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ORIGINAL ARTICLE

The Effect of Using Variable Frequency Trains During Functional Electrical Stimulation Cycling

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ABSTRACT

Objectives. This paper describes an experimental investigation of variable frequency stimulation patterns as a means of increasing torque production and, hence, performance in cycling induced by functional electrical stimulation. **Materials and Methods.** Experiments were conducted on six able-bodied subjects stimulating both quadriceps during isokinetic trials. Constant-frequency trains (CFT) with 50-msec interpulse intervals and four catchlike-inducing trains (CIT) were tested. The CITs had an initial, brief, high-frequency burst of two pulses at the onset of or within a subtetanic low-frequency stimulation train. Each stimulation train consisted of the same number of pulses. The active torques produced by each train were compared. Parametric main effect ANOVA tests were performed on the active torque-time integral (TTI), on the active torque peaks and on the time needed to reach those peaks (T2P). **Results.** The electrical stimulation of the quadriceps produced active torques with mean peak values in the range of 1.6–3.5 Nm and a standard error below 0.2 Nm. CITs produced a significant increase of TTI and torque peaks compared with CFTs in all the experimental conditions. In particular, during the postfatigue trials, the CITs with the doublet placed in the middle of the train produced TTIs and torque peaks about 61% and 28% larger than the CFT pattern, respectively. In addition, the CITs showed the lowest reduction of the performance between prefatigue and postfatigue conditions. **Conclusions.** The use of CITs improves the functional electrical stimulation cycling performance compared with CFT stimulation. This application might have a relevant clinical importance for individuals with stroke where the residual sensation is still present and thus the maximization of the performance without an excessive increase of the stimulation intensity is advisable. Therefore, exercise intensity can be increased yielding a better muscle strength and endurance that may be beneficially for later gait training in individuals with stroke.

KEY WORDS: *Catchlike-property, functional electrical stimulation cycling, variable frequency trains.*

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Introduction

The cycling movement induced by the stimulation of quadriceps, hamstrings, calf, and gluteal muscle groups has become one potential method to rehabilitate individuals with spinal cord injuries (SCI) or stroke. We refer to this artificial movement as functional electrical stimulation (FES) cycling. FES cycling improves muscle strength and trophism (1), reduces joint stiffness (2), and increases cardiopulmonary fitness (3) and blood circulation (4). All these benefits are crucial for the improvement of the general health of individuals with SCI. In addition, FES cycling could be a beneficial method in the rehabilitation of individuals with an acute stroke because it is a bilateral and symmetrical movement such as walking. Different from walking, FES cycling can be performed in a very comfortable and safe posture for the patients without need for external balance support. The use of FES induces afferent and efferent stimulation resulting in limb movements plus cutaneous and proprioceptive inputs. This process, during the acute stage of stroke, could be crucial in "re-educating" patients with hemiplegia how to perform the movement properly (5). Furthermore, muscle strength is preserved, which is a basic prerequisite for walking. Despite these important advantages, one of the main problems that FES faces is a rapid onset of fatigue in the electrically stimulated muscles. Muscle fatigue is a transient decrease in the force-generating ability of a muscle (6,7). A current method used to compensate for fatigue during FES cycling is to increase the current amplitude, which results in the recruitment of additional nonfatigued muscle fibers (8). However, the amplitude cannot be indefinitely increased. In fact, at high levels of stimulation, it is possible that all motor units associated with the target nerve are activated, so that a further increase in stimulation level does not elicit increased muscle response. Because individuals with stroke have intact sensation in their healthy leg and abnormal sensation in the impaired leg, the use of high levels of current amplitude is not feasible because it is painful and not tolerable. Therefore, it is important to find another method to produce a cycling stimulation pattern designed to maximize performance in terms of the produced power output and to delay the occurrence of the fatigue effect.

There have been several approaches in the design of stimulation patterns for FES cycling (9–14). All these strategies differ in the choice of crank-angle ranges over which each muscle group is activated. However, in all these studies the stimulation pattern used is always a constant-frequency pulse train (CFT). The central nervous system optimizes muscle activity with an initial burst followed by a slowing of firing rate (15). Trying to mimic the central nervous system by tailoring stimulation patterns for particular motions might be an interesting method to improve the effectiveness of FES applications. Recently, researchers investigated whether variable frequency trains, instead of CFTs, can be used in FES applications. The variable frequency train can take advantage of the catchlike property; that is, the force augmentation that occurs when an initial, brief, high-frequency burst of two to four pulses is included at the onset of a subtetanic low-frequency stimulation train (16). A stimulation train attempting to exploit the catchlike property of the skeletal muscle is called catchlike-inducing train (CIT).

During sustained stimulation, muscle fatigue is a strong function of stimulation frequency with higher frequencies resulting in a faster rate of force decline (17–20). In addition, fatigue can be directly related to the total number of stimulation pulses received, independent of stimulation frequency (20–22).

The CITs were mainly applied in isometric conditions. However, it has been consistently shown that CITs enhance both isometric (23,24) and nonisometric (25,26) muscle performance compared with CFTs, especially when muscles are fatigued. Binder-Macleod and Kesar suggested that the increase in the occurrences of short interspike intervals in the fatigued state during volitional movements compensates for the loss of muscle force that accompanies fatigue (16). The use of doublets (two fast initial pulses) resulted in a higher isometric force per pulse compared with single pulses both in SCI and able-bodied individuals (24). The effect produced during nonisometric conditions strongly depends on the specific motor task (25). Thus, the only way to understand whether CITs are efficient during FES cycling is to compare the performance generated by CFT and CIT patterns during this movement.

Because muscle fatigue is a major problem in FES cycling, CITs may be especially effective in augmenting force and performance compared to the stimulation with CFTs. Only one study analyzed the effect of CITs during cycling in individuals with SCI, but CITs did not significantly improve the FES cycling performance compared with standard CFT patterns (8). Many reasons may explain these results. First, the current-amplitude values of all the muscles were increased together based on the assumption that the fatigue progresses at the same time and in the same way for all the muscles. Second, all the tested CITs had one pulse more than the CFTs that may induce more muscular fatigue (21). The cycling performance for the different investigated patterns was assessed by the endurance and total mechanical work done during isotonic cycling against a constant resistance. Cadence was controlled by modulation of stimulation intensity to be 50 r.p.m. When maximal stimulation intensity was reached, cadence was allowed to drop to 35 r.p.m. before the cycling trial was stopped. With the used ERGYS isotonic trainer (Therapeutic Alliances Inc., Fairborn, OH, USA), only the work required to move the flywheel is taken into account. The work is calculated from the cadence and the adjusted resistance at the flywheel. The muscles' work to move the legs itself is

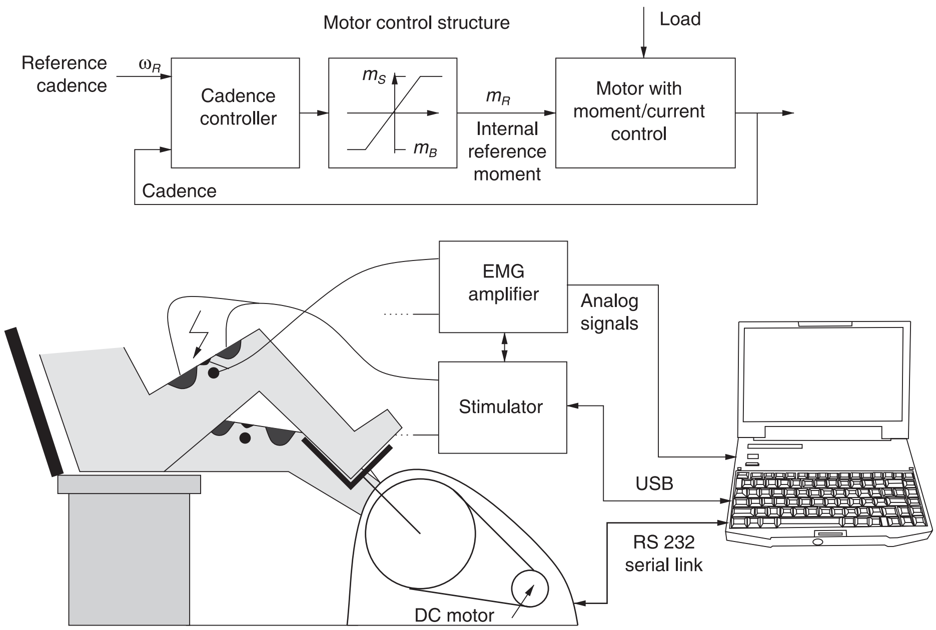

FIGURE 1. Experimental setup and motor controller structure.

not considered. Because the total power output of FES cycling is quite low, this number should not be neglected. The power needed to advance the legs depends strongly on the sitting posture and the muscle tone of the patient and varies from session to session.

The purpose of our study was to understand whether the use of CITs during cycling of able-bodied subjects enhances performance and decreases fatigue in comparison to CFTs. In the pursuit of this aim, we developed a protocol, simpler than the one by Janssen et al. (8), in order to isolate any effects of CITs during FES cycling in terms of torque and generated energy. Therefore, we compared the cycling performance obtained by stimulating only the quadriceps of both legs with different stimulation patterns during isokinetic conditions on a motor-controlled ergometer. It was possible to distinguish the contributions of the two quadriceps because at each instant of time only one of the two generates torque at the crank.

Methods

Subjects and Experimental Setup

After giving written informed consent, six healthy subjects (five men and one woman participated in the experimental sessions. Age, height, and body weight of the subjects were 27.7 ± 3.5 years, 172.0 ± 8.3 cm, and 72.2 ± 15.1 kg, respectively.

The experimental setup was based on a commercially available ergometer equipped with a DC motor (THERA-vital™, medica Medizintechnik, Hochdorf, Germany). A customized eight-bit shaft encoder was installed on the ergometer to measure the crank angle. Two foot orthoses were mounted on the pedals to fix the ankles and stabilize the legs in the sagittal plane. The ergometer can transfer the measured motor torque and cadence to a PC and can receive a command to control the motor through a serial interface (RS 232). The experimental setup is reported in Fig. 1.

A calibration of the torque was carried out by moving different weights of known mass fixed at one crank arm during trials in which constant speed was maintained by the motor. The sensor provided a torque signal with a precision of 0.5 Nm and an accuracy of 0.01 Nm.

Mechanical connection between the shaft of the electric motor and the crank was established through a belt. The electric motor controlled the speed in the range 10–60 r.p.m. whereas the reference cadence ω_R, the maximum support torque m_S and maximum brake torque m_B of the motor could be specified via the serial link (Fig. 1). The torque range was –15 to 15 Nm.

In the case of isokinetic cycling exercises, the motor was controlled to maintain a desired cadence ω_R while the cyclist tried to work against the motor aiming to accelerate the crank by electrical stimulation of the muscles. The measured motor torque was used to estimate the muscular drive moment at the crank.

A motor-equipped FES cycling ergometer was used within the study for the following two reasons:

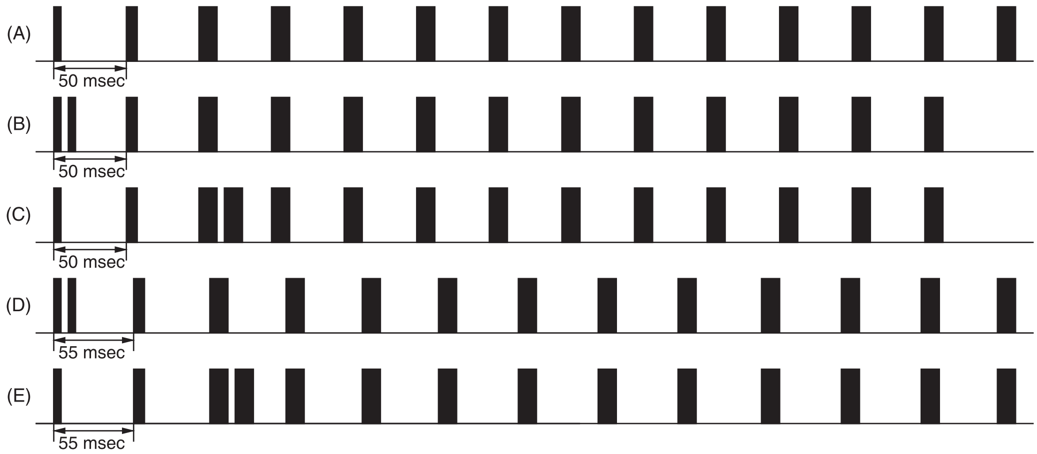

FIGURE 2. Stimulation patterns used during the experiments/sessions/trials. (A) CFT with an IPI of 50 msec (CFT50); (B) CIT with an initial doublet and with an IPI of 50 msec (CITID50); (C) CIT with a doublet in the end of the ramp of the pulse width and with an IPI of 50 msec (CITMD50); (D) CIT with an initial doublet and with an IPI of 55 msec (CITID55); (E) CIT with a doublet in the end of the ramp of the pulse width and with an IPI of 55 msec (CITMD55).

1. Persons with a low sensory threshold for pain can perform cycling exercises as the motor can give adequate support in compensating friction.
2. Exact assessment and control of the total muscular work rate is possible for isokinetic cycling (11,27–29).

The NeuroLog™ System by Digitimer, UK, was used to build a four-channel electromyographic (EMG) amplifier (30). The preamplifier offered a mute input for suppression or reduction of overload artifact signals. Volitional muscle activity of the quadriceps was detected from the EMG readings during the stimulation experiments as described by Schauer et al. (30). The subjects were instructed to relax their leg muscles during the tests.

An eight-channel stimulator (RehaStim Pro, HASOMED, Magdeburg, Germany) was used to stimulate the quadriceps of both legs. Control of the stimulator by the PC was established through an optically isolated USB interface. Electrical stimulation and EMG measurements were synchronized.

All the setup was connected to a Linux-PC running Matlab/Simulink™ for data acquisition and control of the ergometer and stimulation device. The EMG signals were acquired at a rate of 1 kHz through an acquisition board (DAQ board ME-2600i PCI, MEILHAUS electronic, Puchheim, Germany).

Experimental Protocol

Stimulation Patterns

A representation of the five different stimulation trains tested is shown in Fig. 2. To increase the readability of the scheme, only the positive part of each biphasic stimulation pulse is drawn. To avoid a different fatigue effect due to the different number of pulses delivered by the trains, all the tested pulse trains had the same number of pulses. In addition, all the tested patterns started at the same crank angle and consisted of an initial “ramp up” of the pulse width followed by a period of constant pulse width. We decided to use the initial “ramp up” because it is commonly used in clinics to increase the toleration to the stimulation. All the CITs tested included two closely spaced pulses (doublet) with an interpulse interval (IPI) of 5 msec following (24,31–33).

We compared the CFT with an IPI of 50 msec (CFT50; in Fig. 2A) with different CITs: a CIT with a doublet in the beginning of the ramp, and with an IPI of the remaining lower-frequency portion of 50 msec (CITID50; in Fig. 2B); a CIT with a doublet for the third and fourth pulses following the ramp up, and with an IPI for the other pulses of the train of 50 msec (CITMD50; in Fig. 2C); a CIT with an initial doublet with an IPI of the lower-frequency portion of 55 msec (CITID55; in Fig. 2D); a CIT with a doublet in the third and forth pulses and with an IPI for all the other pulses of the train of 55 msec (CITMD55; in Fig. 2E). Also note in Fig. 2, that the 55 msec IPI of the CITID55 and CITMD55 was selected such that these CITs would have the same number of pulses and train duration as the CFT50, and similar frequency (18.2 pulses per second vs. 20 pulses per second).

Experimental Sessions

Once the test subject was seated on the ergometer, the stimulation current amplitudes were selected and the

EMG electrodes were attached. For a fixed pulse width of 500 μsec, the current amplitude for the quadriceps was increased in steps of 5 mA up to the maximal level the subject could tolerate. Current amplitudes during the tests were in the range 25–40 mA yielding visible tetanic muscle contractions. Stimulation settings were leg-specific. During the experiments, pedalling was maintained at 40 r.p.m. by the motorized ergometer. The static stimulation angle range was between 40 and 180 degrees for the right leg and the same range shifted by 180 degrees for the left leg. The zero reference of the crank angle was the point in which the crank was horizontal with the left pedal forward. The static stimulation range is shifted forward of 150 msec in order to take into account the physiological delay, that is, the time between the instant in which the stimulation starts and the beginning of the contraction effect (in terms of torque).

The test consisted of two different sessions performed on two different days. On the first day, CFT, CITID50, and CITID55 (A, B, and D in Fig. 2) were compared and on the second day (1 day after), CFT, CITMD50, and CITMD55 (A, C, and E in Fig. 2) were tested. In both days, a prefatigue test, a fatigue-inducing test, and a postfatigue test were included. A flow diagram of the experimental procedure is shown in Fig. 3.

During the initial 40 sec of the prefatigue test, the subjects were not stimulated at all and cycled passively with the legs moved by the motor only. In the remaining part of the tests both the quadriceps were stimulated in a fixed range of the crank angle. During this phase, the stimulation patterns were alternated and each pattern was delivered to both the quadriceps for 20 sec. Similar to the investigation by Lee et al. (33), the three trains were presented in the chosen order and then they were repeated in reverse, totaling six trains (ie, a 1-2-3-3-2-1 sequence) in order to reduce the fatigue effect. The prefatigue test was repeated twice with a rest of 5 min in between the two trials.

The fatigue inducing test consisted of 10 min of cycling induced by the stimulation of both the quadriceps using a CFT50 pattern.

Postfatigue tests began immediately after the fatigue-producing train and were exactly the same as the prefatigue tests but there was not any rest phase in between the two trials.

The program was approved by the ethical review board of the rehabilitation center of Villa Beretta (Costamasnaga, Como, Italy).

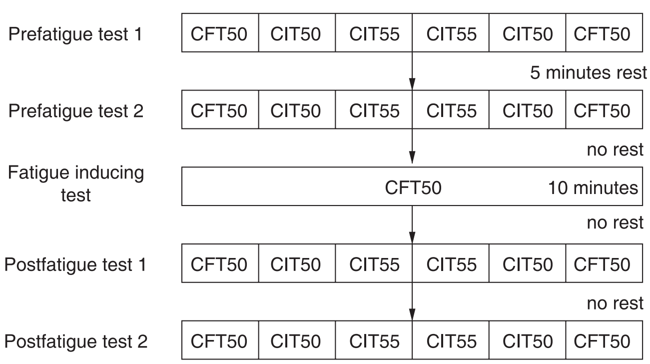

FIGURE 3. Flow chart illustrating prefatigue-testing, fatigue-inducing, and postfatigue test sequences in the experiments. Both the prefatigue and postfatigue tests consisted of two different CITs (CIT50 and CIT55; ie, the CIT with an IPI of 50 msec and 55 msec, respectively), and one CFT. The sequence of the three patterns was repeated in reverse order (1-2-3-3-2-1 sequence). See text for additional details.

Data Analysis

Estimation of the crank torque produced by stimulated muscle contractions is possible for isokinetic cycling. To assess the moment produced by stimulated muscle contractions, the passive crank moment is first measured during a passive cycling trial in which the motor turns the crank and the individual relaxes the lower extremities. To determine the electrically elicited active torque induced by FES, the angle-dependent passive torque is subtracted from the measured crank torque. This "active" torque was used to compute all the considered parameters of cycling performance: the torque-time integral per cycle (TTI), that is, the area under the active torque trajectory (computed as the sum of the positive and negative area), the peak of the active torque obtained for both legs and the time needed to reach the peak (T2P).

To take into account muscle activation history, the torque records produced by the identical stimulation patterns were averaged point by point for each prefatigue and postfatigue test before calculating all the cycling performance parameters (25).

Statistics

After verifying that all the data were normally distributed according to the Kolmogorov–Smirnov test, a parametric main effect analysis of variance (ANOVA) test ($p < 0.05$) was performed to understand how the chosen parameters (ie, the TTI, the active torque peaks, and the T2P), were affected by the different patterns tested. Separate ANOVAS were used to analyze prefatigue and postfatigued muscle performance measures. For significant effects of each ANOVA, Scheffè *post hoc* tests were performed ($p < 0.05$) to determine which pairs of effects were significantly different.

Results

An example of the average active torques produced by a subject with each stimulation pattern is shown in Fig. 4. At onset of stimulation, there was a ramping up of pulse width that smoothed the torque rise. The most rapid

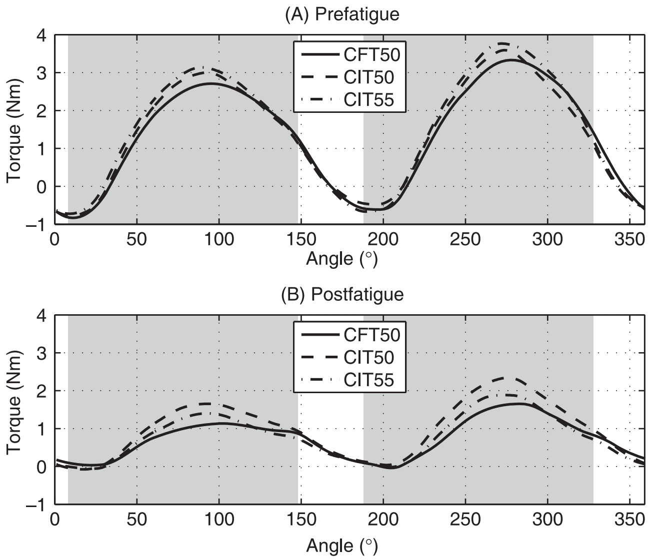

FIGURE 4. Comparison of the average muscle torques obtained from one subject with the different stimulation patterns during the prefatigue (A) and postfatigue tests (B). The gray areas indicate the stimulation ranges in respect to the crank angle.

change of torque occurred at the end of stimulation when the stimulation was switched off without ramping down the pulse width. The negative torques represent partly measurement artifacts caused by the motor control system that possesses a limited band width. Rapid changes in the active muscle torque cannot be compensated fast enough by the cadence controller and will lead to a small variation of cadence. Furthermore, it is possible that the stimulation of the quadriceps was slightly too long, thus a negative torque production by the quadriceps took place.

The CFT produced a lower active torque than the two CIT patterns, both when the muscles were fresh (Fig. 4A) and when fatigue was visible (Fig. 4B). The two torque peaks obtained by the CITs seemed to be a bit shifted to the left with respect to the peaks produced by CFT.

The prefatigue and postfatigue TTI values obtained on both test days are reported in Fig. 5.

The ANOVA statistical analysis for the first day showed a significant difference between the patterns in the postfatigue test only (MS = 0.24, F = 11.25, $p = 0.03$), while in the case of the second day, there was a significant difference in both the prefatigue test (MS = 0.32, F = 7.41, $p = 0.01$) and the postfatigue test (MS = 0.46, F = 11.3, $p = 0.03$). For the first day, the Scheffè *post hoc* analysis revealed a significant difference in the postfatigue test between CITID50 and CFT50 and also between CITID50 and CITID55 as reported in Fig. 5. For the second day, the Scheffè *post hoc* test revealed that in the prefatigue test CITMD50 produced a TTI significantly greater than the ones produced by CFT50. In the postfatigue test, the TTI of CITMD50 was significantly greater than the other two. With the TTI results as a starting point, it also is worthy to calculate the ratio of TTI obtained during the prefatigue and postfatigue tests. The values obtained were CFT50 = 50.8%, CITID50 = 63.8%, and CITID55 = 43.1% for the first day and CFT50 = 44.5%, CITMD50 = 60%, and CITMD55 = 46.2% for the second day. This result implies that CIT50 always produced the lowest reduction of performance in the postfatigue trials.

The torque peak values obtained with fatigued or not fatigued muscles are reported in Fig. 6.

In the first day in which the initial doublet was tested the ANOVA showed a significant difference in the postfatigue test only (MS = 0.33, F = 12.96, $p < 0.05$), and a Scheffè *post hoc* analysis showed that the difference was significant between the CITID50 and CFT50 and between the CITID50 and CITID55. During the second day, the following results were obtained: in the prefatigue test, the ANOVA revealed a significant difference between the three patterns (MS = 0.47, F = 9.86, $p < 0.05$), and the Scheffè *post hoc* analysis underlined that there was a significant difference between the CITMD50 and CFT50 and the CITMD55 and CFT50, as shown in Fig. 6. During the postfatigue test, there was a significant difference between the patterns (MS = 0.64, F = 14.57, $p < 0.05$), and the Scheffè *post hoc* confirmed that the CITMD50 presented a torque peak significantly greater than the others. The percentage ratios of the post to the prefatigue tests also were calculated for the torque peaks. The following values were obtained: CFT50 = 50.9%, CITID50 = 57.0%, and CITID55 = 47.5% for the first day and CFT50 = 48.3%, CITMD50 = 58.4%, and CITMD55 = 50.5% for the second day. Once again the CIT50 patterns showed a lower performance reduction due to fatigue.

In Fig. 7, the mean and standard deviations of the T2P obtained for both legs for all subjects are presented.

Under conditions where cadence is constant, the T2P parameter can be informative when exploring whether the use of a doublet produces a shift in torque profile with respect to the crank angle. A statistical analysis of this parameter showed a significant difference between the patterns only in the postfatigue test of the second day (MS = 0.0033, F = 12.75, $p < 0.05$) and, in particular, the Scheffè *post hoc* test showed that CFT50 produced a significantly longer T2P than the other two patterns.

The numerical results shown in Figs 5–7 are summarized in Tables 1 and 2 and Tables 3 and 4 show, for the three parameters, considered the percentage ratio of CIT50 to CFT and of CIT55 to CFT in the prefatigue and postfatigue conditions.

In particular, the most significant difference between the patterns was obtained in the postfatigue trials performed

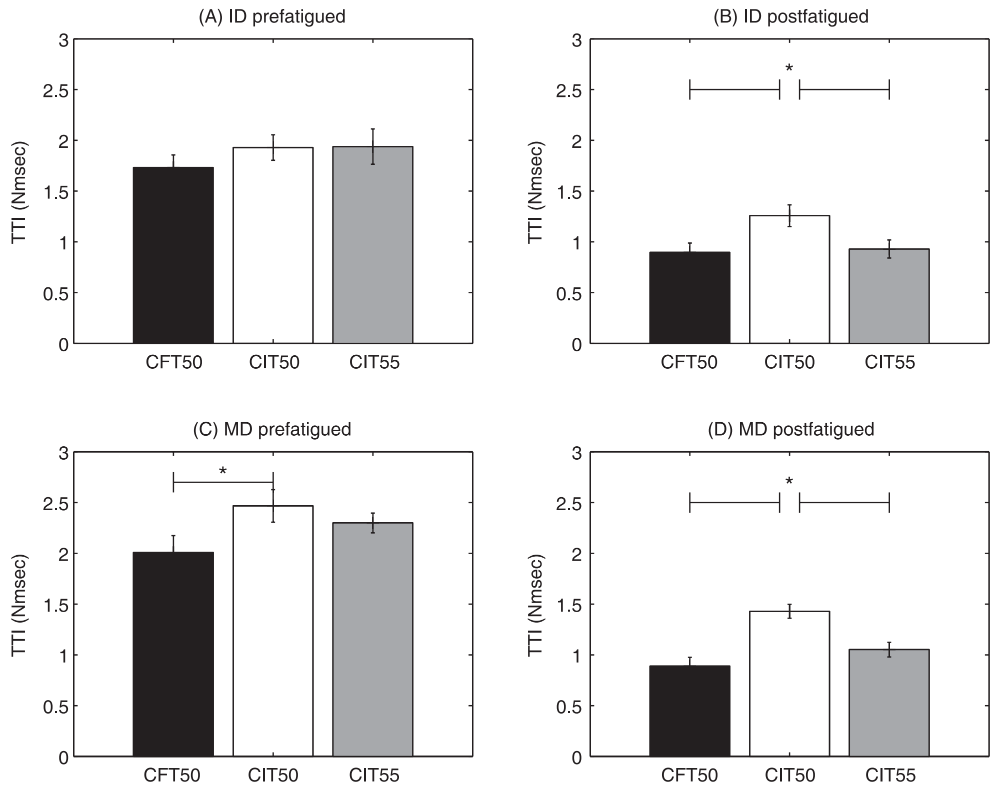

FIGURE 5. Results of the statistical analysis performed to compare the three patterns in terms of TTI obtained during each cycling revolution. Panels (A) and (C) show the comparison during the prefatigue test, and (B) and (D) during the postfatigue tests. The asterisks indicate between which patterns the Sheffè *post hoc* test showed a significant difference.

TABLE 1. Mean Value and Standard Error (SE) of the Analyzed Parameters Obtained by the Three Patterns During the Prefatigue and Postfatigue Trials of the First Day of Sessions

ID	TTI (Nmsec)		Peak (Nm)		T2P (sec)	
Pattern	Mean	SE	Mean	SE	Mean	SE
CFT50 prefatigue	1.73	0.12	3.05	0.13	0.37	0.01
CIT50 prefatigue	1.93	0.13	3.16	0.14	0.37	0.01
CIT55 postfatigue	1.94	0.17	3.13	0.2	0.36	0.01
CFT50 prefatigue	0.90	0.09	1.64	0.11	0.36	0.01
CIT50 prefatigue	1.26	0.11	1.92	0.13	0.37	0.02
CIT55 postfatigue	0.93	0.09	1.59	0.10	0.37	0.01

CFT, constant-frequency train; CIT, catchlike-inducing train; TTI, torque-time integral.

using a middle doublet in the CITs. In fact, the TTI and torque peaks produced by CITs were about 61% and 28% higher than the correspondent values observed with CFT, respectively.

TABLE 2. Mean Value and Standard Error (SE) of the Analyzed Parameters Obtained by the Three Patterns During the Prefatigue and Postfatigue Trials of the Second Day of Sessions

MD	TTI (Nmsec)		Peak (Nm)		T2P (sec)	
Pattern	Mean	SE	Mean	SE	Mean	SE
CFT50 prefatigue	2.01	0.17	3.09	0.12	0.37	0.01
CIT50 prefatigue	2.47	0.16	3.45	0.12	0.38	0.01
CIT55 postfatigue	2.30	0.10	3.42	0.10	0.36	0.01
CFT50 prefatigue	0.89	0.09	1.61	0.07	0.40	0.02
CIT50 prefatigue	1.43	0.11	2.07	0.11	0.38	0.02
CIT55 postfatigue	1.05	0.09	1.78	0.10	0.38	0.02

CFT, constant-frequency train; CIT, catchlike-inducing train; TTI, torque-time integral.

Discussion and Conclusions

The aim of this study was to understand if the application of CITs could be beneficial during FES cycling both with fatigued and not fatigued muscles.

It was already demonstrated that the use of a doublet in the stimulus train resulted in an augmentation of the

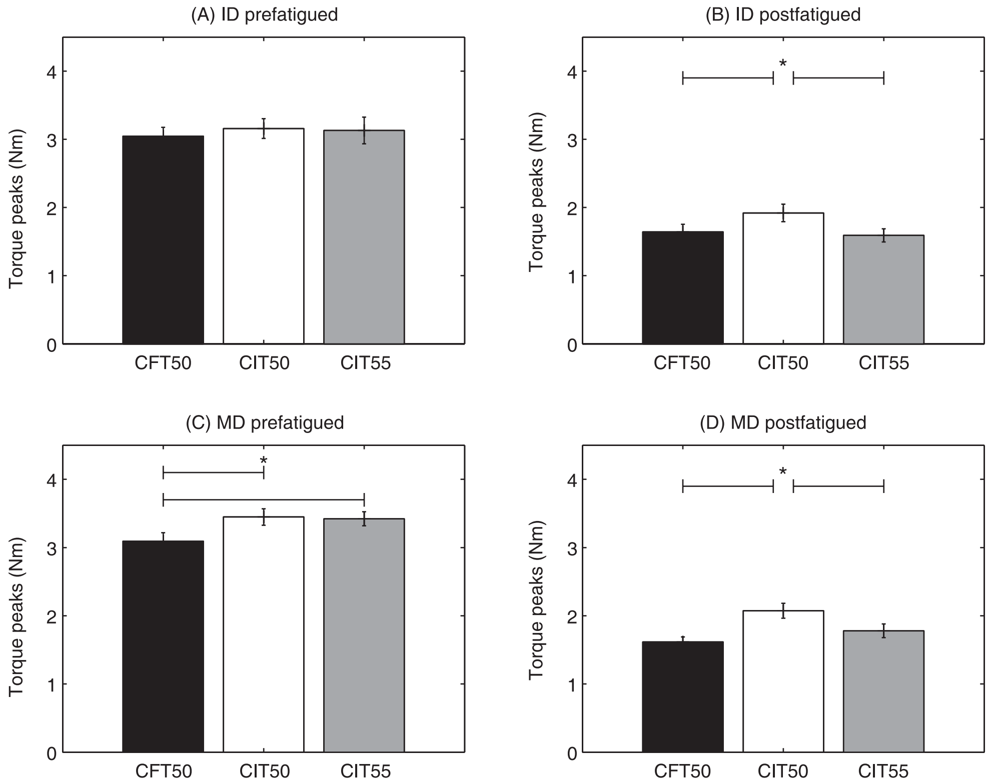

FIGURE 6. Results of the statistical analysis performed to compare the three patterns in terms of torque peaks. Panels (A) and (C) show the comparison during the prefatigue test, and (B) and (D) during the postfatigue tests. The asterisks indicate between which patterns the Sheffè *post hoc* test showed a significant difference.

TABLE 3. The Percentage Ratios of CIT50 to CFT and of CIT55 to CFT Are Shown for TTI, Peak, and T2P. The Ratios Obtained During the First Day With an Initial Doublet for the CITs in Both Prefatigue and Postfatigue Conditions Are Reported

ID	CIT50/CFT50 prefatigue (%)	CIT55/CFT50 prefatigue (%)	CIT50/CFT50 postfatigue (%)	CIT55/CFT50 postfatigue (%)
Peak	103	104	117	97
TTI	111	112	140	104
T2P	99	96	102	102

CFT, constant-frequency train; CIT, catchlike-inducing train; TTI, torque-time integral.

TABLE 4. The Percentage Ratios of CIT50 to CFT and of CIT55 to CFT Are Shown for TTI, Peak, and T2P. The Ratios Obtained During the Second Day With a Middle Doublet for the CITs in Both Prefatigue and Postfatigue Conditions Are Reported

MD	CIT50/CFT50 prefatigue (%)	CIT55/CFT50 prefatigue (%)	CIT50/CFT50 postfatigue (%)	CIT55/CFT50 postfatigue (%)
Peak	112	111	128	110
TTI	123	114	161	118
T2P	101	96	93	93

CFT, constant-frequency train; CIT, catchlike-inducing train; TTI, torque-time integral.

force produced during isometric, isokinetic, and isotonic conditions (23–26). During FES cycling, each muscle is stimulated during a preset crank angle range, and within that range there exists a phase in which the muscle can exhibit the maximal functionality (12). Thus, in such a dynamic movement, it is important to identify the optimum crank angle to deliver the doublet. For this reason, we decided to investigate two different placements of the doublet in the train. In the second test day, the doublet was delivered after the “ramp up”, because we hypothesized that the doublet delivered in that instant results in better timing for force enhancement during the cycling movement.

In both days, the CITs with non-doublet IPI of 50 msec elicited better performance than the other two patterns

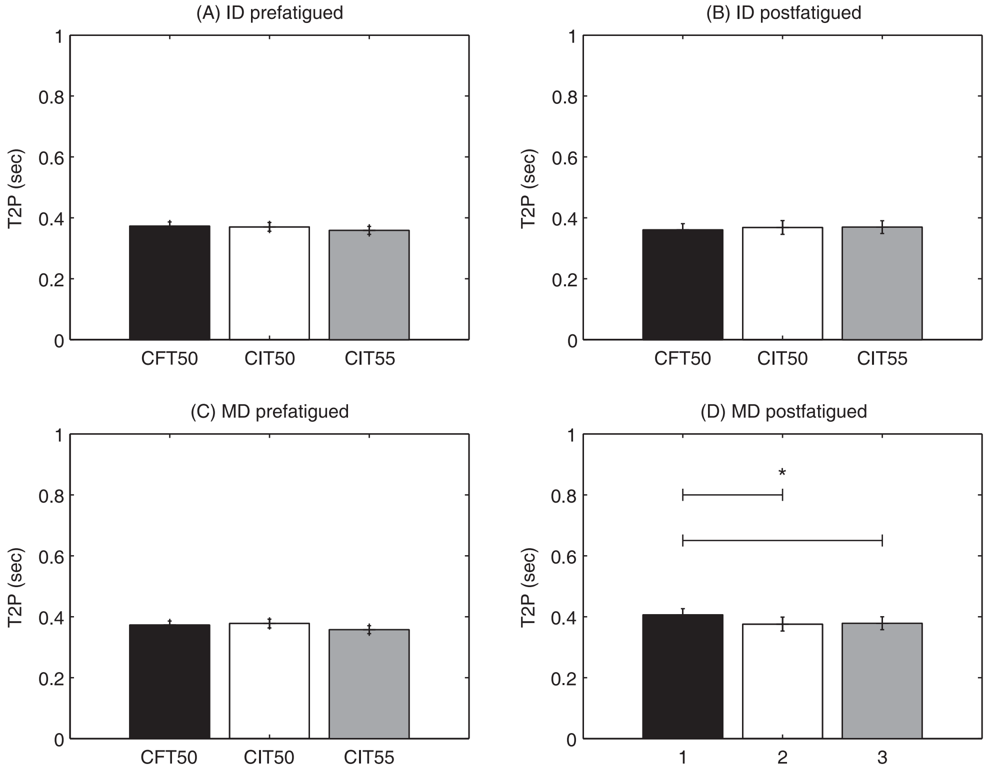

FIGURE 7. Results of the statistical analysis performed to compare the three patterns in terms of T2P. Panels (A) and (C) show the comparison during the prefatigue test, and (B) and (D) during the postfatigue tests. The asterisks indicate between which patterns the Sheffè *post hoc* test showed a significant difference.

(the CFT and the CIT with non-doublet IPI of 55 msec). In fact, in each day, the CIT50 pattern produced the biggest TTI and peak of the torque among all the subjects, and also the reduction of these parameters between the prefatigue and postfatigue tests was less than the one obtained with the other patterns. In particular, the fatigue reduction of TTI for the CFTs was about 13–15% more than the reduction observed for the CITs with a non-doublet IPI of 50 msec.

It is important to explore the T2P parameter when there is a change in peak torque, because the doublet could have altered peak torque by changing the force rise time of the contraction. The statistical analysis showed that CITs produced a significant decrease of the T2P parameter compared to CFT only in the postfatigue test of the second day and only for CITMD50 and CFT50. Therefore, because the TTI and torque peaks were greater and were not delayed, the extra force produced by a doublet resulted from an increase in the rate of increase of the torque as already found in other FES applications (31).

The relative efficacy of CITs to augment force during fatigue may be related to the proposed mechanisms by which CITs augment force. Enhanced muscle stiffness is one of the proposed mechanisms by which CITs augment force production over CFTs (34). Thus, if stiffness decreases with fatigue, then improving muscle stiffness with CITs may produce enhanced dynamic performance because muscle force would be transmitted more effectively to the skeletal system and would allow better take-up of the series elastic components than would CFTs (31).

A direct comparison between the two placements of the doublets in the stimulation pattern was not performed because they were delivered on different days. For this reason, the parameter values would be dependent not only on the pattern tested but also on the different muscle conditions during these days. It is possible to notice that concerning both the TTI and torque peaks, the doublet placed at the third pulse seemed more efficient (as shown in Figs 5 and 7), but it will be worthy to carry out a session in which all the patterns will be tested together. In this way, it would be possible to identify which is the best placement of the doublet in the pattern. It would be possible to exploit the previous study (12) in order to understand which is the crank angle range in which the torque produced by the muscle group is optimally transferred to the crank.

It would be interesting to understand if the obtained results could be different when CITs are applied at a higher constant angular speed during cycling. In fact, for increasing cadence, the number of pulses in the remaining lower-frequency portion of the train decreases. Therefore, the CITs could become similar to high-frequency CFT.

Our results seem to be quite in discordance with the only study found in literature on the application of variable frequency trains during FES cycling (8). The reasons could be that Janssen et al. analyzed SCI people while we performed the experiments on intact subjects. In addition, Janssen et al. compared patterns having a different number of pulses in the train and that the protocol used was too complex to isolate the effect of the pattern on the results. Furthermore, test conditions were not well-controlled with the employed isotonic cycling ergometer.

The importance of this study is that CITs were demonstrated to produce more power output and less fatigue than CFTs both with not fatigued and tired muscles in healthy subjects. In particular, the most interesting result was that the TTI and torque peaks produced by the CITMD50 was 61% and 28% greater than the ones produced by CFT, respectively.

There seems to be a real potential for the use of doublets on patients. Concerning individuals with SCI, Bickel et al. demonstrated that, in fatigue state, the enhancement in the TTI and in the rate of increase of the torque due to CITs was less than that observed in healthy subjects. It was hypothesized that the decreased augmentation due to the catchlike property in the quadriceps femoris muscles of individuals with SCI may be due to smaller twitch durations of the paralyzed muscles. This could mean that the muscle composition could affect the results.

It would be even more interesting to extend our results to patients with stroke instead of to individuals with SCI. In these patients, and particularly in individuals with a stroke in an acute stage, there is not any transformation of the fiber composition and the effect of CIT might be still visible as in able-bodied subjects. In addition, because patients with stroke often have residual sensation in their impaired limb, maximum stimulation intensity is often severely limited by low pain tolerance. For this reason, our objective was to deliver a CIT aiming at maximizing cycling performance by exploiting the greater the temporal summation of force generated by the use of a doublet. Finally, if the rate at which fatigue develops is reduced, individuals with stroke will be able to exercise more intensely, leading to greater enhancements in cycling ability and rehabilitative effects. Although the obtained results are encouraging, a deeper study on patients is required before integrating CITs into the stimulation strategy for FES cycling.

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Conflict of Interest

The authors reported no conflict of interest.

References

1. Mohr T, Andersen JL, Biering-Sørensen F et al. Long-term adaptation to electrically induced cycle training in severe spinal cord injured individuals. *Spinal Cord* 1997;35:1–16.
2. Mirbagheri MM, Ladouceur M, Barbeau H, Kearney RE. The effects of long-term FES-assisted walking on intrinsic and reflex dynamic stiffness in spastic spinal-cord-injured subjects. *IEEE Trans Neural Syst Rehabil Eng* 2002;10:280–289.
3. Raymond J, Davis GM, van der Plas M. Cardiovascular responses during submaximal electrical stimulation-induced leg cycling in individuals with paraplegia. *Clin Physiol Funct Imaging* 2002;22:92–98.
4. Janssen TWJ, Glaser RM, Shuster DB. Clinical efficacy of electrical stimulation exercise training: effects on health, fitness, and function. *Top Spinal Cord Inj Rehabil* 1998;3:33–49.
5. Chae J, Yu D. Neuromuscular stimulation for motor relearning in hemiplegia. *Crit Rev Phys Rehabil Med* 1999;11:279–297.
6. Burke RE, Rudomin P, Zajac FE 3rd. The effect of activation history on tension production by individual muscle units. *Brain Res* 1976;109:515–529.
7. Williams JH. Contractile apparatus and sarcoplasmic reticulum function: effects of fatigue, recovery, and elevated Ca^{2+}. *J Appl Physiol* 1997;83:444–450.
8. Janssen TW, Bakker M, Wyngaert A, Gerrits KH, de Haan A. Effects of stimulation pattern on electrical stimulation-induced leg cycling performance. *J Rehabil Res Dev* 2002;41:787–796.
9. Perkins TA, Donaldson N de N, Fitzwater R, Phillips GF, Wood DE. *Leg powered paraplegic cycling system using surface functional electrical stimulation*. Proceedings of 7th Vienna International Workshop on FES, Vienna, Austria, 2001:36–39.
10. Petrofsky JS. New algorithm to control a cycle ergometer using electrical stimulation. *Med Biol Eng Comput* 2003;41:18–27.
11. Hunt KJ, Stone B, Negård NO et al. Control strategies for integration of electric motor assist and functional electrical stimulation in paraplegic cycling: utility for exercise testing and mobile cycling. *IEEE Trans Neural Syst Rehabil Eng* 2004;12:88–101.
12. Ferrante S, Saunders B, Duffell L et al. *Quantitative evaluation of stimulation patterns for FES cycling*. Proceedings of 10th Annual Conference of the International FES Society, Montreal, Canada, 2005:94–96.
13. Chen JJ, Yu NY, Huang DG, Ann BT, Chang GC. Applying fuzzy logic to control cycling movement induced by functional electrical stimulation. *IEEE Trans Rehabil Eng* 1997;5:158–169.
14. Gföhler M, Lugner P. Cycling by means of functional electrical stimulation. *IEEE Trans Rehabil Eng* 2000;8:233–243.
15. Desmedt JE, Godaux E. Ballistic contractions in fast or slow human muscles: discharge patterns of single motor units. *J Physiol* 1978;285:185–196.

16. Binder-Macleod SA, Kesar T. Catchlike property of skeletal muscle: recent findings and clinical implications. *Muscle Nerve* 2005;31:681–693.

17. Binder-Macleod SA. Force-frequency relation in skeletal muscle. In: Cumer DP, Nelson RM, eds. *Dynamics of human biologic tissues*. Philadelphia, PA: Davis, 1992:97–113.

18. 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;36:644–653.

19. Levy M, Mizrahi J, Susak Z. Recruitment, force, and fatigue characteristics of quadriceps muscles of paraplegics isometrically activated by surface functional electrical stimulation. *J Biomed Eng* 1990;12:150–156.

20. Bigland-Ritchie B, Zijdewind I, Thomas CK. Muscle fatigue induced by stimulation with and without doublets. *Muscle Nerve* 2000;23:1348–1355.

21. Garland SJ, Garner SH, McComas AJ. Relationship between numbers and frequencies of stimuli in human muscle fatigue. *J Appl Physiol* 1988;65:89–93.

22. Marsden CD, Meadows JC, Merton PA. Muscular wisdom that minimizes fatigue during prolonged effort in man. Peak rates of motoneuron discharge and slowing of discharge during fatigue. In: Desmedt M, ed. *Motor control mechanism in health und disease*. New York: Raven Press, 1983: 169–211.

23. Bickel SC, Slade JM, VanHiel LR, Warren GL, Dudley GA. Variable-frequency-train stimulation of skeletal muscle after spinal cord injury. *J Rehabil Res Dev* 2004;41:33–40.

24. Karu ZZ, Durfee WK, Barzilai AM. Reducing muscle fatigue in FES applications by stimulating with N-let pulse trains. *IEEE Trans Biomed Eng* 1995;42:809–817.

25. Lee SC, Binder-Macleod SA. Effects of activation frequency on dynamic performance of human fresh and fatigued muscles. *J Appl Physiol* 2000;88:2166–2175.

26. Kebaetse MB, Turner AE, Binder-Macleod SA. Effects of stimulation frequencies and patterns on performance of repetitive, nonisometric tasks. *J Appl Physiol* 2002;92:109–116.

27. Schauer T, Behling C, Liedecke W, Negård NO, Raisch J. *Feedback control of an FES lower limb cycling ergometer*. Proceedings of 11th Annual Conference of the International FES Society, Miyagi-Zao, Japan, 2006:130–132.

28. Schauer T, Salbert RC, Negård NO, Hunt K, Raisch J. Power control of electrical stimulation induced cycle ergometry (in German). *at—Automatisierungstechnik* 2005;53:607–614.

29. Fornusek C, Davis GM, Sinclair PJ, Milthorpe B. Development of an isokinetic functional electrical stimulation cycle ergometer. *Neuromodulation* 2004;7:56–64.

30. Schauer T, Salbert RC, Negård NO, Raisch J. *Detection and filtering of EMG for assessing voluntary muscle activity during FES*. Proceedings of 9th Annual Conference of the International FES Society, Bournemouth, UK, 2004:185–187.

31. Binder-Macleod SA, Lee SC. Catchlike property of human muscle during isovelocity movements. *J Appl Physiol* 1996;80:2051–2059.

32. Binder-Macleod SA, Lee SC, Baadte SA. Reduction of the fatigue-induced force decline in human skeletal muscle by optimized stimulation trains. *Arch Phys Med Rehabil* 1997;78:1129–1137.

33. Lee SC, Becker CN, Binder-Macleod SA. Catchlike-inducing train activation of human muscle during isotonic contractions: burst modulation. *J Appl Physiol* 1999;87:1758–1767.

34. Parmigianni F, Stein RB. Nonlinear summation of contractions in cat muscles. II. Later facilitation and stiffness changes. *J Gen Physiol* 1981;78:295–311.