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EFFECTS OF CATCH-LIKE PROPERTY ON MUSCLE FATIGUE IN INTERMITTENT ELECTRICAL STIMULATION

Hiroki Ito[1)], Yoichi Shimada[2)], Toshiki Matsunaga[2)],
Masahito Kawatani[3)] and Eiji Itoi[1)]

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[1)]*Division of Orthopedic Surgery, Department of Neuro and Locomotor Science,*
[2)]*Rehabilitation Division and* [3)]*Division of Neurophysiology and Applied Physiology,*
Department of Physiology and pharmacology,
Akita University School of Medicine, Akita 010-8543, Japan

Abstract : Catch-like property is a force enhancement produced in the muscle when a brief, high frequency burst of pulses is added to a low frequency electrical stimulation train. In functional electrical stimulation (FES), low frequency stimulation of approximately 20 Hz has primarily been used to reduce muscle fatigue. In the present study, the effects of catch-like property on muscle fatigue were analyzed using intermittent electrical stimulation. The results showed that, compared to conventional low frequency stimulation, low frequency stimulation taking advantage of the catch-like property significantly increased the maximum muscle force and workload and decreased muscle fatigue. The results of the present study suggest that catch-like property is useful in clinical administration of FES.

Key words : Catch-like property, functional electrical stimulation (FES), muscle fatigue, intermittent stimulation, animal study

Introduction

Functional electrical stimulation (FES) is a method of restoring functionality to upper or lower extremities by electrically stimulating the lower motor neurons of patients with paraplegia, quadriplegia, or hemiplegia. Today, FES makes it possible for quadriplegics to eat and write, and for paraplegics to walk[1-4)]. Since 1990, we have been performing FES to restore leg function in paraplegics, and have had success in restoring their ability to stand up and to walk[5-7)]. When FES restored leg functions, muscle fatigue usually occurred much earlier than under normal physiological conditions. In restoration of standing and walking, muscle fatigue leads to knee buckling, thus hindering restorative efforts[4,6,8,9)]. For these reasons, it is important to reduce muscle fatigue for FES and thus to select an appropriate stimulation frequency.

In the existing FES systems, practical tetanic muscle contraction and functional restoration is primarily achieved through continuous stimulation. At the same time, it is necessary to apply stimulation at frequencies that are less likely to cause muscle fatigue, so that low frequency stimulation (typically at less than 50 Hz) is used[1,3,9)]. Recent advances in medical engineering have made it possible to perform more efficient intermittent FES incorporating closed-loop control[2,4,7,8)]. There have been reports of high frequency stimulation of approximately 50-100 Hz[10)], however, the optimal stimulation frequency for restoring leg function has not been conclusively determined.

In 1970, Burke and colleagues applied a single electrical stimulation of 100 Hz at the start of low frequency stimulation of excised feline muscles, and reported increased and sustained muscle force[11]. This phenomenon was later confirmed by various researchers and is now referred to as a catch-like property of a muscle[12,13]. For instance, Ratkevicius and colleagues intermittently stimulated the quadriceps femoris of healthy individuals by applying short-term (300 msec) continuous stimulation at the low frequency of 14.3 Hz every 2.5 seconds[14]. They reported that the catch-like property increased the maximum isometric muscle force and workload, and that this effect was marked when the muscle was fatigued. These findings suggest that the catch-like property could be used for controlling muscle fatigue in FES. However, previous reports only investigated short-term stimulation with short cycles, and there have been no studies on the catch-like property associated with intermittent FES using long-term electrical stimulation lasting several seconds, which is required for FES in clinical settings.

The aims of the present study were 1) to ascertain whether or not the catch-like property can be observed following intermittent application of low frequency continuous stimulation lasting several seconds; and 2) to investigate the effects of the catch-like property on muscle fatigue in relation to conventional low frequency stimulation.

Materials and Methods

Subjects

Eighteen adult male Wistar rats with an average age of 13±1 weeks and an average body weight of 283.2±18.4 g, were divided into two groups.

(1) Low frequency stimulation group (LFS group): 4-second low frequency electrical stimulation of 20 Hz applied intermittently (Figure 1-a).

(2) Catch-like property stimulation group (CLPS group): 4-second low frequency electrical stimulation of 20 Hz was applied intermittently with

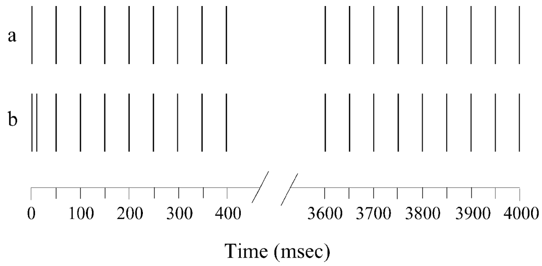

Fig. 1 Schematic representation of the 4-second stimulation trains used during the study. Each vertical line represents a 200-μsec stimulation pulse.
a) Low frequency stimulation (LFS): constant-frequency stimulation train with interpulse intervals of 50 msec (20 Hz).
b) Catch-like property stimulation (CLPS): stimulation train (20 Hz) with one initial interpulse interval of 10 msec (100 Hz).

a single electrical burst of 100 Hz applied at the start of every 4-second continuous stimulation (Figure 1-b).

In both groups, a monophasic rectangular pulse with a pulse width of 0.2 msec and a stimulation intensity of −4 V was used. The isometric muscle force of the medial gastrocnemius was measured at regular intervals while stimulating the sciatic nerve.

Experimental Setup

General anesthesia was induced by administering sodium barbiturate (30 mg/kg) intraperitoneally. After opening the posterior surface of the leg to expose the sciatic nerve, a bipolar cuff electrode (interelectrode distance: 5 mm; MD Giken, Tokyo, Japan) was attached to the sciatic nerve at the center of the femur. Next, the medial gastrocnemius was severed at the tendon near the insertion area to the calcaneus. A transducer (ORIENTEC Corp., Tokyo, Japan) was attached and fixed with a load of approximately 1 N next to the stump[15]. Signals transmitted from the force transducer during isometric muscular contraction were recorded on a force-time curve using a paper recorder (Nihon Kohden Corp., Tokyo, Japan) (Figure 2).

For both LFS and CLPS groups, the maximum potentiation effect (constant maximum isometric

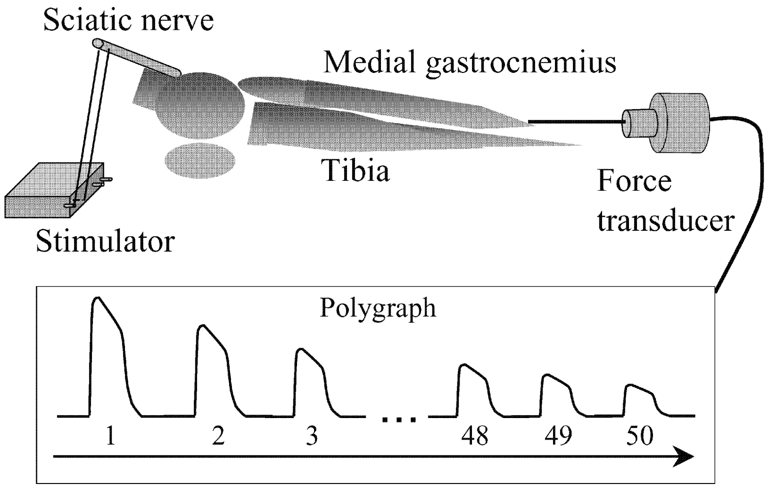

Fig. 2 Schematic representation of the experimental procedure

muscle force) was confirmed by applying low frequency stimulation of 20 Hz for 4 seconds (4-second "on" period) followed by a 15-second "off" period: this procedure was repeated 4-5 times[12]. The muscle fatigue test was then conducted as follows: In the LFS group, low frequency stimulation of 20 Hz was applied for 4 seconds with a break of 15 seconds before the next stimulation. This procedure was repeated 50 times to record the isometric muscle force for a 16-minute period. Similarly, in the CLPS group, the isometric muscle force was recorded to ascertain the effects of the catch-like property.

To prevent the muscles from desiccation during the study, mineral oil was used to cover the exposed area[16]. The study was conducted at a constant room temperature of 25-27°C, while the rectal temperature of the rats was maintained between 35 and 36°C. At the end of the study, the rats were euthanized by carbon monoxide inhalation. The protocols for animal experimentation described in this paper were previously approved by the Animal Research Committee, Akita University; All subsequent animal experiments adhered to the "Guidelines for Animal Experimentation" of the University.

Assessment of muscle force, fatigue, and workload

The maximum isometric muscle force (F_{Peak}, unit: N), the muscle force at the fourth second (F_{4sec}, unit: N) (Figure 3), and the integral muscle force (force-time integral: FTI, unit: NS) (Figure 4) were determined for each 4-second muscle force-time curve during the muscle fatigue test. FTI parameters were calculated using image software analysis (Mac Scope version 2.5, Mitani Corporation, Chiba, Japan).

Muscle fatigue was defined as attenuation in F_{Peak} (maximum muscle force) at the n-th 4-second stimulation [$F_{Peak}(n)$] in relation to the F_{Peak} at the initial 4-second stimulation in the muscle fatigue test [$F_{Peak}(i)$]. To ascertain the time course of muscle fatigue, the percentage of initial $F_{Peak}(n)$ was calculated using the formula:

$$\text{Percentage of initial } F_{Peak}(n) = [F_{Peak}(n) / F_{Peak}(i)] \times 100$$

To assess the time course of muscle fatigue at the end of each 4-second stimulation, attenuation in F_{4sec} at the n-th stimulation [$F_{4sec}(n)$] in relation to that at the initial 4-second stimulation in the muscle fatigue test [$F_{4sec}(i)$] was calculated using the for-

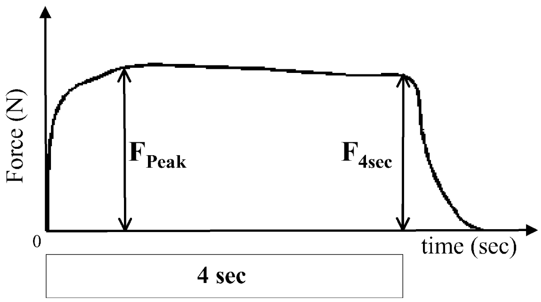

Fig. 3 The force-time curve during 4-second stimulation. Maximum isometric muscle force (F_{Peak}) and muscle force at the fourth second just before start of the "off" period (F_{4sec}) were determined as shown.

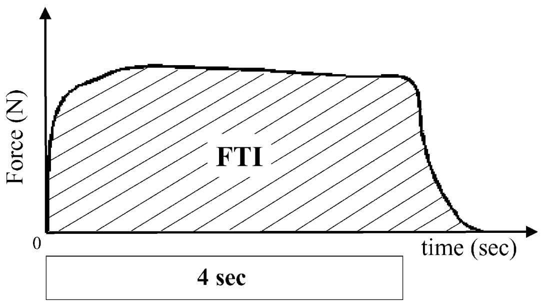

Fig. 4 Calculation of the force-time integral (FTI) from the force-time curves. FTI indicates the entire muscle workload during the 4-second stimulation period.

mula:

$$\text{Percentage of initial } F_{4sec}(n) = [F_{4sec}(n)/F_{4sec}(i)] \times 100.$$

The percentage of FTI at the n-th stimulation [FTI(n)] to the FTI at the initial 4-second stimulation in the muscle fatigue test [FTI(i)] was calculated using the formula:

$$\text{Percentage of initial } FTI(n) = [FTI(n)/FTI(i)] \times 100.$$

The time course of FTI was determined for every ten stimulations.

Statistical analysis

Significant differences in the maximum muscle force over the 4-second stimulation period (F_{Peak}), and the muscle force at the fourth second (F_{4sec}) between LFS and CLPS groups at the start and end of the muscle fatigue test were evaluated with a *t*-test with a significance level of 5%. Repeated measure ANOVA (Stat-View version 5, Cary, North Caroline, USA) was used to statistically analyze differences in the percentage of initial F_{Peak} (n), percentage of initial F_{4sec} (n) and percentage of initial FTI between LFS and CLPS groups at a significance level of 5%. Numerical values were expressed as mean±standard deviation.

Results

Muscle force

At the start of the muscle fatigue test, the F_{Peak} (maximum muscle force over the 4-second stimulation period) was 5.64±0.72 N (mean±SD) and 5.71±0.42 N for the LFS and CLPS groups, respectively: the difference was not statistically significant (*t*-test, $p=0.7974$). At the end of the muscle fatigue test, the F_{Peak} values for the LFS and CLPS groups (2.51±0.40 N and 3.37±0.44 N, respectively) were statistically significant (*t*-test, $p=0.0005$). No significant differences were found between the LFS and CLPS groups for the F_{4sec} (muscle force at the fourth second) at the start of the muscle fatigue test (5.38±0.68 N and 5.62±0.37 N, respectively; *t*-test, $p=0.3647$). At the end of the muscle fatigue test F_{4sec} values for the LFS and CLPS groups (2.07±0.30 N and 2.42±0.30 N, respectively) were statistically significant (*t*-test, $p=0.0248$). Force-time curves for one case from the LFS and CLPS groups at the start and end of the muscle fatigue test are shown in Figure 5.

Time course of muscle fatigue

Over time, the percentage of initial F_{Peak} decreased for both groups, and the percentage of initial F_{Peak} became significantly greater for the CLPS group (repeated measure ANOVA, $p<0.0001$) (Figure 6), indicating that the level of muscle fatigue for the CLPS group was significantly

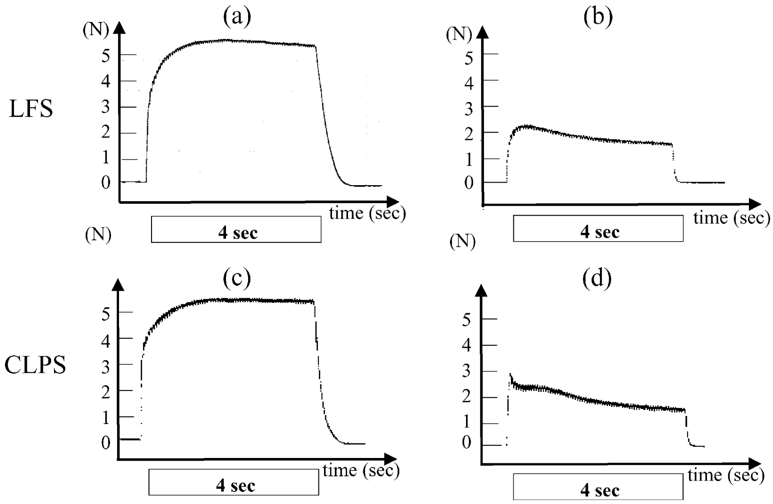

Fig. 5 Representative force-time curves at the start and the end of the muscle fatigue test for LFS and CLPS groups. At the start of the muscle fatigue test (unfatigued), shifts in muscle force were similar for the LFS and CLPS groups (5-(a), 5-(c)). However, at the end of the test (fatigued), the muscle force increased more quickly and remained higher for the CLPS group, but there was no marked difference in muscle force just before the completion of the stimulation between the LFS and CLPS group (5-(b), 5-(d)).

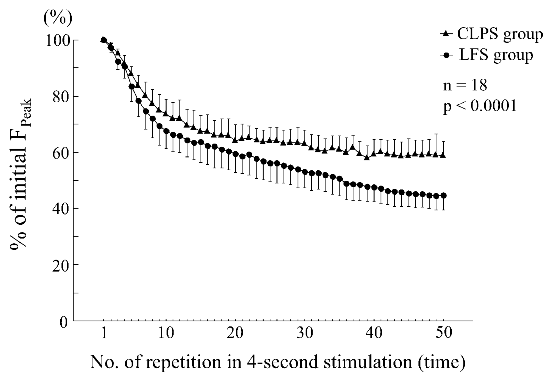

Fig. 6 Time course of % of initial F_{Peak} for LFS and CLPS groups during the muscle fatigue test. Differences in muscle fatigue between LFS and CLPS were statistically significant (repeated measure ANOVA ; $p<0.0001$), and muscle fatigue was greater for LFS. Symbols and bars represent mean±SD.

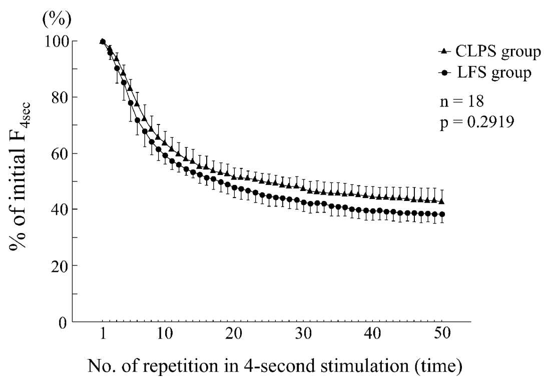

Fig. 7 Time course of % of initial F_{4sec} for LFS and CLPS during the muscle fatigue test. No statistical different was found (repeated measure ANOVA ; $p=0.2780$). Symbols and bars represent mean±SD.

reduced. At the end of the muscle fatigue test, the percentage of initial F_{Peak} for the LFS and CLPS groups was 44.7±5.3% and 58.9±4.9%, respectively. There were no significant differences in the percentage of initial F_{4sec} between the two groups (repeated measure ANOVA, $p=0.2919$) (Figure 7). At the end of the muscle fatigue test, the percentage of initial F_{4sec} for the LFS and CLPS groups was 38.6±3.2% and 43.0±4.1%, respectively.

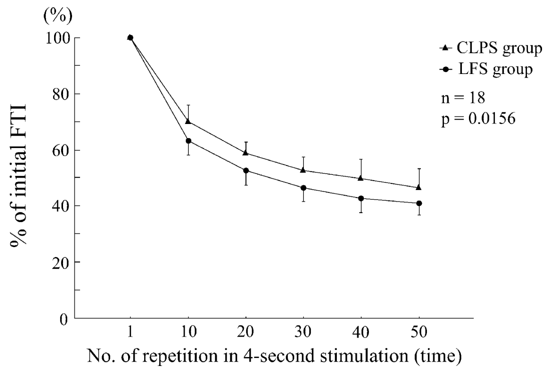

Fig. 8 Time course of % of initial FTI for LFS and CLPS during the muscle fatigue test. Differences in FTI between LFS and CLPS were statistically significant (repeated measure ANOVA ; $p=0.001$). Symbols and bars represent mean±SD.

Time course of muscular workload

Over time, the percentage of initial FTI decreased for both groups, but was significantly higher for the CLPS group (repeated measure ANOVA, $p=0.0156$) (Figure 8). At the end of the muscle fatigue test, the percent of initial FTI_{0-4} for the LFS and CLPS groups was 41.0±4.3% and 46.5±6.8%, respectively.

Discussion

In the present study, low frequency electrical stimulation was intermittently applied for 4 seconds and the effects of the catch-like property on muscle force, muscle fatigue, and muscular workload were then investigated. The results showed that the catch-like property significantly increased the maximum muscular force and workload, and significantly decreased muscle fatigue. According to previous reports, the catch-like property has been confirmed for short-term stimulation of less than one second in a short cycle[12-14,16-18]. The present study showed that the catch-like property could be observed with 4-second continuous stimulation. This finding should be beneficial for taking advantage of the catch-like property in long-term continuous FES.

Kagaya and colleagues reported that it took 3.0±0.3 seconds on average for paraplegics to stand and 3.0±0.1 seconds to sit[5]. Marsolais and colleagues applied 1-3 seconds of continuous stimulation intermittently to the quadriceps femoris, biceps femoris and tibialis anterior for restoring locomotion in paraplegia by FES[1]. Therefore, the conditions used in the present study, 4-second low frequency stimulation of 20 Hz applied intermittently, is similar to FES used in clinical settings.

Of many reports on the physiological mechanisms of the catch-like property, Duchateau and colleagues reported that the catch-like property occurs when high frequency stimulation increases Ca release from the sarcoplasmic reticulum[19]. Parmiggiani and colleagues stated that increased muscle stiffness correlated with the catch-like property[20]. In the present study, the difference in muscle fatigue between LFS and CLPS groups was greater in the latter half of the muscle fatigue test. We suppose that the catch-like property was more efficiently expressed under low-frequency fatigue because Ca released from sarcoplasmic reticulum is reduced. In future, it will be necessary to investigate the physiological mechanism of the catch-like property under various conditions for intermittent application of long-term continuous stimulation.

One of the advantages associated with the catch-like property is that muscle force peaks earlier[17,18]. In the restoration of standing based on FES closed-loop control, quick muscular contraction in response to stimulation is needed[10]. As a result, stimulation that takes advantage of the catch-like property should be useful. Ratkevicius and colleagues clarified that the catch-like property increased the maximum muscle force and workload regardless of ATP consumption[14]. They applied continuous low frequency stimulation for 300 msec, whereas the results of our study showed that 4-second continuous stimulation also increased muscular workload. Further studies are necessary to investigate the ATP consumption associated with 4-second continuous stimulation.

When FES closed-loop control is used for the restoration of lower extremities, paraplegics can remain standing for 30 to 60 minutes with conventional low frequency stimulation[7,21]. The results of the present study showed that the low frequency stimulation taking advantage of the catch-like property increased the maximum muscle force and workload and decreased muscle fatigue, and that the muscle force at the end of 4-second continuous stimulation for this catch-like property-combined stimulation was comparable to that of conventional low frequency stimulation. The results of the present study suggest that the catch-like property is useful for restoring functions such as standing and walking, and that longer restoration should be possible by combining the catch-like property with the currently available systems. In future, we are planning to further investigate the clinical application of stimulation that takes advantage of the catch-like property.

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