Functional Electrical Stimulation of skeletal muscle – Implications for cardiovascular support

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Abstract

Cardiomyoplasty (CMP) was developed as a potential treatment for chronic heart failure. In CMP the latissimus dorsi muscle (LDM) is wrapped the heart ventricles and stimulated with a burst of electrical pulses to contract in synchrony with the heart. Due to it the poor muscle performance of the LDM during CMP, this treatment is not currently an accepted intervention. We posit that one factor contributing to the poor muscle performance during CMP was the use of sub-optimal stimulation parameters. In this paper, we outline recent evidence regarding stimulation strategies that have been shown to maximize muscle performance. These strategies include rearranging the stimulus pulse patterns within stimulation trains to take advantage of the catchlike property of the skeletal muscle and systemically modulation the pulse frequency and intensity to produce greater power compared to traditionally used approaches. If these strategies are able to produce greater forces from the LDM, CMP performance may be able to be improved.

Key Words: Cardiomyoplasty, ventricular assistance, functional electrical stimulation

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Functional electrical stimulation (FES) has been used to replace or augment the function of paralyzed muscles to enable performance of functional movements such as standing and walking in individuals with neurological dysfunctions [22, 24]. Another potential application of FES is in cardiomyoplasty (CMP). Dynamic CPM was developed as a surgical treatment for chronic heart failure in which the latissimus dorsi muscle (LDM) was wrapped around the heart ventricles and stimulated with a burst of electrical impulses to contract in synchrony with the heart [7]. This procedure was designed to provide an optional therapy for heart failure patients who were refractory to medical therapy or who were not heart transplant candidates. Most clinical CMP studies have reported a significant improvement in functional class without any measurable improvements in left ventricular (LV) systolic function [7]. In experimental and clinical studies, systolic augmentation of LV function by the LDM has not been routinely observed; LV ejection fraction and peak systolic pressure remained almost identical in the presence versus absence of electrical stimulation [14]. LDM atrophy, loss of contractile function, muscle degeneration, and necrosis have been suggested as possible reasons for these disappointing results [20]. Acute mobilization and wrapping of the LDM around the heart causes LDM ischemia. Furthermore, continuous 24-hour per day stimulation is detrimental to the LDM. By stimulating the LDM for only part of the day (CMP on-demand), Rigatelli and colleagues were able to preserve LDM integrity, leading to increased LDM cardiac assistance [26]. By combining a two-stage vascular delay procedure with CMP on-demand, Kashem and colleagues showed that intermittent LDM stimulation increased peak LV pressure by 19%, stroke volume by 34%, and stroke work by 68% [17]. Although CMP is currently not an accepted intervention for congestive heart failure, its inherent advantages still make this an attractive technology. One limitation of CMP may have been the use of sub-optimal electrical stimulation parameters. This paper will outline recent evidence about stimulation strategies that can maximize muscle performance, as related to CMP.

Electrical stimulation parameters and CMP

When skeletal muscle contraction is elicited through artificial electrical stimulation, the electrical stimulation parameters markedly influence the strength and time course of muscle contraction. In CMP, it is advantageous to have the LDM muscle contract rapidly and strongly to provide maximum cardiac assistance. Also, after a rapid and strong contraction, relaxation is important to allow adequate diastolic ventricular filling [13]. During clinical applications of CMP, the LDM was typically electrically activated with a pattern of uniformly spaced electrical pulses, i.e., constant-frequency train (CFT), consisting of 6 monophasic pulses, each 210 µs in duration, with an intraburst frequency of 30 pulses/s [8]. While a 30-pulse/s CFT may be a reasonable choice, trains of nonuniformly spaced nerve impulses have been recorded during volitional contractions in a variety of muscles in both animals and humans [1, 15]. Similarly, it has been shown that the strength of skeletal muscle cardiac assistance obtained with FES can be further increased by using complex stimulation patterns [12].

The rate of fatigue of repeatedly stimulated skeletal muscle is partly determined by the number of pulses within the stimulus pattern [16]. During skeletal muscle cardiac assist using FES, the LDM was converted into a fatigue-resistant phenotype through chronic electrical stimulation [20]. Unfortunately, this conversion process decreases muscle strength, speed, and power, thereby diminishing potential cardiac assist [27]. If electrical stimulation pattern(s) could be identified that contained fewer stimulus pulses and still elicited similar or enhanced muscle contractile performance, decreased rate of muscle fatigue would be possible. The use of an improved stimulus train parameters may obviate the need for conversion of the muscle to a fully fatigue-resistant phenotype and reduce the decline in muscle performance presently noted.

Enhancement of muscle performance using the catchlike property

During FES, stimulation is delivered in the form of groups of pulses called trains. The frequency of the stimulation train and the intensity (i.e., the product of amplitude and duration) of the individual pulses are the two main parameters affecting muscle performance during FES. The instantaneous stimulation frequency can be varied within the train on a pulse-by-pulse basis by changing the pattern or arrangement of pulses within the train. Such variable-frequency trains (VFTs) that take advantage of the “catchlike” property of skeletal muscle have been shown to augment muscle performance compared to CFTs [2]. The catchlike property of skeletal muscle is the tension enhancement seen when an initial high-frequency burst of pulses (see Figure 1) is added to the beginning of a subtetanic train of pulses [4]. The catchlike property has been demonstrated in single motor units [6], whole animal muscles,[4] and human muscles[5]. It is an inherent property of skeletal muscle cells and its primary mechanism is probably an increased sarcoplasmic Ca2+ concentration.[11, 25] Consistent with this mechanism of increased Ca2+ release is the observation that force augmentation due to the catchlike property is more pronounced during fatigue[5].

Typically during CMP, CFTs, which consist of single pulses separated by equal interpulse intervals (IPIs) throughout the train, have been used to activate muscles [12]. However, VFTs, which consist of a high-frequency burst of two to four pulses included at the onset of a subtetanic low-frequency stimulation train, have ben show to augment muscle performance during electrical stimulation. VFTs have been shown to enhance rate of rise of force and force-time integral compared with CFTs of similar frequency, especially in the fatigued state [2, 12] (See Table 1). In addition, during nonisometric contractions, VFTs produced greater work, excursion, peak power, average power, and rates of rise of force from fatigued human quadriceps femoris muscle than CFTs [2, 21]. In a recent study, using our mathematical muscle model to help identify the optimal stimulation pattern, we showed for the first time that CFTs can be replaced by VFTs, with fewer pulses, to produce identical motion trajectories as that produced in response to the CFTs [23]. Hence, we showed that by varying the pattern of the stimulation train it was possible to reduce the number of pulses and the mean frequency required to achieve a targeted trajectory [23]. Thus, varying the instantaneous frequency within a train of pulses to take advantage of the catchlike property can help improve dynamic muscle performance during electrical stimulation [23].

Taking advantage of the catchlike property during CMP

Two previous studies tested the hypotheses that increased mechanical performance from the LDM could be achieved by activating the muscle with variable-frequency trains [12]. The mechanical performance of the canine LDM (n = 7) during shortening contractions in which the LDM lifted a weight was measured while the muscle was stimulated with 5- and 6-pulse CFTs (of duration 132 and 165 ms, respectively) and 5- and 6-pulse VFTs (of duration 104 and 143 ms, respectively) that were designed to take advantage of the catchlike property of skeletal muscle. The VFTs elicited significantly greater peak power than did the 6-pulse CFT. When the muscles were fatigued, VFT stimulation significantly improved both the peak and mean power produced compared with stimulation by CFTs [12].

In the second study, six dogs underwent a vascular delay of the LDM, followed by intracoronary microsphere injections to induce LV dysfunction [17] Two weeks later, cardiomyoplasty surgery was performed. Over 9 weeks, the LDM was incrementally stimulated. At the end of 9 weeks in a terminal study, VFT and CFT pulse trains were compared. VFT stimulation caused significantly greater increases in stroke power, maximum aortic flow, and LV dP/dt compared to CFT stimulation. For the same number of pulses, VFT increased stroke power by 20.6% ($p<0.05$), maximum peak aortic flow by 20.1% ($p<0.05$) and max LV dP/dt by 14.6% ($p<0.01$) compared to CFT.

Designing novel strategies to maximize skeletal muscle performance during FES

Typically during FES, the frequency used to activate muscles is kept the same and the users increase the stimulation intensity (pulse-duration or pulse-amplitude) to maintain targeted performance as the muscles fatigue. However, during CMP, different stimulation strategies can be used to maintain cardiac output for a greater number of contractions. Stimulation parameters can be varied across trains during repetitive stimulation in an attempt to maintain the targeted muscle output for prolonged durations. Recent studies in our laboratory investigated the effectiveness of novel strategies of modulating stimulation frequency [18] as well as modulating both stimulation intensity and frequency on muscle performance during repetitive activation of human quadriceps femoris muscles [9, 10, 19]. Chou and colleagues showed that in paralyzed quadriceps muscle, for an initial stimulation frequency of 30-Hz, progressively increasing the pulse intensity followed by the train frequency using a customized modulation strategy produced more successful contractions compared to progressively increasing frequency followed by intensity[10]. Also, the starting frequency affected task performance and fatigability during repetitive electrical stimulation. We found that the electrical stimulation protocol that began with 30-Hz trains and progressively increased stimulation intensity followed by frequency produced a greater number of successful contractions compared to protocols that started with 20-Hz or 40-Hz trains (Fig. 2) [9]. In addition, because VFTs are known to produce force enhancement in the fatigued muscle compared to CFTs, it is hypothesized that another potential strategy to maximize muscle performance during repetitive stimulation may be to start with CFTs and switch to VFTs as the muscle fatigues. Scott and colleagues tested this hypothesis and showed that switching the stimulation train pattern from a CFT to a VFT produced more successful contractions of the human quadriceps muscle compared to stimulating with either CFTs alone of VFTs alone [28]. Scott and colleagues used a special type of VFTthat consists of high-frequency doublet pulses throughout the train [28]. Hence, a judicious manipulation of stimulation frequency, intensity, and pattern is necessary to maximize muscle performance during application of electrical stimulation for CMP.

Conclusion

Strong, fatigue-resistant, muscle contractions would be ideal for skeletal muscle cardiac assistance. The lessons learnt from recent electrical stimulation studies provide potential approaches to accomplish this goal. Recent studies suggest that rearranging the stimulus pulse pattern to form VFTs that takes advantage of the catchlike property of skeletal muscle for can help to produce greater power compared to traditionally used CFTs during cardiomyoplasty, even when using fewer pulses.

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