THE USE OF IMPLANTED INTRAMUSCULAR FES SYSTEM FOR AMELIORATING FOOT DROP DURING LOCOMOTION

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THE USE OF IMPLANTED INTRAMUSCULAR FES SYSTEM FOR AMELIORATING FOOT DROP DURING LOCOMOTION

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"This integrative action in virtue of which the nervous system unifies from separate organs an animal possessing solidarity, an individual, is the problem before us".

-Sir Charles Scott Sherrington

This thesis is respectfully dedicated to all the individuals inculcating me with a love of learning.

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LIST OF SYMBOLS AND ABBREVIATIONS

Abbreviation	Name
FES	Functional Electrical Stimulation
ALS	Amyotrophic Lateral Sclerosis
PFFB	Positive Force Feedback

SUMMARY

Functional Electrical Stimulation (FES) is an assistive method for patients with dysfunctional nervous system who cannot functionally contract skeletal muscle to generate voluntary movement. By applying electrical stimulation on the skin, the muscle is able to generate the contractile force in which it previously wasn't able to. Current FES systems rely on control systems that use external physical cues, such as a tilt sensor, to determine the timing of stimulation. This method still reflects some problems, as it doesn't reflect individuality of patients and cannot function properly when the user walks on an inclined surface. This clinical research targets on examining the feasibility of developing an alternative control system that can control the muscle volitionally through the nervous signals generated by the user. A model of the FES system is created by stretching the gastrocnemius muscle and apply intramuscular stimulation in the decerebrated cat. It is hypothesized that the force of the muscle after electrical stimulation is higher than that without stimulation and this positive force feedback is only viable within a range of electrical stimulation. To test this hypothesis, a target tension of muscle contraction in an isolated feline muscle was used as the cue for electrical stimulation with the intent to boost that muscle contraction, that is, positive force feedback was used to initiate intramuscular stimulation as a means of increasing the force of muscle contraction in a decerebrate feline model. The maximum force and duration of contraction were compared when the muscle was stretched with and without stimulation. By varying the initial frequency of stimulation and the amount of stimulation relative to the force output of the muscle, the strength of distinct muscle contractions was increased.

It is found out that using one tailed nonparametric, unpaired students' t test, the p value of the controlled group($n_1 = 9$) and the threshold 1.2N($n_2 = 10$) is $2.48 * 10^{-5} < 0.05$, which rejects the null hypothesis. It is also observed that below threshold values of these parameters no effect was observed and above threshold values tetanic contraction was initiated, but between the range of the intermediate values, the force of muscle contraction between the stimulated groups and the control group increased. These findings suggest that positive force feedback could be a potentially viable control system for FES systems.

CHAPTER 1

INTRODUCTION

Functional electrical stimulation (FES) system is a widely used technique that can greatly improve the quality of life of a person by restoring or assisting his or her voluntary ability such as walking, standing, breathing, coughing, arm reaching or bladder and bowel evacuation (Peckham, 2005). By applying current via the electrode pair, FES system can generate muscle contraction assisting the patient to achieve specific motor tasks. The idea behind the FES system is that electrical pulses applied to the nerve can create action potentials which, if propagated distally, can be transmitted to the neuromuscular junction and direct the muscle to contract. Because the threshold required for activation of a muscle fiber is much greater than the threshold for producing action potentials in a nerve fiber, the electrical stimulation of muscle occurs by stimulation of motor axons with the muscle. An alternative approach is to stimulate muscle nerves, but this approach has the disadvantage of stimulating sensory afferents as well. Additionally, recent evidence suggests that functional electrical stimulation has significant therapeutic effects in reversing muscle atrophy, increasing cortico-spinal connections, controlling muscle spasticity and recovering the damaged reflex circuit closer to its normal neurological functions (Ragnarsson, 2008).

The FES system is commonly used to treat foot drop symptom. Foot drop, the inability to lift the foot during ambulation, is commonly observed in patients with ALS (amyotrophic lateral sclerosis), Parkinson's disease, multiple sclerosis, stroke or incomplete spinal cord injury (Stevens, 2010). This could be seriously debilitating because the ability of lifting a foot is an essential part of the swing phase in the gait cycle. Foot drop can happen to one or both feet at the same time and can be rooted from underlying neurological, muscular or anatomical problem. Patients with foot drop show high stepping gait and exaggerated swing motion. They have difficulty performing

activities that require the use of the front foot and experience muscle atrophy in the leg. By using electrically stimulation on the peroneal nerve during footfall in the swing phase of the gait cycle (figure 1-1), the muscle contraction could be amplified, allowing dorsiflexion in the ankle joints. This can help patients return to their regular gait cycle. The current FES system uses a tilt sensor for controlling the gait of the person during walking (Dai, 1996). This external physical cue will determine the activation of the stimulation in the FES system during swing phase based on the angle between the sensing axis to the reference axis with respect to the gravity. This method, however, creates inaccuracy in mimicking the gait cycle because of the discrepancy in stride lengths and sagittal plane joint movements across individuals. Moreover, the hemiplegic patients adopting this type of controlled system will have difficulties walking on an incline because the reference axis doesn't align with that of the inclined surface (Ghoussayni, 2004).

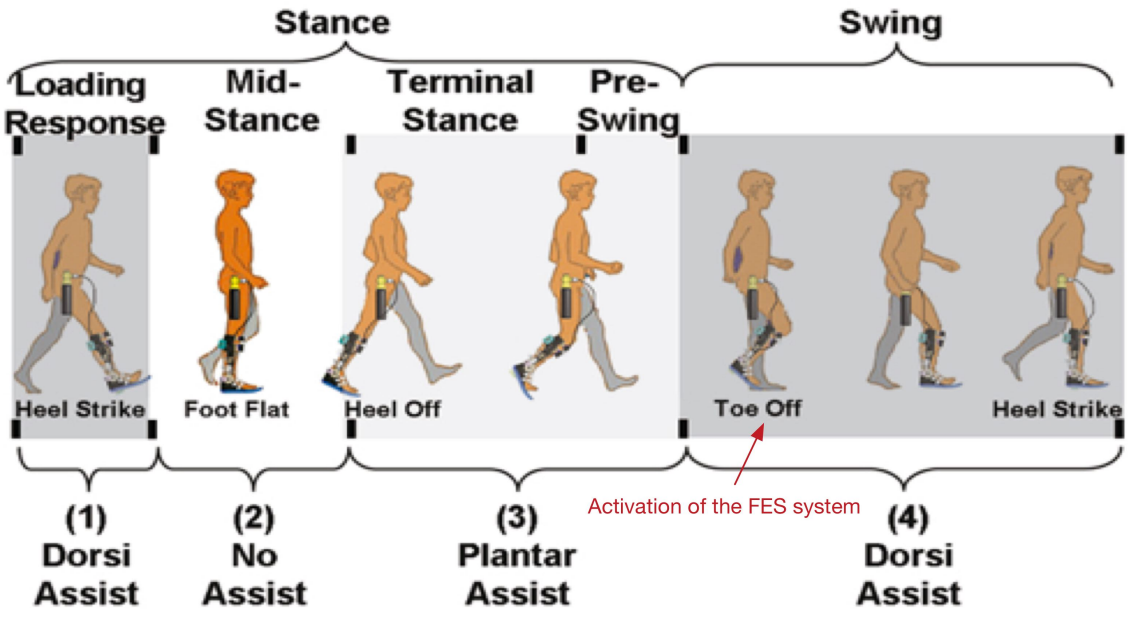


Figure 1-1. The Gait Cycle. The FES system activates at the beginning of the swing phase when the toe is lifting up from the ground.

Recent neurophysiological research shows accumulating evidence for positive feedback in the control of motor tasks in animals, which can possibly substitute the current activation mechanism for the FES system. Positive force feedback is the excitatory effect of the muscle once perturbation is applied. Two prominent sensory receptors in muscle are the muscle spindle and the Golgi tendon organ neuron (Figure 2.1). The muscle spindle detects the length of the muscle. The tendon organs, locating between the muscle and its tendon, senses muscle force. Positive force feedback increases the force of muscular contraction in concert with length feedback from the muscle spindle. The patient who has foot drop will have deficit muscular or neural activities. This means that the patient has the willingness to lift the feet but is unable to exert enough muscular contraction during the foot lifting process. The FES system can detect the modest forces developed by the patient using the intramuscular EMG signal to apply electrical stimulation in the muscle to amplify the muscular contraction. This pilot study shows a preliminary result demonstrating the clinical potential of developing a new technique to enhance the current FES system to reduce the potential problems in which the current predicate device encounters.

CHAPTER 2

LITERATURE REVIEW

The ability to move efficiently is directed by the neural circuits called the locomotor central pattern generators which receive low-dimensional and simple sensory information signal and produce high dimensional and rhythmic movement (Goodman et.al, 2000). The central pattern generators consist of two types of muscle proprioceptors categorized as muscle spindle and Golgi tendon organs that sense the relative position of the body and maintain the spring-like property of the muscle. These proprioceptors input the length and force feedback signals into the central nervous system and mediate the output motor signals (Houk, 1997). These overall effects create the feed-forward control loop called the sensory feedback. Sensory feedback plays an important role in the modulation of posture since it alters the muscular stiffness. Sensory feedback could be categorized into heterogenic feedback and autogenic feedback. Heterogenic feedback happens between two distinct different muscles and autogenic feedback is the feedback that the muscle sends to itself. These feedbacks could be either excitatory or inhibitory. Typically, the excitatory feedback comes from the muscle spindle, and the inhibitory feedback comes from the Golgi tendon organ (Bonasera et.al., 1994). The muscle spindles generally dominate in length feedback while the Golgi tendon organs dominate in force feedback. The length related excitation and the force related inhibition are important because they are strongly correlated with the mechanical properties of the limbs. The length feedback can enhance the muscular stiffness and reduce the muscular stiffness's dependency on the disturbance of the background force (figure 2-1). This adjustment to the muscular stiffness is termed as stiffness regulation (Houk, 1979). In a

static state, positive force feedback could contribute to instability and oscillation. However, during locomotion, the positive force feedback contributes to maintaining the spring-like property of the muscle and reducing the sensitivity of the perturbation in posture, increasing the movement's stability and control (Prochazka et.al., 1997).

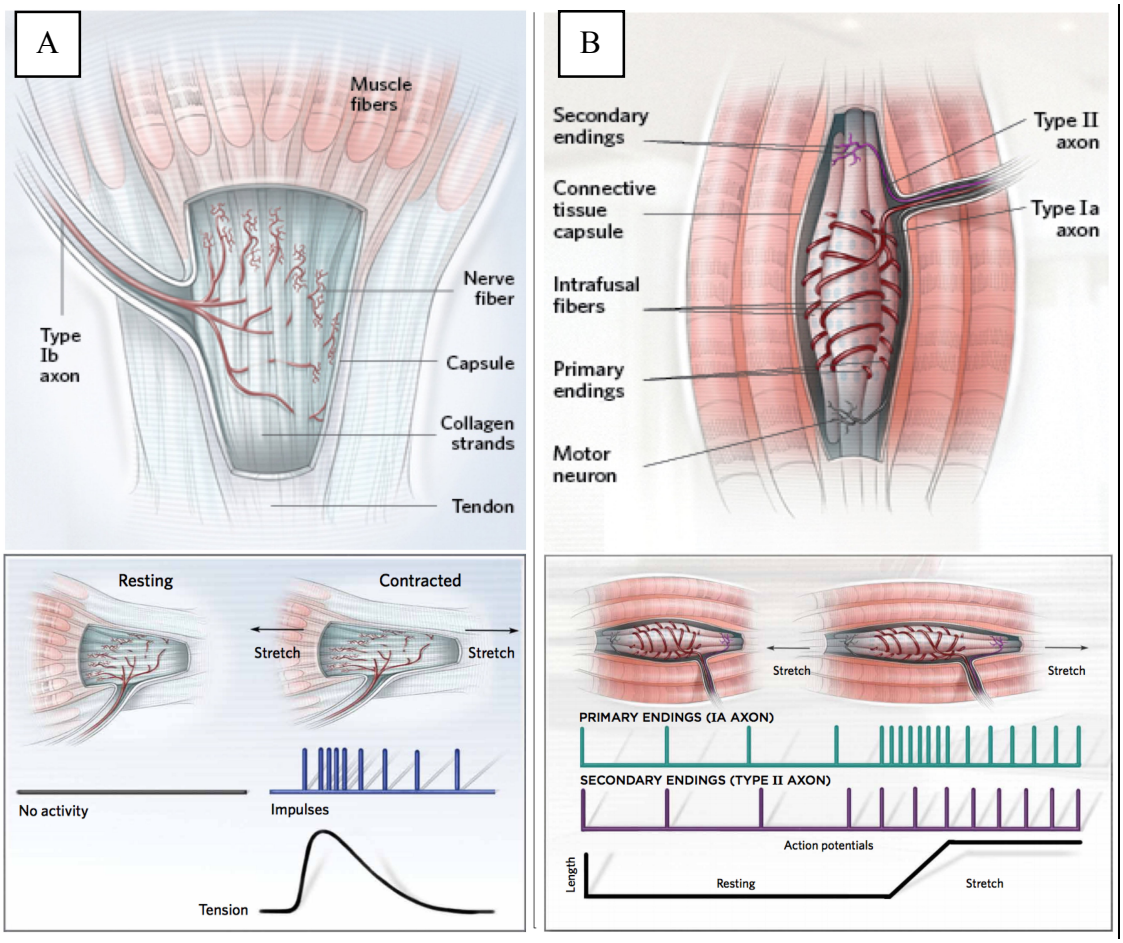


Figure 2-1. ***Sensory Neurons. Figure 2-1-A represents the tendon organ. Tendons contain nerve capsules in the connective end of the skeletal muscle and connect the muscles with bones. The sensory axons in the nerve capsule, called the type Ib axon, detects the muscle force. Figure 2-1-B represents the muscle spindle. It is located in the middle part of the skeletal muscle. The sensory axons of the muscle spindles composed of Type Ia axon and Type II axon. The muscle spindle detects the length change of the muscle. Collectively, the tendon organ and the muscle spindle creates proprioception, the ability to sense the relative position of neighboring parts of the body and strength employed in movement. (Delphia, 2016).***

CHAPTER 3

METHOD AND MATERIALS

All animal procedures were approved by the GT IACUC and followed guidance from the NIH.

A schema of the experiment design and arrangement of the apparatus is shown in figure 3-1. A female cat was decerebrated under isoflurane anesthesia with all the brain tissue rostral to the transection was removed (Nichols, 1987). Anesthesia was removed after the completion of the decerebration. Two experiments were performed in two different days. Day one consists of 51 trials and day two consists of 11 trials. The tendon of the gastrocnemius muscle was detached from the decerbrated cat and connected to a linear motor that can mechanically stretch the muscle for 0.1ms for every 0.25ms period. Strain gauge myograph lied between the linear motor and the muscle providing measurement in the skeletal muscle force. The computer took the measurement and outputted the force diagram as shown on figure 3-2. Figure 3-3 shows an example of the individual force signal in the force diagram. A value of the skeletal muscle force is set up in the computer prior to the stretching as the threshold value for activating the electrical stimulation. Intramuscular wire electrodes were placed within the gastrocnemius muscle and only activated if the force measured by the myograph exceeded the threshold value and the stimulation stopped once the muscle force dropped below the threshold value(<0.1ms). In the day one's experiment, three electrodes with different amplitudes (5.5V, 2.7V and 2V) electrical stimulations pulsed at a square waveform once the force crosses the threshold value were placed in the right medial gastrocnemius muscle. In the second day's experiment, only one electrode electrical stimulation pulsed at 1V

amplitude with the same waveform and frequency as the first day's experiment was placed at the right gastrocnemius muscle.

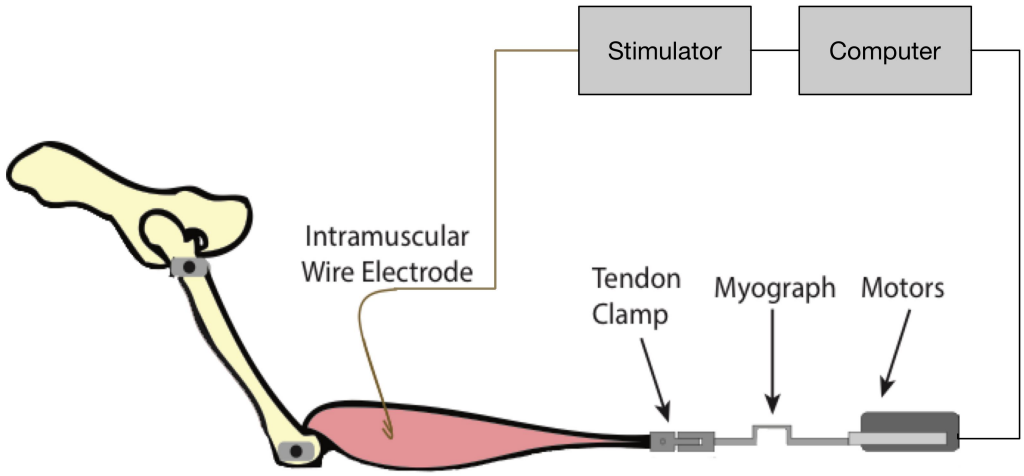


Figure 3-1. Schema of Experimental Design and the Arrangement of the Apparatus. The tendon of the gastrocnemius muscle is detached from the decerbrated cat and connected to a linear motor that mechanically stretches the muscle for 0.1ms for every 0.25ms period. Strain gauge myograph lies between the linear motor and the muscle providing measurement in the muscle force. Intramuscular wire electrode is inserted in the gastrocnemius muscle and stimulates electrical current to the muscles. The constant electrical stimulation is a square waveform with 80 Hz saturation frequency.

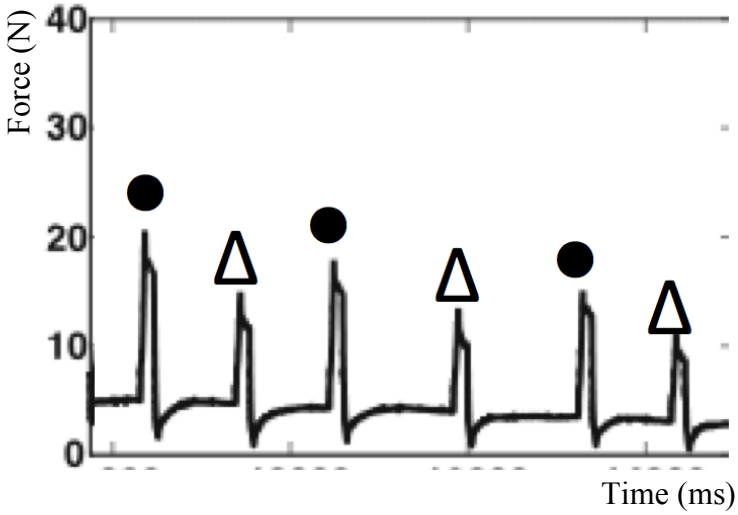


Figure 3-2. The Force Diagram Recorded by the Computer. Stimulation is applied every two force pulses. The black round dot indicates that electrical stimulation and mechanical stretch coexist while the triangle sign indicates when only stretch exists.

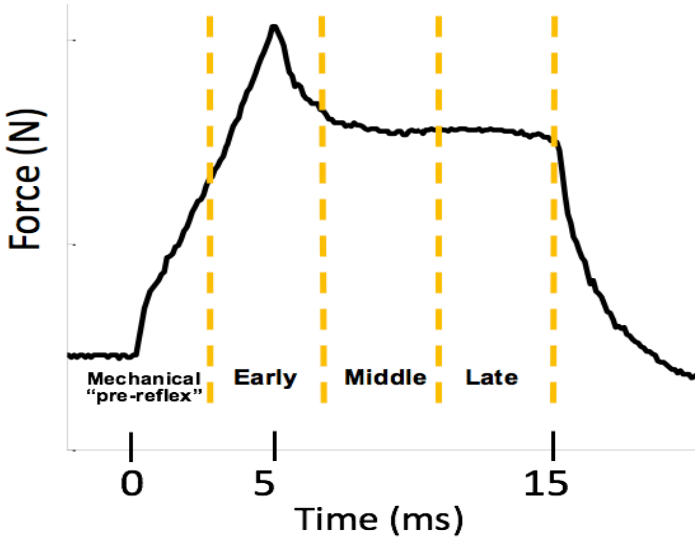


Figure 3-3. The Different Phases of Force Signal in the Force Diagram. Beginning phase is the mechanical pre-reflex resulted from the mechanical stretch of the linear motor. The early epoch phase of the force usually reaches to the highest level in force magnitude. In the middle phase, force amplitude is regulated to a stable level. The late epoch phase is the phase when force reaches the stable level before the force effect fades.

Statistical Analysis

To assess the difference between the control trials and the experimental trials, the late epoch of the muscle contraction, the maximum muscle contraction and the duration of the muscle contraction are compared. Significance is examined by using one way nonparametric, unpaired students' t test ($p<0.05$ means the result is significant) for day one's trial. Bar graph would be displayed to show the difference between experimental trial and control trial. Box and whisker plot would also be used to graphically display a difference between the control and experimental groups in day 1's trial. Because day 2 has relatively small sample size, day 2's table will be displayed showing the average of all the trials with the magnitude of late epoch, maximum force and the time duration.

CHAPTER 4

RESULTS

The experiment compared force of muscle at the late epoch period of the control trial to a corresponding time point of experimental trials. Figure 4-1 demonstrates different scenarios of muscle contraction, including the contraction without positive force feedback(control), with positive force feedback and with excessive positive force feedback. Figure 4-1 shows examples of muscle force in different circumstance: without positive force feedback, with positive force feedback and with excessive positive force feedback. Below a threshold level of stimulation, there was no observed change in the muscle reaction (figure 4-1-A). Once threshold of stimulation was surpassed there was an increase in the force output (figure 4-1-B). Below threshold values of these parameters, no effect was observed and above threshold level of stimulation, the muscle would exhibit a sustained contraction until the trial was ended and stimulation removed (figure 4-1-C). The late epoch is measured as the end point of the force signal when force reaches the stable level, and is taken at the first relatively horizontal curve's end (figure 4-2). The observed results show that within a range of intermediate values of electrical stimulation, the force of muscle contraction increased (figure 4-3). Across the trials, there is an increase of force response comparing the control and experiment group($p<0.05$) with students' t test and is further verified by the box plot (figure 4-5). However, it is also shown that there was no correlation between amount of PFFB and the increase in force at late epoch and between amount of PFFB and amount of increase of maximum force output (figure 4-3). There is no correlation between the amount of positive force feedback and the time duration of the muscle contraction (figure 4-4). Table 4-1 is the result from the 11 trials day 2's experiment and shows a similar outcome.

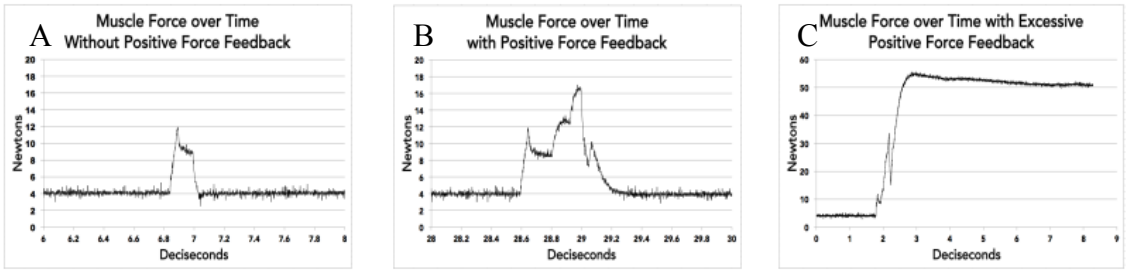


Figure 4-1. Muscle Force over time with Different Level of Current Stimulation. 4-1-A represents the muscle over time without positive force feedback. 4-1-B represents the muscle force over time with positive force feedback. 4-1-C represents the muscle force over time with excessive positive force feedback.

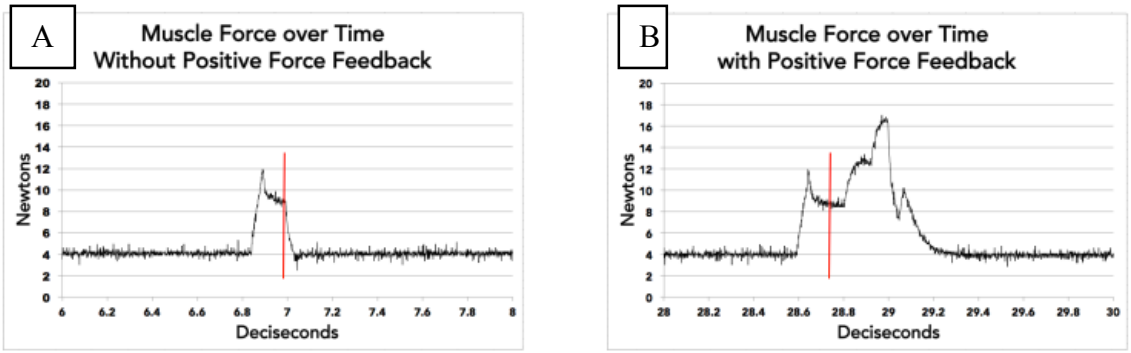


Figure 4-2. The Late Epoch Labeling. The late epoch phase is the phase when force reaches the stable level, and is taken at the first relatively horizontal curve's end. 4-2-A shows the late epoch labeling of muscle force over time without positive force feedback. 4-2-B shows the late epoch labeling of muscle force over time with positive force feedback. This example shows that if there is an increase of force after the force goes relatively stable, the late epoch is still taken at the end of the first horizontal curve. The late epoch labeling is to be differentiated with the maximum force amplitude, which is taken at the maximum force level of each force signal.

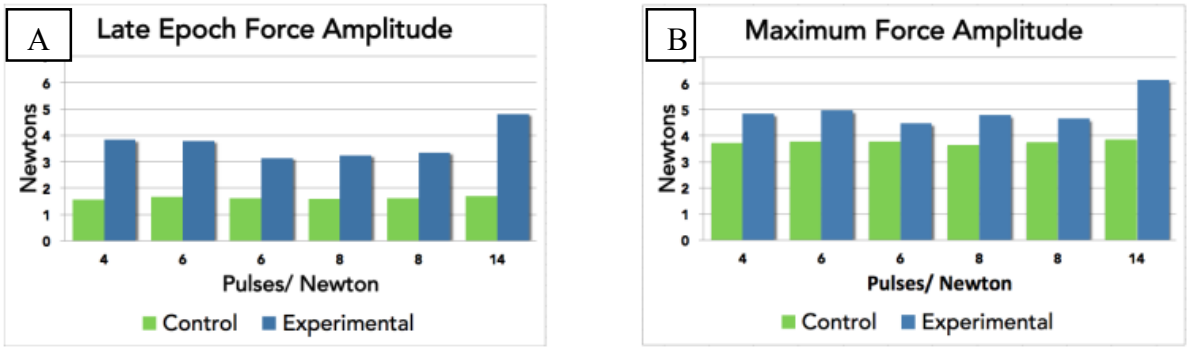


Figure 4-3. the Bar Graph of Force Amplitude result. 4-3-A shows that there was no correlation between amount of PFFB and the increase in force at late epoch. 4-3-B shows that there was no correlation between amount of PFFB and amount of increase of maximum force output

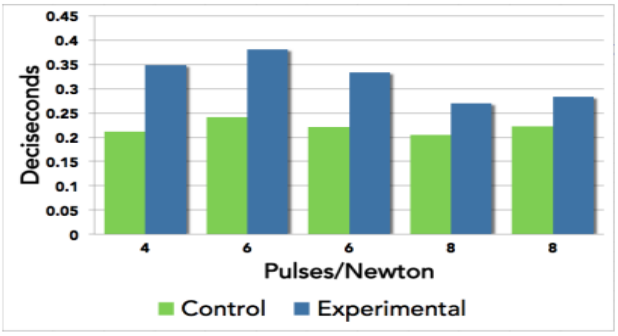
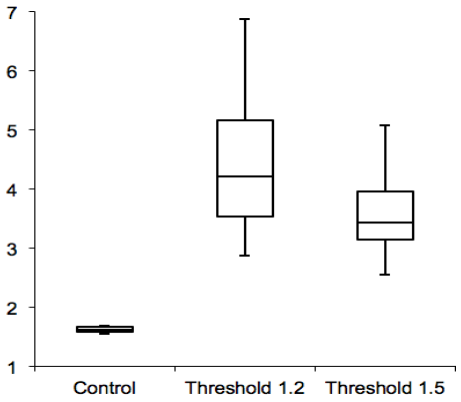


Figure 4-4. the Bar Graph of Duration Results: there is no correlation between amount of positive force feedback and the time duration of the muscle contraction



Labels	Control	Threshold 1.2	Threshold 1.5
Min	1.5581	2.8855	2.556
Q_1	1.591925	3.53965	3.14695
Median	1.6195	4.2227	3.4414
Q_3	1.6793	5.16875	3.96565
Max	1.6992	6.8742	5.0762
IQR	0.087375	1.6291	0.8187
Upper Outliers	0	0	0
Lower Outliers	0	0	0

Figure 4-5. The Box and Whisker Plot of the first day's Experimental Data: the median of the experimental groups (threshold 1.2 and 1.5) is significantly higher than the threshold of the control group. This box plot shows that the electrical current stimulating the muscle elevate the force output and verifies that the existence of positive force feedback. Using nonparametric one tail t test with unequal variance, the p value between control and threshold 1.2N is $2.48 * 10^{-5}$ and the p value between the control and threshold 1.5N is is $1.26 * 10^{-10}$, which both reject the null hypothesis ($p<0.05$)

	N	Late Epoch(N)	Max (N)	ime Duration (ms)
Control	4	0.21	0.24	0.61
Threshold 4N	3	0.32	0.74	1.16
Threshold 6N	5	0.38	0.60	0.62

Table 4-6. The Data Analysis of the trials in control, and electrically stimulating the muscle above 4N and 6N in the second day's experiment. N is the sample size. Late epoch means the magnitude of the late epoch. Max means the magnitude of the maximum point in a single force response. Time duration takes the time of a single force response.

CHAPTER 5

DISCUSSION

The results show that below a threshold level of stimulation, there was no observed change in the muscle force output. Once the force of the muscle exceeds the threshold of stimulation, electrical current is applied to the muscle and demonstrates a higher force output. An increase in the duration of the contraction is also observed in the addition of an electrical stimulation. However, at a certain range of threshold, the muscle would exhibit a sustained contraction until the trial was ended and stimulation removed. This behavior is expected from a positive feedback system with sufficient loop gain. The comparison of force of muscle at the late epoch period of the control trial to a corresponding time point of experimental trials shows that there was no correlation between amount of PFFB and the increase in force at late epoch, the amount of increase of maximum force output or the duration of contraction of the muscle. However, the study shows that the intramuscular stimulation does exhibit a positive force feedback response and verifies the fact that the electrical stimulation applied to the muscle can trigger an elevated force magnitude. The boundary point is still yet to be known for a stable positive force feedback where the ankle yield is low. It is determined that there was a wide range of parameters within which the system was stable during locomotion.

CHAPTER 6

CONCLUSION AND FUTURE WORK

In this experiment, the relationship between the increment of force output and the stimulation threshold was unpredictable, but this study was able to show that there existed a range of gains where the behavior was stable, and a threshold beyond which the stabilized feedback system disappeared and became tetanic contraction. The result of this study shows that positive force feedback can be viable trigger system for activating the FES system. The technique currently approved for human use uses a tilt sensor, which has limitations when the user is walking on an incline (Ghoussayni et.al., 2004). This study shows that within a certain range, a stable effect of the positive force feedback exists. The next step is to find the boundary point where positive force feedback exists and use those theories to apply to an algorithm for the FES system to activate the muscle contraction. An EMG will be implemented in the muscle detecting the force response. When the user intends to move, the positive force feedback will activate the electrode of the FES system. Using the positive force feedback is potentially better than the other predicate device in the market. The device will work independently of terrain and will not alter its response arising from the change in angle. The device is also expected to function as a muscle modulator that provides muscle with a more spring-like behavior.

In a proposed design of the functional electrical stimulation device, Fiber optic micro sensor would be implanted to take the measurement of tendon force of the tibialis anterior (Behrmann et. al., 2012). Self-adhesive surface electrodes will be placed on the skin covering the motor points of tibialis anterior to stimulate. Once the initiation of toe

off action is detected through the measurement of the muscular force is higher above a certain threshold, the electrodes will electrically stimulate the muscle and stopped once the recorded force is beyond another upper boundary threshold. These lower and upper boundary threshold value will be further investigate to depict a more accurate range to maintain the stability of the muscle and avoid tetanic actions. To avoid instability, the electrical stimulation could be programmed to turn off once the tetanic contraction is detected by the fiber optic micro sensor.

This study still has several limitations. The sample size is small and the placements of electrodes were not uniform throughout all trials. The electrodes have resistance and might move during stimulation, therefore providing inconsistent responses. The voltage of the electrodes are different in order to attempt similar responses from the muscle. The medial gastrocnemius muscle was used for other studies prior to this experiment and might affect the muscle. To resolve the current issue, future studies will incorporate more experimental trials with more treatment groups and control groups. A selection matrix will be made to select trials that could be useful in the data analysis. To resolve the issue of the different placement of electrode in the muscle, a microelectrode array will be implemented to allow precise stimulation in the muscle.

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