the most times for four individual subjects (see Table 1). The average C10 value was very high because the subjects who performed the best with that train performed very well.



Figure 6. Average number of target-meeting excursions for all sixteen train types, n=12. F and p values from each significant ANOVA are listed below. Two-way ANOVA:

Train: F=8.984, p=.001 Frequency: F=53.341, p=.000

Interaction: F=4.349, p=.000

One-way ANOVAs:

Effect of train type at IPI50: F=5.323, p=.013, at IPI70: F=10.827, p=.001, at IPI90: F=5.434, p=.012, at IPI110: F=8.230, p=.002

Effect of frequency within CFTs: F=16.926, p=.000,

within VFTs: F=21.090, p=.000, within DFTs: F=7.470, p=.000

x indicates significantly greater than 70, 90 and 110 of the same train type (x $p \le .05$, xx $p \le .01$)

* indicates significantly less than DFT of corresponding IPI (* $p \le .05$, ** $p \le .01$) o indicates DFTs that are significantly greater than D110 (o $p \le .05$, oo $p \le .01$) ^ indicates DFTs that are significantly less than D50 (o $p \le .05$, oo $p \le .01$) Error bars represent standard error.

Table 1. Individual subject data for the average number of target-meeting contractions produced by each train, n=12. "S" refers to subject #. No subjects met the target with the C110 or V110, and the C90 only produced one successful contraction. The train that produced the most successful contractions for each subject is in bold.

S	C10	CFTs			VFTs				DFTs							
		30	50	70	90	110	30	50	70	90 1	10	30	50	70	90	110
1	43	38	13	0	0	0	98	79	76	84	0	40	44	21	24	25
2	28	29	22	0	0	0	35	34	1	0	0	32	35	28	29	10
3	25	38	29	7	0	0	20	24	2	0	0	31	41	31	24	5
4	26	32	30	0	0	0	34	29	0	0	0	33	36	44	31	25
5	68	53	36	0	0	0	42	16	0	0	0	59	27	33	0	0
6	150	34	10	0	0	0	36	30	0	0	0	32	39	33	0	3
7	39	37	0	0	0	0	38	0	0	0	0	19	21	16	0	0
8	25	27	0	0	0	0	43	0	0	0	0	33	40	7	0	0
9	150	90	0	0	0	0	79	98	1	0	0	55	84	26	55	57
10	51	69	41	1	1	0	47	56	10	0	0	58	63	50	67	59
11	37	31	26	12	0	0	39	28	20	0	0	33	34	30	34	35
12	34	52	33	0	0	0	60	49	0	0	0	51	55	78	34	0
⊼:	56.33	44.17	7 20	1.67	.08	0	47.58	36.9	9.17	7	0	39.7	43.25	33.1	24.8	18.3
SD:	45.48	18.9	14.9	3.8	.29	0	21.6	29.5	21.9	24.2	0	12.9	17.02	18.2	22.1	22.0

As demonstrated in the typical subject data, the average time to target for the first and last successful contraction clearly indicated that more time was required to reach the target at the end of a test than at the beginning. By the last successful contraction, all but five trains needed at least 1000ms to reach the target, but for the first contraction, all trains met the target in well under 1000ms (see Figure 7). In addition, the group DFT time to target data illustrated the same phenomenon as the typical subject DFT data in that the D30 and D50 both required about the same amount of time to reach the target, and the low-frequency DFTs also required about the same amount of time to reach the target (see Figures 5b and 7). This effect was not observed for the CFTs or VFTs.

Although the results of each train were examined, the C90, C110 and V110 data were not included in Figures 7-9. No subjects met the target with the C110 or V110, and only one subject met the target with the C90, and she met the target only one time. The average C90 value for the first contraction was therefore equal to the average C90 value for the last contraction. This offered misleading evidence suggesting that with the C90, no increase in time was required to reach the target over the course of a test. In addition, it should be noted that the results for the V90 reflected only one subject's data, because she was the only one to meet the target with that train (see Table 1). However, her data were included in Figures 7-9 because she met the target 84 times indicating that the V90 could be successful for some individuals.

The average rest times (time without stimulation) for the first and last targetmeeting contractions indicated that much more rest time was available after the first contraction than after the last contraction. By the last contraction, most trains were delivered in entirety so the subjects had the minimum rest time of 1000ms. For the first contraction however, some trains met the target as fast as 503ms (\pm 132) (D50), therefore allowing for a rest time of 1497ms. In addition, the high-frequency trains allowed for a longer rest-time than the low-frequency trains (see Figure 8).





Figure 7. Average time to target for the first target-meeting contraction, n=12. C90, C110, and V110 values are not included. Error bars represent standard error.



Rest Time for FIRST Contraction

Figure 8. Average time without stimulation (rest time) for the first target-meeting contraction, n=12. C90, C110 and V110 values are not included. Error bars represent standard error.

The average number of pulses delivered for the first and last contractions indicated that subjects received many more pulses in the last successful contraction than in the first. Table 2 lists the number of pulses for each train when the train lasted 1s. This maximum number of pulses was delivered in the last successful contraction for the trains that lasted longer than 1s (all but five trains). However, for the first contraction, most subjects reached the target in less than 1s causing termination of the pulse delivery before the full-length train was administered (see Figure 9).

Table 2. Number of pulses in 1000ms trains for each train type and frequency. This number of pulses was only delivered when the subject required 1s or more to reach the target. Each pulse was 600μ s in duration. Due to the doublets, DFTs contained many more pulses than CFTs and VFTs with comparable IPIs.

	NUMBER OF		NUMBER OF		NUMBER OF
IRAIN	PULSES	IRAIN	PULSES	IKAIN	FULSES
C10	101				
C30	34	V30	36	D30	58
C50	21	V50	22	D50	38
C70	15	$\mathbf{V70}$	17	D70	28
C90	12	V90	14	D90	22
C110	10	V110	12	D110	18

100 90 80 Number of Pulses 70 60 50 40 30 20 10 0 C⁹ C⁹ C¹⁰ 230 250 270 290 03° 05° 01° 08° 010 CJ0

Number of pulses to target for FIRST contraction

Figure 9. Average number of pulses to target for the first successful contraction, n=12. C90, C110 and V110 values are not included. Error bars represent standard error.

Chapter 4

DISCUSSION

4.1 Train Performance

The purpose of this study was to test sixteen different stimulation trains to determine which would produce the greatest number of target-meeting excursions. Overall, the DFTs met the target more often than the CFTs for the five common frequencies tested (IPI30-110ms). This finding supports the previous findings from this laboratory (unpublished observations). However, to our surprise, the high frequency trains (IPIs of 30 and 50ms) were the most successful within each train type (they met the target the most times), and the C10 burst was the most successful train overall.

The averages used to measure the success of the trains were misleading in some cases. Although the C10 burst was determined to be the most successful train on average (56.33 target-meeting excursions), the standard deviation was large (\pm 45.48). In addition, although the overall mean number of times to target was greater for the C10 burst than all other trains, the C30 and V30 each outperformed the C10 for six individual subjects, and the D50 outperformed the C10 for seven out of twelve

subjects. However, two subjects met the target the maximum 150 times with the C10, markedly increasing the average for that train. In addition, those subjects may have continued far past 150 successful contractions with the C10, and in this respect, our average may underestimate the ability of the C10 for those subjects. We did not test a D10 (5ms doublets each separated by 10ms) or a V10 (an initial triplet followed by pulses evenly spaced by 10ms) because it was thought that the frequency of those trains would be too high and therefore too fatiguing for clinical use and also because we did not anticipate a great difference in performance between a 5 and 10ms IPI.

In addition to the unexpected success of the C10, the C30 and the V30 performed better than predicted. Based on previous results from our laboratory for dynamic contractions in fresh muscle, we predicted that the C50 would be the most successful CFT (17). The results indicated that the C10 and C30 were both superior to the C50, but the C10, C30 and C50 were all more successful than the low-frequency CFTs (IPIs of 70, 90 and 110ms). Based on previous work in this laboratory we also predicted that the V50 would be the most successful VFT (17). The V30, however, produced the most target-meeting excursions among VFTs. As with the CFTs, the V30 and V50 both met the target significantly more times than the V70, V90 and V110. Despite our prediction that they would be too fatiguing, the C30s and V30s were able to produce more target-meeting excursions than the C50s and V50s.

Within the DFTs, the D50 and the D30 were the most successful trains. Due to the findings of Karu and colleagues for isometric contractions, we predicted that

DFTs with inter-doublet intervals of 50-80ms would be the optimal DFTs (12). Our prediction therefore did not account for the relative success of the D30. The results also indicated that the D50, D70, D90 and D110 were able to produce many more target-meeting contractions than the corresponding CFTs and the V110 indicating that the DFTs were clearly the most successful trains at low frequencies (IPIs of 70, 90 and 110ms).

One possible reason why the DFTs were more successful at low frequencies (IPI 70-110ms) is because those DFTs reached the target faster (653.86 ± 4.59 ms, first contraction) than low-frequency (IPI 70-110ms) CFTs (750.5 ± 58.69 ms) and VFTs (707.17 ± 66.70). This quick movement allowed the muscle to have a longer rest time (time without stimulation) per contraction cycle when being tested with DFTs, therefore possibly minimizing the fatigue. This may also explain the success of the C10 burst for some subjects, for on average it was able to reach the target faster than all of the other trains (437 ± 47.49 ms, first contraction) therefore giving it a longer rest time between contractions. Interestingly, despite the quick time to target, the DFTs (all trains) and the C10 both delivered more pulses to the muscle in the first contraction (21.01 ± 8.11 and 46.75 ± 10.49 , respectively) than the other CFTs (12.48 ± 5.06) and all of the VFTs (15.47 ± 4.36), suggesting that perhaps the number of pulses did not have a major effect on fatigue.

The relative failure of the low-frequency VFTs (V70, 90 and 110) was a surprising result since these trains were thought to be catch-like inducing. A possible explanation for this is the length of the trains that were tested. The VFTs that were

previously found to be superior to CFTs were short trains, such as the six-pulse VFTs used by Lee and colleagues (15,17). The present study suggested that 1000ms VFTs (with 12-36 pulses) might have been too long to produce a marked improvement over comparable CFTs.

Despite the great differences between the CFTs, VFTs, and DFTs at low frequencies, when the best DFT (D50), VFT (V30), and CFT (C30) were all compared to each other and to the C10 burst, there were no significant differences between the four trains' abilities to produce successful contractions. However, the D50 was better than the C30 for all but four subjects and the success of the DFTs across a wide range of frequencies was unique only to that train type. In addition, for the first contraction, the D30 and D50 required about the same amount of time to reach the target (513 ± 179 ms and 503 ± 132 ms, respectively) and the D70, D90 and D110 also required about the same amount of time to meet the target (649 ± 220 ms, 656 ± 159 ms, and 657 ± 141 ms, respectively). This phenomenon was observed for the typical subject as well as for the group averages and it suggested that perhaps one low-frequency pattern was needed to reach the target in ~515ms and another highfrequency pattern was needed to reach the target in ~660ms.

4.2 Muscle Differences

A trend observed in this study was that individual differences among subjects allowed some trains to work well for certain subjects and not at all for others. As described above for the C10, these differences may explain why the low-frequency VFTs worked extremely well for one subject (she met the target 76 times with V70 and 84 times with V90), but hardly worked at all for the others. Ding and colleagues predicted that these differences would occur (9). They developed a mathematical model to predict such differences in an individual muscle responding to different train types and explained that it is very difficult to identify optimal muscle activation patterns due to individual differences in muscle contractile properties (9).

In addition to inherent physiological differences among subjects, the subjects in this study were tested over six experimental sessions and were therefore vulnerable to other factors such as variations in temperature and time of testing that may have affected their responses to different trains (8,18). In an attempt to minimize these within-subject effects, we separated each test by at least 48 hours and requested that subjects refrain from strenuous exercise for at least 24 hours before testing. We used a MVIC burst superimposition technique to be sure that the muscle was performing at its maximum ability for each testing session (22). The subject who performed so well with the V70 (met target 76 times) and V90 (met target 84 times) offered an example of such an individual difference; she met the target only 21 times with the D70 and 24 times with the D90.

4.3 The Catch-like Property

Despite any individual differences observed in this study, the success of trains with an initial burst of pulses (doublet or triplet-initiated VFTs) over CFTs is generally thought to be due to their catch-like inducing nature. The catch-like property of skeletal muscle is the tension enhancement produced by trains with a high-frequency burst of pulses followed by much longer, constant IPIs (7). Trains with initial bursts of pulses followed by longer IPIs are therefore referred to as catchlike inducing trains, for they exploit the inherent catch-like property of skeletal muscle and increase the force output previously produced by CFTs (15).

Studies of catch-like inducing trains have suggested that their ability to augment force is due to increased muscle stiffness and increased release of calcium caused by the initial doublet of pulses (4,10,21). The initial doublet is thought to increase force and stiffness in the muscle, therefore allowing the rest of the train to produce greater forces (21). The other proposed mechanism for the force augmentation produced by the initial doublet in catch-like inducing trains is an increase in calcium release from the sarcoplasmic reticulum during muscle contraction (10).

In the present study, the DFTs were clearly the most successful trains at low frequencies and the C10 was the most successful train overall. The DFTs consisted of a series of repetitive doublets (bursts) throughout the train. These doublets may have repeatedly increased calcium release and muscle stiffness throughout the train, therefore producing force augmentation many times within a train rather than only at the start of the train as in VFTs. As the muscle fatigued, the initial burst provided by VFTs may not have produced enough force to maintain functional contractions, but the repetitive doublet activation offered by DFTs may have been optimal in fatigued muscle (9).

Interestingly, Kudina and Alexeeva and Bawa and Calancie observed naturally-occurring repetitive doublets in human motorneurons at the beginning of voluntary muscle contractions (1,14). It was thought that these doublets were the result of an increase in excitatory synaptic input and were also due to afterdepolarization (electrical excitation immediately after neuron firing) of the cell membrane which caused an additional pulse to fire directly after the initial pulse (14). One could speculate that the neurons were using repetitive doublets to exploit the catch-like property and maximize force output at the beginning of a contraction.

Previous DFT work in this laboratory including the unpublished observation of DFT success in repetitive dynamic contractions, and the modeling work by Ding and colleagues, allowed us to predict the success of DFTs over CFTs (4,9). The success of the C10 however, was surprising because it was a very high-frequency train (100Hz) and was therefore expected to be very fatiguing (2). In addition, since the C10 consisted of a constant series of single pulses (rather than a burst followed by longer IPIs), it was not expected to be as successful as the catch-like inducing trains, because they had previously been shown to improve performance over CFTs (4,7,15).

Although the C10 was a constant-frequency train, the 10ms IPIs that separated each pulse were so short that the C10 may have activated the same mechanisms responsible for force augmentation as those caused by doublet stimulation. The C10 was quite unlike the other CFTs tested (they had a minimum of 30ms between pulses) and was really more like a DFT composed of closely spaced 10ms doublets. Burke and colleagues reported that trains with a 10ms initial doublet caused an

augmentation in the force time integral, indicating that trains initiated with a C10 activated the catch-like property (7). However, the C10 tested in the present study was a 1000ms burst of equally spaced pulses and was not followed by a series of longer, constant IPIs. The success of this CFT (even as the muscle fatigued) suggests that for some individuals, trains other than the catch-like inducing trains (a burst followed by longer, constant IPIs) could be useful in producing functional movements.

Clearly the C10 was a successful train, however, as previously mentioned it was only more successful than the C30 for six subjects, the V30 for six subjects and the D50 for five subjects. The C10 burst was the best train for only four individuals, and the V30 was the also best train for four individuals. Therefore, although it produced the greatest average number of target-meeting contractions, the C10 was not the optimal train for the majority of subjects. None of the trains tested in this study proved to be optimal across subjects for moving the lower leg through a target excursion. This was partially due to inherent physiological differences among individual subjects, but general trends were observed that could now be used to construct trains that may be more successful (9).

4.4 Proposed Optimal Train

Considering the outstanding performance by the C10 and the success of DFTs observed both in the present study and previously in this lab (unpublished observations), we suggest that the optimal train for producing target-meeting

contractions may involve a combination of these two train types. In addition, because many studies have now shown that trains with an initial high-frequency burst followed by a lower-frequency portion best exploit the catch-like property of skeletal muscle, we propose that trains with a burst of three or more pulses at the onset of a DFT with longer inter-doublet intervals may be optimal (4,7,23). Such a train would utilize the high forces produced by the burst to initially meet the target, and then sustain the movement and minimize fatigue with the lower-frequency repetitive doublets.

Interestingly, Van Lunteren & Sankey recently examined the effects of VFT stimulation of the rat diaphragm muscle and found that the best train for inducing the catch-like property (it caused the greatest increase in the force-time integral) was initiated by a four pulse C10 followed by a low frequency (15-25Hz) series of equally spaced pulses (23). This finding supports our prediction that initiating trains with a longer burst (\geq 3 pulses) may increase force output and therefore help to improve the target-meeting ability of the trains. In addition, we propose that due to the ability of doublets to augment force in fatigued muscle, using repetitive doublets (low-frequency DFTs) subsequent to the burst will further help to maintain functional movement and minimize fatigue (9). Future research could examine trains initiated with a high-frequency burst followed by lower frequency doublets to determine their ability to produce target-meeting contractions.

Chapter 5

CONCLUSION

The DFTs were the most successful train type for producing target-meeting contractions over a wide range of frequencies, and the C10 burst was the most successful train overall. It appeared as though a high-frequency burst (i.e. doublets or trains) was needed to augment force levels as the muscle fatigued and to maintain movement through the target excursion. In addition, the success of the C10 indicated that for some subjects, a high-frequency burst was able to produce high forces without causing a detrimental amount of fatigue. Due to the success of these trains and the nature of catch-like inducing trains, it is proposed that the optimal train for producing target-meeting contractions may be an initial burst at the onset of a DFT with longer inter-doublet intervals. Identification of an optimal train for producing functional movements of the lower leg could be helpful in the clinical treatment of individuals with central nervous system dysfunction.

APPENDIX

Amande Turner

49-178

HUMAN SUBJECTS PROTOCOL RENEWAL University of Delaware

Protocol title	Force Optim Contraction	ization in Huma s	an Skele	etal Muscle Du	iring Isotonic
Current HS number	'HS 98-146				
Principal Investigator	Stuart Binde	er-Macleod; Phy	sical Th	erapy	
Other investigators	Samuel Lee				
Type of review	Expe	dited	X	Full board	
Original approval date	06/15/98				
Most recent approval date	06/15/98		Appro	val expires	06/14/99
HSRB Approval Signature_ New HS number <u>99 -</u>	Critil . 178	Densur	al next	Date 2 expires <u>6/2</u>	June 1999

PROTOCOL STATUS. Please indicate (/) the status of this project.

Request protocol continuance

- A. Active--project ongoing.
- B. D Currently inactive-project was initiated but is presently inactive.
- C. D Inactive--project never initiated but anticipated start date is _____

Request protocol termination

- D. D Inactive--project never initiated.
- E. Completed-no further activities will involve human subjects.
- 2. SUBJECTS

4-8

Number of subjects who have completed protocol

Estimated number of additional subjects needed to complete the project

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