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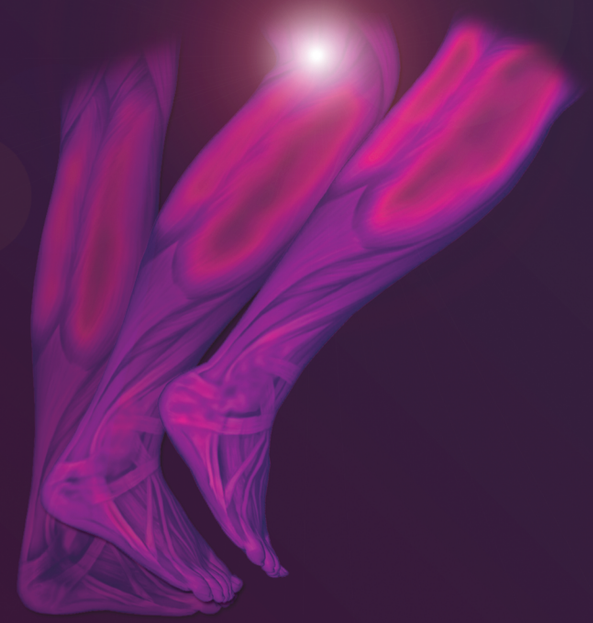
FES OF THE TRICEPS SURAE DURING GAIT

Colleen C. Monaghan

FUNCTIONAL ELECTRICAL STIMULATION OF THE TRICEPS SURAE DURING GAIT



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Prof. dr. ir. P. H. Veltink
Prof. dr. ir. H. J. Hermens
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List of Abbreviations

Δφ	Change in angle since heel strike
AGLR	Approximated likelihood ratio principle
cGM	Gastrocnemius Medialis of leg contralateral to stimulation
CoM	Centre of Mass
CoP	Centre of Pressure
cRF	Rectus Femoris of leg contralateral to stimulation
cST	Semitendinosus of leg contralateral to stimulation
cTA	Tibialis Anterior of leg contralateral to stimulation
CVA	Cerebrovascular Accident (stroke)
EMG	Electromyography
FES	Functional Electrical Stimulation
F_Z	Ground reaction force. Force in the Z direction.
iGM	Gastrocnemius Medialis ipsilateral to stimulation
iRF	Rectus Femoris of leg ipsilateral to stimulation
iST	Semitendinosus of leg ipsilateral to stimulation
iTA	Tibialis Anterior of leg ipsilateral to stimulation
NSe	No stimulation applied during gait. This stimulation condition was measured prior to the Se condition
NSf	The final non-stimulated trial carried out at the end of the healthy subject experiments
NSl	No stimulation applied during gait. This stimulation condition was measured prior to the Sl condition
NSm	No stimulation applied during gait. This stimulation condition was measured prior to the Sm condition
SCI	Spinal Cord Injury
Se	Early stimulation. Stimulation applied early in the gait cycle
Sl	Late stimulation. Stimulation applied during late stance
Sm	Mid stimulation. Stimulation applied during mid stance
TS	The triceps surae muscle, contributing to plantar flexion and push-off during gait.

Chapter 1

General Introduction

1.1 Introduction

Stroke, also known as a cerebrovascular accident (CVA), is the third most common cause of death in developed countries [1] and the leading cause of disability [2,3,4,5]. While the incidence of stroke is declining in many developed countries, the figures are still high. Annually, stroke affects approximately 15 million people worldwide [5]. Approximately one third of this number will die, another third will live with permanent disabilities caused by the stroke [5], the others will eventually recover. Recovery can be within 24 hours in the case of a transient ischaemic attack (TIA) [5], commonly known as a mini stroke, or it can take many months.

A CVA can occur due to a blockage, causing decreased blood flow to the brain. This is an ischemic stroke and accounts for around 80 [4]-87% [6] of all occurrences. The remaining 10 [6]-20% [4] of occurrences are due to a brain haemorrhage, caused by a rupture of a blood vessel in the brain. High blood pressure, high cholesterol, diabetes, smoking, obesity and excessive alcohol intake [1-6] can increase the risk of having a CVA.

A CVA causes a lack of neuromuscular control and complete or incomplete loss of sensation on one side of the body (hemiparesis). While CVA affects every aspect of the survivor's life, including upper and lower body movement and coordination as well as psychological aspects, the work described in this thesis will focus on the push-off phase of gait.

1.2 Recovery Stages of Stroke

At the event of a CVA, limbs become completely flaccid and no movement can be initiated. The recovery process has a specific pattern and is generally considered to be complete at approximately six months post-stroke. Over time, slight movement can be initiated; spasticity develops, and then reduces; and eventually, improvement of movement and coordination [7] occurs. Patients can form a plateau at any stage of recovery, but the sequence of events remains the same [7].

1.2.1 Recovery of Gait after Stroke

Investigations of changes to muscle activation patterns of both paretic and non-paretic legs of stroke subjects during gait [8,9,10] have been conducted using

electromyography (EMG). Studies have also involved the development of these changes over the period of recovery [10]. The EMG results [10,11] show that the activation patterns of the non-paretic muscles are also affected due to a CVA and that these patterns, for a select group of subjects, may change over time [11]. However others noted [10] that although the walking pattern clearly improved during the recovery period, the coordination patterns did not.

1.2.2 Classification of Stroke Gait

In general, the effects of stroke are varied; people also deal with these changes in an individual way. Both the Rankin [11] and modified Rankin [12] scales are used in practice, to assess motor damage and self-sufficiency of the survivor. The European Stroke Scale [13], also used in practice, categorises the effects. On the European Stroke Scale, 50% of the assessment is based on cognitive abilities and the other 50% on physical abilities, a total of 26% given to lower limb assessment, including: maintain leg position (4%), flex leg (4%), dorsiflex foot (8%) and gait (10%). While practical, in order to determine how much support is required, these scales are subjective and not quantitative. Knutsson and Richards [14,15,16,17,18,19,20] carried out extensive research, aiming to classify stroke according to the resulting neuromuscular changes, using EMG. As a result, they propose treatment according to how each specific type is likely to respond.

In summary, they found three types of stroke based on disturbed motor control and four, when a combination of effects is present. It should be stressed that all EMG activity of the muscles of the paretic side decreases compared to normal activity.

Type I is classified by premature activation of the triceps surae (TS) leading to poor push-off due to biomechanical constraints. This premature activation, as seen in EMG recordings [14,18] can occur at any time after foot-floor contact. The cause is unknown, but may be due to decreased stretch reflex threshold. The result is pulling back of the lower leg and knee hyperextension [14-20]. In this group, during the transition from stance to swing, the hip hikes the leg upwards, in order to swing it forward. Along with insufficient plantar flexion this ensures inadequate push-off power.

EMG activity of Type II subjects shows a complete lack of, or largely decreased EMG activity on the paretic side [14-20] resulting in knee hyperextension during

stance. EMG shows that there is a lack of phasic activation of triceps surae and low activity in the tibialis anterior. As with Type I, in Type II stroke, activation is too low for sufficient propulsion at push-off [14].

In Type III, excessive co-activations of muscle groups, patterned activity becomes completely disorganised. These activation patterns are more characteristic of activation patterns seen in cerebral palsy subjects than in CVA subjects. The co-activation generally involves quadriceps, hamstrings and calf muscles [15-20].

From this literature, it is clear that a CVA results in inadequate push-off ability.

1.3 Push Off

Before describing the planned treatment to restore stroke push-off, the events, muscles and characteristics of the muscles required for normal gait, specifically for push-off, should be outlined. Gait has been described as a series of repeated falling. A stride begins when calf muscles relax and the body sways forward [21]. At this time, the lower leg pivots forward over the foot, which remains fixed in place, stretching the calf muscles. This places the centre of mass in front of the supporting foot. As a result the other leg must swing forward to make contact with the ground. The calf muscles of the stance leg – the leg still to the rear of the body's centre of mass –contract and shorten, pushing the centre of pressure from the heel to the big toe, generating ankle plantar flexion torque, causing the heel to lift from the ground. As the body weight is shifted from the stance leg, the calf muscles actively flex the knee and push the body forwards [16]. This action constitutes the "push off" [21]. The pelvis is also important here, as its degree of rotation determines the forward distance that the swinging leg can make [21].

1.3.1 The Ankle Joint

The ankle joint complex is composed of the talocrural joint and the subtalar joint [22]. The talocrural joint is a hinge joint between the tibia/fibula bones of the lower leg and the talus bone of the foot. The subtalar joint is the joint between the calcaneus and the talus bones of the foot [22]. The talocrural joint has one degree of freedom, with its rotation axis between the tips of the malleoli. The foot rotates around this mediolateral axis, approximately perpendicular to the sagittal plane, resulting in dorsal or plantar flexion. Plantar flexion is the movement of the foot

away from the anterior surface of the tibia and dorsiflexion is movement in the opposite direction [23]. However, the subtalar joint of the foot allows for additional degrees of freedom including inversion/eversion and internal/external rotation [22]. Orientation changes around these axes may occur during the swing phase of gait. However, during stance, the ground prevents major orientation changes around these additional axes. Therefore, in the event of push-off, movement and torque generated around the mediolateral axis, which are induced by contraction of the triceps surae (TS) are the most important.

1.3.2 The Triceps Surae

The main muscle groups responsible for push-off are the calf muscles; the superficial layer is known as the triceps surae (TS). The TS contains three muscles, however, in humans, the plantaris muscle is rudimentary, so the TS concerns two main muscles, the gastrocnemius and the soleus. The soleus is monoarticular. It has origins on both the upper posterior surface of the tibia and fibula and insertion at the Achilles tendon [24]. The primary function of the soleus is plantar flexion. The gastrocnemius is biarticular, with a medial and lateral head, which originate from the respective medial and lateral condyles of the femur. Like the soleus, the insertion of the gastrocnemius is at the Achilles tendon [24]. Because of their biarticular nature, the gastrocnemii can cause both plantar flexion and knee flexion. The soleus is mainly comprised of small, slow-twitch, low-force-output motor units. The gastrocnemius contains approximately equal amounts of fast and slow units, and can therefore produce a large range of force output [24].

Muscle mass and muscle spindle density are larger in the soleus than in the gastrocnemii combined. Soleus volume is approximately 450 cm^3 in a human adult. The lateral gastrocnemius is 145 cm^3 and the medial gastrocnemius is 260 cm^3. The amount and density of spindles in the soleus is much greater than in the gastrocnemius, the soleus has approximately 400 spindles, with a spindle density of 0.94 spindles/g and the gastrocnemius has approximately 150 spindles and a density of 0.4 spindles/g [24]. With a larger volume and cross sectional area than both the lateral and medial gastrocnemius, the soleus has a larger force generating capacity [25].

The TS provide the majority of energy needed for movement during push-off [26,27] and swing initiation [28].

1.4 Treatment Methods in Stroke

Treatment of stroke patients takes on a variety of forms, including physiotherapy, functional electrical stimulation (FES) treatment, and a combination of these methods, on both upper and lower limbs. Furthermore, subjects are provided with mechanical supports such as a walking stick or an ankle foot orthosis to facilitate locomotion [29,30].

Knutsson and Richards proposed treatments for each type of motor disturbance [19] that they identified in stroke. They found that Type I responds to antispastic therapy. In addition, subjects can be trained to prevent knee hyperextension by rotating the pelvis forward when the paretic leg is in swing. This moves the body weight further over the support foot at weight acceptance [7,18]. Consequently, only forward progression is possible when the TS contracts prematurely [17]. Alternatively, placing a block into the shoe may prevent the TS from stretching at initial contact, delaying any stretch reflex activation [17,19]. Use of the shoe inlay may be included in a FES program [16]. Type II responds to strengthening techniques [15], especially eccentric contractions, which do not stretch the spastic antagonists [7], a gait re-learning program, electrical stimulation (see 1.5) or an orthosis [7,15,19]. Bedside checks may reveal that Type II subjects exhibit enhanced stretch reflex characteristics, therefore antispastic therapy such a as Baclofen, which is medication for reducing spasticity, may be advisable for such circumstances, however, this will not improve the gait of these subjects [15,19]. Type III is resistant to therapy [7,15] although Knutsson has described Baclofen as being useful at times for diminishing the effects observed in the EMG patterns of these subjects [15].

Other researchers have found that task-specific training has added benefits. Task-specific training has improved the ability of the hip muscles to pull the leg and the ankle to push-off [14,18] at terminal stance.

1.5 Functional Electrical Stimulation

Electrical stimulation of muscles uses electrical current to activate nerve fibres, which contract muscle fibres of intact muscles. The intention of this technique is to cause a contraction in a similar way to physiological activation. Electrical stimulation can be used therapeutically to improve muscle strength or motor function [31,32,33] and relearning [34] or as a treatment to replace a lost function (Functional Electrical Stimulation [FES]).

Physiological recruitment of muscle fibres, while asynchronous, has a pattern initially involving small, slow-contracting, slow fatiguing fibres and, when needed, recruitment of fast contracting, fast-fatiguing and forceful fibres. This is known as the size principal [35,36,37]. Electrical stimulation induces synchronous recruitment of fibres and the recruitment order is reversed [35,36,37]. In this sense, FES is still not optimal. However, under very specific conditions, the recruitment order can be manipulated.

1.5.1 The Motor Response and the H-Reflex

Electrical stimulation excites nerves, which contain both motor and sensory fibres. The tibial nerve, which innervates the soleus and gastrocnemii [24], contains many kinds of efferent and afferent fibres. These fibres have a range of diameters and functions. As described above, during electrical stimulation, larger diameter fibres are activated at lower stimulation levels than fibres with smaller diameters. The largest diameter fibres in a mixed nerve such as the tibial nerve are the Ia afferents carrying information from the primary endings of the muscle spindles and efferent α-motor neuron fibres, innervating the motor units of the muscle. Therefore, stimulation of the tibial nerve induces two responses, seen in EMG as M- and H-waves. The M-wave is a direct motor response due to activation of the α-motor neuron fibres [24,36]. It occurs at approximately 5-8 ms [24] after the onset of the stimulation. The subsequent H-wave, occurring at approximately 30-45 ms after stimulation onset [24], is due to stimulation of the Ia afferents, sending a sensory signal to the central nervous system, which reflexively induces a motor response in the α-motor neurons. This monosynaptic reflex is called the Hoffman reflex (H-reflex) [24,36]. The shorter latency of the M-wave compared to the H-reflex is due to the shorter distance travelled before generating a motor response, the M-wave

travels along only part of the motor aspect of the H-reflex trajectory. The M-wave generally has a higher activation threshold than the H-reflex because the efferent α-motor neuron fibres are, on average, thinner than the sensory Ia afferents [24,36]. The H-reflex is also known as the electrical equivalent stretch reflex, induced, for example by the tendon tap [36].

1.5.2 Applications of FES

FES can be applied to nerves or muscles that have not been damaged as a result of injury. For this reason it is more commonly used in cases where the lesion occurs high in the central nervous system. FES is used to restore functions of spinal cord injured (SCI) subjects [38] when the lesion is in the spinal column, or in CVA subjects [29] when the injury is in the brain. This is because the problem of muscle contraction in these subject groups does not lie with the muscle or nerve itself. FES is used to restore upper [39,40] and lower [39,41] limb, as well as internal organ function [42]. Internally, for example, bladder function can be restored by stimulating the sacral nerve roots via implanted hook electrodes on the intradural or extradural nerve roots [42,43,44]. In the past, bladder control was achieved by stimulating the detrusor muscle, with electrodes stitched onto the bladder wall [42]. On the upper limbs, FES can restore reaching, lifting and grasping functions, to enable everyday activities such as washing, or eating. Lower limb function restoration, using FES, serves to enable rising from a (wheel) chair, to standing balanced, to actually performing gait.

1.5.2.1 Drop Foot

To date, efforts to restore gait functions have focussed on the problem of drop-foot [29,41,45]. Drop foot is the inability to voluntarily dorsiflex the foot, creating a trailing of the injured foot, reducing swing, distance covered and gait speed. Often individuals with a drop foot are offered an ankle foot orthosis, which keeps the foot and lower leg at a 90^{o} angle. This serves to prevent the toes from dropping and helps to prevent falling. Liberson et al. [45] first reported the use of the drop-foot stimulator in the 1960's. The drop-foot stimulator uses FES of the peroneal nerve, to activate the tibialis anterior, causing ankle dorsiflexion. When timed correctly, ankle dorsiflexion enables the foot to lift, from initial swing until heel strike. There

have also been reports of the therapeutic value of the drop-foot stimulator [29], where subjects have stated that without the stimulator being switched on, they can still dorsiflex during swing. This effect is known as carry-over. The drop-foot stimulator is a relative success story in the field of FES and is developed to the stage of implantation [46,47,48]. See Figure 1-1 for an example of the implantable drop foot stimulator.

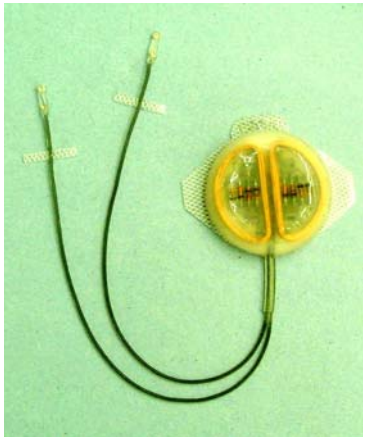

Figure 1-1: Two-channel implantable drop foot stimulator

1.5.2.2 Spinal Cord Injury and Push- Off

SCI is damage to the spinal cord that results in complete or incomplete loss of function or feeling below the level of injury. Causes include car and motorcycle accidents, gunshot wounds or disease [49]. Bajd et al. [28,50] stimulated the plantar flexors of spinal cord injured (SCI) subjects, during gait, inducing push-off. The stimulation caused heel-rise and knee flexion, shortening the leg as it entered into swing, at end stance; as well as providing upward and forward propulsion to swinging leg [28,50]. Bajd et al. [14] found that using FES, force between standing still and push-off increased by 40% and the duration of push-off decreased significantly. They stated [28] that stimulation of calf muscles alone can provoke swing. The subjects in these experiments underwent a muscle strengthening training program and FES gait training program [14]. To date, such research has not been carried out on the plantar flexors of stroke subjects. However, we

hypothesise that FES of the plantar flexors of CVA subjects can provide the same improved push-off observed with SCI subjects.

Munih and Ichie [40] applied FES to the calf muscles, and found that ankle plantar flexion and knee flexion were efferently provoked, and that the flexion withdrawal response was afferently provoked. Duysens et al. [51,52] showed that timing of stimulation influences the responses obtained. They tested stimulation frequencies at different phases of gait, finding that reversal of induced reflexes occurs, depending on the frequency and phase of stimulation. Furthermore, Jones and Yang [53] activated the soleus during the swing phase of gait, producing plantar flexion and falling. This is expected when plantar flexion during swing is triggered.

1.5.3 Changes to Neuromuscular Control due to FES

Stimulation may cause reflexive changes to the stimulated muscle, as well as to muscles and muscle groups ipsilateral to stimulation, or muscles and groups of the leg contralateral to stimulation [24,26,51,52,54]. It is logical to assume that contraction of the stimulated muscles is not the only change that occurs in the body as the result of FES. This hypothesis may be applicable to healthy subjects, as well as patient groups, particularly when considering that over the course of the recovery period following a stroke, changes in neural control of the paretic and non-paretic side occurs, as has been observed in EMG measurements [9]. Therefore, when FES is applied to one muscle group of a CVA subject, this may be considered replacing a lost function and potentially speeding up recovery. In that case, EMG patterns of both legs can be expected to change. Because this has not yet been investigated, it is important that neurophysiological changes during the application of FES are studied [34] in order to understand the interaction between the FES and the nervous system.

1.6 Aims and Objectives

This research was carried out to understand the interactions between FES and the activation patterns of stimulated and non-stimulated muscles during gait. These physiological changes will be measured using EMG. The triceps surae were

chosen because of the potential to improve the lost function of push-off of CVA subjects using FES of this muscle group.

1.7 Thesis Structure

Prior to experimentation on CVA subjects, tests were carried out on healthy subjects, in order to optimise the methodology.

1.7.1 Methodology (I): Comparison of Isometric Ankle Torque Generation Using Surface Stimulation of the Tibialis Nerve or Triceps Surae Muscle

Chapter 2 is an isometric study of electrical stimulation. This study was focussed on a small group of healthy subjects. Two electrode setups were tested, one with the stimulation electrodes directly over the muscle and the other with surface stimulation of the tibial nerve, the nerve responsible for contraction of the plantar flexion group. This nerve lies at the popliteal fossa behind the knee. The aim of the research was to determine if electrical stimulation of the plantar flexors could generate forceful contractions, and if so, what stimulation setup generated best results.

1.7.2 Methodology (II): Stimulation Timing Control

Chapter 3 is the second methodological paper. Trials involving FES of the TS of healthy subjects during gait were carried out successfully using the heel switch as a trigger for stimulation. Upon transfer of this experimental protocol to CVA subjects, it was discovered that the heel switch was an insufficient method for control of stimulation for push-off. For this reason an alternative method was designed, using a gyroscope on the lower leg of the stimulated side.

1.7.3 Healthy Subject Evaluation (I): Interaction of Artificial and Physiological Activation of the Gastrocnemius During Gait

Chapter 4 is the first presentation of the healthy subject gait experiments. FES was applied to the tibial nerve of healthy subjects during gait. EMG measurements were made of all muscles, however only the results of the effects of FES on the medial gastrocnemius ipsilateral to stimulation (iGM) were reported.

1.7.4 Healthy Subject Evaluation (II): The Effect of FES of the Tibial Nerve on Physiological Activation of Leg Muscles During Gait

Chapter 5 is the second of the healthy subject gait experiments. In this paper, EMG of the tibialis anterior (TA), gastrocnemius medialis (GM), semitendinosus (ST) and rectus femoris (RF) muscles of both legs was analysed, with and without stimulation, during gait. Kinematics of the thigh, lower leg and foot of the stimulated side and the lower leg of the non-stimulated side were measured using inertial sensors. Results of the EMG patterns and angular velocity changes are reported.

1.7.5 Patient Evaluation: Effects of FES of CVA Subjects on Stimulated and Non-Stimulated Muscles and Kinematics

Chapter 6 details the results from the patient gait experiments. Like Chapter 5, this paper compares results from EMG measurements from the TA, GM, ST and RF of both legs, as well as kinematic results from the thigh, lower leg and foot of the paretic side and the lower leg of the non-paretic side, with and without surface stimulation, applied to the paretic tibial nerve during gait.

1.7.6 General Discussion & Recommendations for Future Work

This chapter takes into account the work that has been carried out. Overall results are discussed and recommendations are provided to researchers who may wish to develop concepts in the future.

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Chapter 2 Methodology (I)

Comparison of Isometric Ankle Torque Generation Using Surface Stimulation of the Tibial Nerve or Triceps Surae

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Abstract

Objectives: To determine the best electrode setup for maximum plantar flexion torque generation, in an isometric setup. The sub-aim is to transfer the optimal electrode setup to stroke subjects who will benefit from improved push-off during gait.

Methods: Five healthy subjects sat in an isometric setup, while stimulation amplitude was increased in five steps from threshold stimulation to maximum stimulation. At each stimulation level, one burst of 15 pulses of stimulation was applied. The stimulation frequency was 50Hz, and pulse width was 300μs. Six isometric positions were tested, with the leg outstretched, and with the knee flexed, at both knee positions, ankle angles of 20^0 dorsiflexion, neutral (90^0) and 20^0 plantar flexion. At each leg orientation, two different electrode positions were tested, one involved surface nerve stimulation, with a small cathode over the tibial nerve, at the popliteal fossa and the anode at the lower leg. The other electrode setup involved direct muscle stimulation, with both the cathode and anode placed directly on top of the calf muscles.

Results: The tests show that both electrode setups generated large ankle plantar flexion torques, reaching above 70Nm with nerve stimulation and above 90 Nm with direct muscle stimulation. With the leg outstretched, the nerve stimulation generally performed slightly better than muscle stimulation, but this was not the case when the knee was flexed. Recruitment curves were considerably varied in shape and amplitude. Saturation was not always possible to achieve, due to pain sensation of the stimulation.

Conclusions: Stimulation electrode placement is not critical for good stimulation of the plantar flexors. Recruitment characteristics were variable over and within subjects. Pain is induced at very high levels, which is unacceptable for subjects undergoing experimentation. To implement push-off improvement as a functional therapy, considerations should be made to implant the stimulation electrodes to improve the chance of saturation and minimise the chance of pain.

2.1 Introduction

Functional electrical stimulation (FES) is used to replace or facilitate functions that have been lost or reduced [1,2] due to e.g. a stroke (CVA) or a spinal cord injury (SCI). While FES is useful, for example on the tibialis anterior muscle to reduce drop foot, or on the shoulder, arm and hand, for reaching and grasping [1] the effects of FES are not fully understood. Fundamental research is needed in order to understand and eventually predict the outcomes of FES applied under different conditions. These conditions include the choice of muscles, the muscle fibre types, whether the muscle is bi- or mono-articular, the length of the muscle, the load acting on it, as well as, various interactions with the central nervous system [3,4,5]. As these effects can be complex, study of the stimulation in a controlled environment is desired. This can be achieved by stimulation under isometric conditions.

Isometric stimulation of muscles of the triceps surae has been demonstrated in the past [5,6,7] and as expected, torque increase with increased muscle length is reported in most studies. Previous work [6,7,8] involved measurements of ankle plantar flexor torque, with the knee fixed to 60 or 90 degrees flexion, to intentionally minimise the effects of the bi-articular gastrocnemii and to investigate the influence of only the soleus on plantar flexor torque. However in general, these studies do not entail the combination of measurements of plantar flexor torque with electrical stimulation of the tibial nerve and of the muscle bulk, when changes are made to both the knee and the ankle angles.

As the triceps surae are the main muscles responsible for push-off [6], ankle plantar flexion and knee flexion during healthy gait and as they are activated by the tibial nerve, the work described in this chapter involves isometric stimulation of the triceps surae, directly on the muscle and also via the tibial nerve. This work was conducted to investigate if one electrode setup generates larger torques than the other, as it is known the electrode positioning influences the shape of the recruitment curve [9]. Because the gastrocnemii are bi-articular, crossing both the knee and ankle, and the soleus is mono-articular [3,10], crossing only the ankle joint, tests will be carried out with the knee and ankle in flexion and extension, to assess the influence of both joints on the generated ankle torques. The optimal electrode

set up will be transferred to CVA subjects to improve the lost function of push-off[11-16] of these subjects.

In summary, the goal of this research is to determine the best electrode setup for maximum plantar flexion torque, in an isometric setup. The sub-aim is to later transfer the optimal electrode setup to stroke subjects who will benefit from improved push-off during gait.

2.2 Methods

Four subjects, three male and one female, aged between 24 and 27 years old participated in the study. All subjects were right-handed and had no known history of neurological disorders. Each subject signed an informed consent.

Figure 2-1 shows the experimental set up. A custom-made chair was built for isometric torque measurements. The chair was designed to accommodate measurements from the left leg, which could be secured to a metal supporting arm, onto which a rotatable footplate was fixed. The axis of rotation of the leg support could be aligned to the knee joint. The axis of the ankle joint could be aligned to the axis of the footplate. The lower leg and foot orientations could be altered to change both knee and ankle angle. The fixtures were subsequently secured into position. As rotation was prevented, contraction of the triceps surae generated isometric plantar flexor torques. Isometric torque was sensed by a strain gauge force transducer, measuring the force, applied to a beam, which was connected perpendicularly to the axis of the footplate. The torque signal was transmitted directly to a custom-built recording program, in LabView.

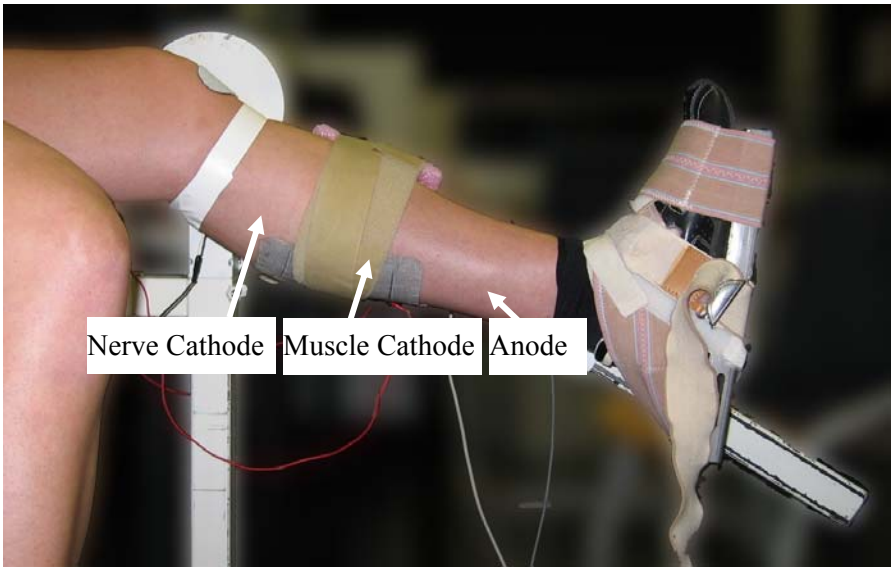

Figure 2-1: Isometric experiment showing the leg and foot fixated to the rig. Knee and ankle rotation was possible to position the lower leg segments for testing. During stimulation, the knee and foot were fixated preventing movement.

Two stimulation scenarios were tested, one involved stimulating the muscle directly, the other via the tibial nerve. Stimulation was provided using a custom-built, bi-phasic electrical stimulator. Each rectangular, charge-balanced pulse had an initial 300µs phase, a 50µs dead space, followed by a second phase lasting 500µs. Stimulation frequency was 50Hz, 15 pulses were delivered per burst. Burst duration was thus approximately 300ms. The burst duration was in accordance with work of Bajd et al.[17] on plantar flexor stimulation of SCI subjects, during gait. Stimulation parameters were modified on a laptop and transmitted to the stimulator via Bluetooth. This ensured that the stimulator and subject could remain physically disconnected from any mains power supply. Stimulation electrodes for muscle stimulation and the indifferent electrode for nerve stimulation, were 50 x 90 mm adhesive electrodes. A Kendall/Tyco Healthcare (USA) ARBO Disposable solid gel Ag/AgCl EMG electrode 22mm x 35mm was used for nerve stimulation.

2.2.1 Procedure

The skin was cleaned abrasively with alcohol, at the popliteal fossa and the triceps surae (TS), where the stimulation electrodes were to be placed, on the left leg. When the skin was dry, the self-adhesive stimulation electrodes were adhered. The tests were carried out at two main electrode setups, one where a stimulation electrode was placed at the popliteal fossa, just above the plantaris, in order to target the tibial nerve of the stimulated leg. To improve selectivity of stimulation, an EMG electrode was used for the cathode above the tibial nerve. This electrode was taped firmly in place, held pressed as close to the underlying nerve as possible, to achieve low-threshold activation. For muscle stimulation, the larger electrodes were placed across the muscle bulk of the gastrocnemii. The cathode was adhered to the widest part of the muscle belly, stretching across both the medial and lateral gastrocnemius. The anode placed approximately 5 cm below the cathode. Electrode placement is highlighted in Figure 2-1. Following electrode placement, subjects took upright-seated position in the custom-built chair. The knee and foot were securely fastened, such that at each set position, no movement was possible. Figure 2-1 provides a visual representation of the experimental setup. Visible in the image is the fixation of the foot into the isometric set up. It should be noted that this photograph, does not display knee fixation.

Measurements were made with a knee angle of 150^0 and 120^0. At the ankle, measurements were made at 90^0 between the tibia and sole of foot (referred to as Ank 0) and 20^0 in the plantar flexion (Ank -20) and 20^0 in the dorsiflexion (Ank +20) directions.

When the subject was fastened to the chair with the knee extended and the ankle in a neutral position, threshold (Thrsh. Stim) and maximum stimulation (Max. Stim.) levels were determined for both electrode setups. Stimulation amplitude was slowly increased until threshold. Threshold in this case was defined as the stimulation level needed to generate a measurable muscle twitch. The amplitude was subsequently increased to a maximum level, where preferably saturation occurred. Saturation can be determined using the torque measurements; when stimulation amplitude increases, no further increase of torque is measured, meaning that the contraction force of the muscle has reached its limit. However, stimulation level was generally painful at such high levels, therefore increase of stimulation

level stopped before saturation was reached, when the subject indicated that no further increase could be tolerated. See Table 2-1 for the stimulation levels used.
Five stimulation bursts were delivered at each leg orientation and electrode setup combination. Stimulation was applied, ramping in equal increments between threshold and maximum. The time between the application of each burst, was approximately 30s, to prevent muscle fatigue. It has been reported that 3 to 5 seconds is enough [10] however others have an interval of one minute. The order of leg orientation and electrode setup was randomised, to prevent the effect of timing (warming up and fatigue effects) on the generated torques.
Peak torques per stimulation amplitude were determined, using Matlab.

2.3 Results

Table 2-1 shows the stimulation levels used for each subject at each electrode set up.
Based on the experimental data, peak torques at each stimulation level, leg orientation and electrode set up were determined and recruitments curve created. These are represented in Figure 2-2 below. Based on this data, Table 2-2 was constructed to find the maximum torque for each electrode setup and leg orientation.
Table 2-1 shows that except for Subject 1, it was possible to increase the stimulation level to larger values using muscle stimulation (Mus), than nerve stimulation (Nrv). With the exception of Subject 3, Thrsh. Stim was lower for nerve stimulation than muscle. This means that nerve stimulation resulted in a muscle contraction at a lower stimulation amplitude than direct muscle stimulation. However, since the stimulation electrode was considerably smaller for nerve stimulation, the current density, is higher at equal stimulation levels, possibly explaining the higher tolerance levels during muscle stimulation and the lower threshold in response to nerve stimulation.

Table 2-1: Comparison of stimulation levels delivered under muscle (Mus) and nerve (Nrv) electrode setups.

	Subject 1		Subject 2		Subject 3		Subject 4	
	Nrv	**Mus**	**Nrv**	**Mus**	**Nrv**	**Mus**	**Nrv**	**Mus**
Thrsh. Stim. (mA)	30.0	34.0	34.0	40.0	33.5	26.0	38.0	46.5
Max. Stim. (mA)	142.0	110.0	67.0	128.0	125.0	157.0	114.0	127.5
Max./Thrsh.	4.7	3.2	2.0	3.2	3.7	6.1	3.0	2.8

*Thrsh. Stim is stimulation level at threshold.

*Max. Stim is the maximum stimulation that subjects could tolerate.

*Max./Thrsh is the ratio of maximum stimulation to threshold stimulation.

*Nrv is the electrode setup involving stimulation of the tibial nerve.

*Mus is the electrode setup involving direct muscle stimulation.

It is clear from Figure 2-2 that, for each individual, the exact shapes of the recruitment curves were different. This figure shows that for stimulation levels above threshold and below maximum, stimulation delivered via the nerve, particularly when the knee was extended, generated larger peak torques than via direct muscle stimulation.

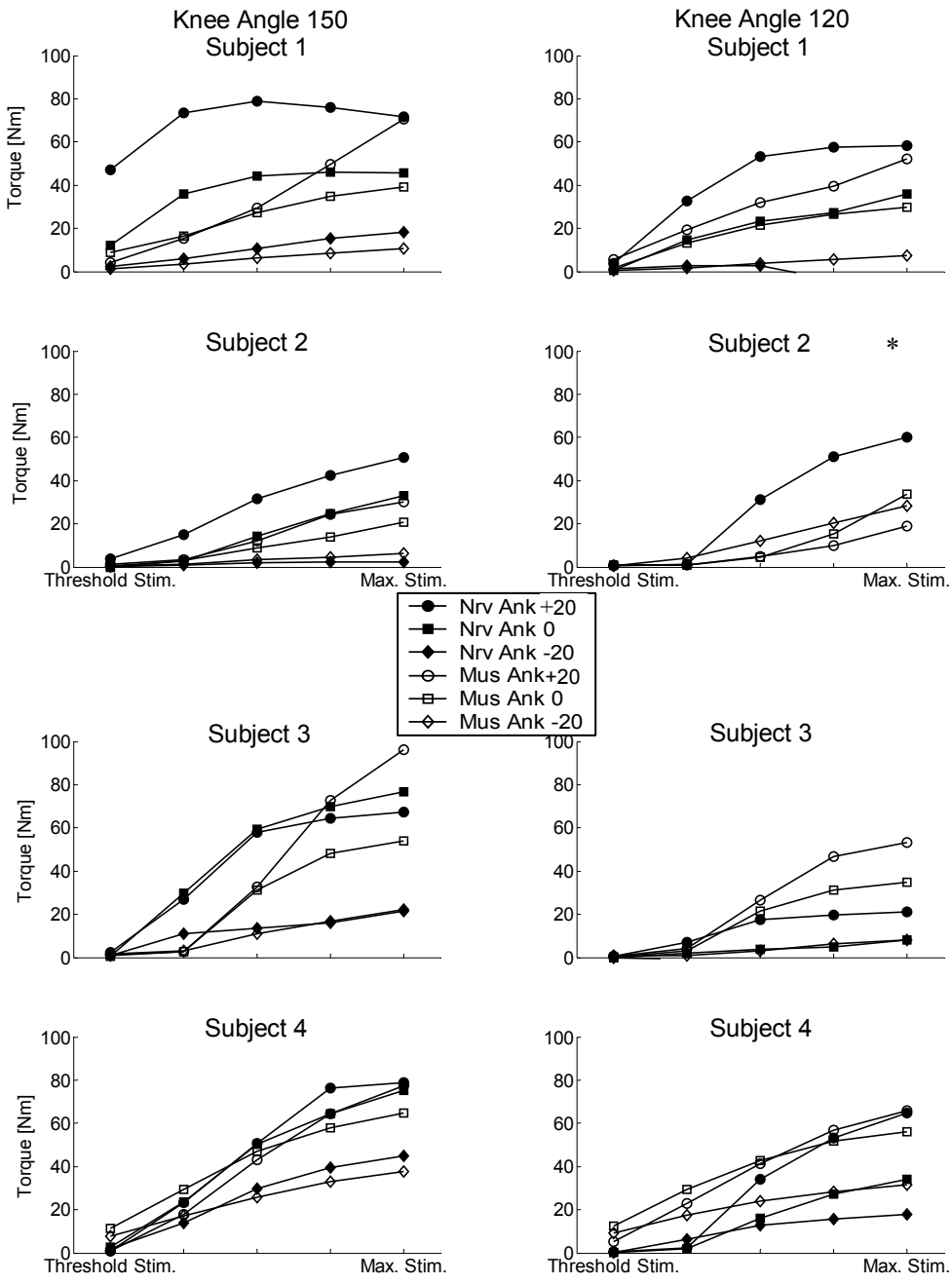

Figure 2-2: Ankle torque generation, for knee angle 150^{o} and 120^{o}, and ankle: Ank +20, Ank 0 and Ank -20 and muscle (Mus) or nerve (Nrv) electrode setup

Table 2-2: Maximum torque generated, for each leg orientation and electrode setup, per subject.*

Sub	Electrode Setup	$Torque_{max}$ Knee Angle 150° [Nm]			$Torque_{max}$ Knee Angle 120° [Nm]		
		Ank +20	Ank 0	Ank -20	Ank +20	Ank 0	Ank -20
1	Mus	71	39	11	52	30	7
2	Mus	30	21	6	19	34	28
3	Mus	96	54	22	53	35	8
4	Mus	77	65	38	66	56	31
Mean		68.5	44.75	19.25	47.5	38.75	18.5
Std		27.8	19.1	14.2	20.0	11.7	12.8
1	Nrv	79 (3)	46 (4)	18	58	36	3 (2)
2	Nrv	51	33	2 (4)	60	-	-4 (3)
3	Nrv	67	77	22	21	8	0 (1)
4	Nrv	79	75	45	65	34	18
Mean		69.0	57.8	21.8	51.0	26.0	4.3
Std		13.3	21.7	17.7	20.2	15.6	9.6

* All maxima were generated at maximum stimulation level, unless indicated in the bracketed number after the Torque value (Threshold = 1, Maximum Stimulation Level= 5). The shaded cells show where the nerve stimulation generated lower torques than muscle stimulation.

During muscle stimulation, maximum peak torques were always found at maximum stimulation level. This was also usually the case with nerve stimulation, except where the numbers in brackets of Table 2-2 indicate another stimulation level at which maximum torque occurred (this happened six times out of 24). However, it should be noted that subjects found maximum stimulation level painful and could tolerate it only because it was not applied frequently, or for prolonged periods (i.e. one 300ms burst was applied 30 times in total over the entire experiment duration of approximately 3 hours). The mean torques on the left-hand side of Table 2-2 are larger than the corresponding torques on the right hand side,

for the same electrode setup. The values on the left-hand side result from the knee extended, which means that the gastrocnemius is more stretched. Table 2-2 show that at Ank +20 and knee angle at 150^0 the mean torques were largest. This result was expected, because all three triceps surae muscles were stretched, therefore contributing maximally, in the range of leg orientations tested, to the plantar flexion torque. In general, when the knee is extended to 150^0, the torque generated is larger with nerve stimulation than with muscle, except for Subject 2 at Ank -20 and Subject 3 at Ank +20, at this knee angle. At knee angle 120^0, maximum torques generated at a given electrode setup are more variable, but more than half show that muscle stimulation at this knee angle generates larger torques.

2.4 Discussion

The results show a general and expected trend that as stimulation level increased, the peak torque generated also increased. This is true for both nerve and muscle stimulation. As the muscle was stretched, the torque generated was larger. The results also show that there was some inter and intra-subject variability as the degree of increase of torque was not always equal, with each change of leg orientation or electrode set up. Furthermore, due to maximum stimulation level reaching the pain threshold, not all recruitment curves show saturation; therefore the triceps surae were not always fully activated, even at this maximum stimulation level.

There is a range of previous literature present to support our findings that as the muscle stretches, torque generation increases [6,7,19]. This is influenced by the increased length of the sarcomeres in the muscles, the moment arms of the passive tendons to the joint, and the amount of slack between the muscle and the tendon; which are influenced by the angle of the joint [18]. In addition to the shortened muscle length, the electrode to nerve distance is less optimal when the knee is bent, because the nerve shifts further from the electrode. While all precautions were taken to minimise this, it may have influenced the ability to stimulate the nerve adequately.

At Ank +20 and the knee angle at 150^0, the largest torques were generated, because the triceps surae muscles were more stretched in this leg orientation. Because the gastrocnemii are biarticular, the knee angle influences their length, but not the

soleus length. Therefore knee angle change influences the torque production of gastrocnemii but not the torque production of the soleus. This implies that the gastrocnemius has a considerable contribution to plantar flexion torque. This is in agreement with literature [6]. Sale et al. [7] state that theoretically, gastrocnemii should contribute more to ankle plantar flexion torque than the soleus, but their measurements did not show this to be the case. Furthermore, the soleus muscle is made primarily (70-90%) of slow twitch, low force fibres. The gastrocnemii have an almost equal distribution of fibre types [10], however this is also known to vary [10]. The greater proportion of fast-twitch, high-force fibres in the gastrocnemii compared to the soleus explains the ability of the gastrocnemii to generate larger torques than the soleus. The variability of fibre types, as well as the wide range of lengths of sarcomeres in the gastrocnemii has been used in the past to explain the broad range of torque generation by gastrocnemius contraction. It has also been reported, by Rassier et al. [5] that even when a muscle is considered to be at an optimal length for force or torque generation, the individual motor units of the muscle will have different lengths, some will be at an optimal length for force production, however others will not. This would help explain the apparent inter- and intra- subject variability, which was also found by Munih et al. [18]. The reasoning given by Rassier is of particular importance to plantar flexor torque generated by the triceps surae, because the distribution of fibre types in the gastrocnemii are not uniform; therefore increasing the chances that not all fibres will be at their optimum lengths at any given leg orientation.

Furthermore, it has been reported [20] that stimulation at 200Hz of the triceps surae did not generate saturation. Therefore stimulating at a lower frequency, of 50Hz may not be sufficient to produce saturation, during electrical stimulation. However, it should be noted that this would also depend heavily on the stimulation levels used, which in general are not reported in literature. Furthermore, FES applied at 200Hz for prolonged use would not be feasible, e.g. for stimulation at every step taken during gait, as this would rapidly increase the chance of fatigue of the stimulated muscle.

The results show that many factors influence the peak torque that can be generated by electrically stimulating the triceps surae, of healthy subjects. Isometric conditions are relatively stable and controlled for generating and measuring the

influence of stimulation on torque production, and yet the results show a considerable degree of variability. This variability is influenced by the angle of the ankle and knee, the area chosen for stimulation and the subject being stimulated.

As indicated in the introduction, the purpose of these experiments was to determine the best electrode configuration, stimulation amplitude and leg orientation for maximum torque generation. The ultimate goal is to restore push-off of stroke subjects who have lost this function, by electrically stimulating the calf plantar flexors. Torques reported in Table 2-2 show that isometric electrical stimulation of the triceps surae generates plantar flexion torques in the same order of magnitude as those generated during gait. During gait, this usually ranges between 70 and 150 Nm [21]. Therefore we can expect similar torques during FES, during gait.

The results of the tests presented here show, that at the leg orientation at push-off, nerve stimulation produces larger torques, and generally (with the exception of Subject 2) with lower stimulation levels, as Table 2-1 shows. Although the torques generated were not of a large magnitude more than those generated by muscle stimulation, they were still larger. We should also consider that current density is large with equal stimulation levels and small surface area of the stimulating electrode. Moreover, stimulation amplitudes should be kept as low as possible not only to prevent discomfort, but also the occurrence of irreversible damage induced by frequent, high amplitude stimulation. This can lead to changes of ionic concentrations in the blood, below the skin's surface, causing damage [22, 23].

The results of this work will be transferred to subjects with a stroke, with the aim of improving their push-off during gait. However, as a functional therapy, considerations should eventually be made to implant the stimulation electrodes to improve the chance of saturation and minimise the chance of pain.

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Chapter 3 Methodology (II)

Stimulation Timing Control

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Abstract

Objectives: To create a stimulation control method, to replace the heel switch for push-off stimulation control during gait in subjects with a stroke.

Methods: Using a gyroscope on the lateral side of the lower leg, an angular velocity is sent to the stimulation control. The algorithm is triggered during each swing phase of gait when the angular velocity of the lower leg is relatively high. Subsequently, the start of the stance phase is detected by a change of sign of the gyroscope signal at approximately the same time as heel strike. Stimulation is triggered when the lower leg angle reaches a preset value since the beginning of stance. The change of angle is determined by integrating angular velocity from the moment of change of sign.

Results: Real-time reliability of stimulation control was at least 95% for four of the five stroke subjects tested, two of which were 100% reliable. For the remaining subject, the reliability was increased from 50% found during the experiment, to 99% during offline processing.

Conclusions: A gyroscope, measuring angular velocity of the lower leg in the sagittal plane is a simple more reliable alternative to the heel switch to control functional electrical stimulation of the triceps surae to improve push-off of stroke subjects during gait.

3.1 Introduction

Timing control of a functional electrical stimulation (FES) system is vital for the success of the device. Different FES applications rely on different control methods, which depend on the function to be replaced, as well as the remaining abilities of the user. FES is used in a range of applications, including restoration of control of internal organs, reaching and grasping, sit-to-stance and gait. The focus of this work is timing control of FES during gait.

To facilitate gait on a daily basis, an FES controller must meet a few basic requirements. Functionally, the controller must have high detection probability, high sensitivity, high selectivity as well as low chance of false detections. The device must operate in real-time and provide stimulation frequently over the duration of each day. Physically, the combined stimulation and control system must be limited in size and weight to facilitate ease of mobility for the users.

A common application of FES for gait improvement is the drop-foot stimulator. This application enables energy efficient gait and prevents falls [1,2]. The drop-foot stimulator stimulates the superficial branches of the peroneal nerve, contracting the tibialis anterior muscle, raising the toes during the swing phase of gait. As stimulation of the peroneal nerve causes the toes to rise, this stimulation facilitates not only swing, but also ensures that heel strike occurs at initial contact. This is important, because initial contact of stroke subjects may involve toe or mid-foot strike, instead of heel strike. Currently, the most common device for controlling stimulation timing of the drop-foot stimulator is the heel switch. This is a force sensitive resistor, placed under the heel during gait. Upon application or removal of force on the sensor, the continuous signal from the heel switch changes in amplitude. When a preset threshold is crossed, stimulation is triggered. In the case of drop foot, stimulation is initiated when the heel lifts from the ground, removing force from the heel switch. Stimulation terminates when force is re-applied to the sensor, at the next heel strike of the stimulated foot.

In addition to the drop-foot problem, other research has shown that in stroke, push-off is severely affected due to early, low amplitude activation of the triceps surae [3,4,5,6,7,8,9]. For this reason, our research efforts aim at improving push-off of stroke subjects by electrically stimulating the paretic triceps surae during gait. The

timing of stimulation must be optimal. Because the heel switch has been widely used for stimulation control, and no prior research has focussed on improving push-off of stroke subjects, during gait, the heel switch was also our initial choice for control of FES to induce push-off. Since the heel rises during push-off, heel-off occurs too late to facilitate push-off stimulation. For this reason, heel strike and a time delay must be used to trigger stimulation to induce push-off. Heel switch control was adequate for preparatory trials involving healthy subjects. However, problems arose when this control method was transferred to stroke subjects. These problems were predominantly of technical and mechanical nature, resulting in inadequate and unreliable triggering of stimulation. Changing pressure on the heel switch inside the shoe during gait often triggered the stimulator more than once during one gait cycle. Other irregular stimulation was due to missing step detections, therefore not activating the heel switch and not triggering stimulation. To correct this, it was often necessary to change the location of the heel switch and make adjustments, such as inserting an extra insole or rigid piece of material at the heel. Insertions, in combination with the heel switch, often caused discomfort after some time, disrupting continuous use. For one subject, the amendments were painful and the heel switch had to be completely removed from inside the shoe and taped to the bottom of the outer sole. In general, it took a relatively long time to place the heel switch adequately and determine correct threshold values, increasing the chance that the stroke subjects became fatigued before actual use. Other researchers have also found the heel switch to be problematic due to a number of factors including incorrect positioning in the shoe, extra stimulation due to change in pressure of the heel switch [10], mechanical breakage of the heel switch and related cables [11], loading and unloading decreasing its life expectancy [12]. Furthermore, users must always wear shoes [12] making it difficult to consider the entire system as a daily treatment.

In addition to problems with the application of the sensors, our preliminary evaluation showed that heel switches are unreliable for controlling calf muscle stimulation. Because absolute time delays are used to trigger push-off stimulation and the duration of gait cycle intervals varies with gait speed [13], the heel switch control method for FES of push-off restoration is highly dependent on gait speed. Initial contact of stroke subjects is not always heel strike, and may vary from step

to step of the same subject. Additionally, unlike the drop foot stimulator, push-off stimulation does not improve heel strike, so a good heel strike and good triggering of the heel switch is not ensured. Therefore control of stimulation to improve push-off, using the heel switch with a preset time delay cannot be relied upon. Another problem that we encountered using heel switch control was continuous cycles of unwanted stimulation, which we refer to as "limit-cycling"[14]. Contraction of the calf muscle due to stimulation causes the heel to lift. This supports push-off by generating momentum to move the body forward. In some of the subjects, however, the heel returned to the ground, triggering the heel switch again, resulting in limit cycling. Instead of propulsion, this may lead to deceleration of the movement, if stimulation was triggered before the centre of mass progressed enough over the foot. Due to the variability of gait in stroke, time since heel strike is not an adequate criterion to start stimulation of the triceps surae for push-off. Sufficient progression of the body over the foot is a more accurate criterion to evaluate. We also concluded that the sensory information used to control stimulation should not be primarily effected by the activation of the contracting muscle, because this can lead to unstable control and limit cycling. This was seen when the heel switch caused the heel to rise and reactivate the heel switch prematurely. Therefore, alternative sensing on the leg is preferable.

Pappas et al.[10] proposed a gyroscope and three force sensitive resistors built into an insole. While effective for their purposes and removing the problem of heel switch positioning, signals originating from the foot still have the other drawbacks mentioned.

A number of researchers have shifted control away from the foot. In most cases, the application was for a drop foot stimulator, and not for push-off. The lower leg has been the preferred location for stimulation control. This is likely to be due to the potential for implantation and minimalisation of cables, when implemented in an implant[11,15]. Willemsen et al.[15] used accelerometers on the lower leg. Later, Dai et al.[12] low-pass filtered signals from clusters of accelerometers on the lower leg to obtain inclinations. Both studies focussed on drop foot stimulation, but inclination of the lower leg may also be an important option for control of timing of push-off facilitation. Other researchers have used accelerometer clusters[16], or natural nerve signals[10,17,18] as well as manual switches built into crutches[10,19].

When using manual switches, subjects have to press a button to activate a stimulation burst at every step taken. Reportedly, subjects can be trained to do this without conscious thought [19].

Bajd et al. [20,21,22] have applied FES to the plantarflexors of spinal cord injured (SCI) subjects. The subjects manually triggered the stimulation using a push button [20,21,22]. Other researchers have controlled FES using gait phase detection systems [23] and finite state control mechanisms [24], using variants of force sensitive resistors and predictive algorithms.

Others have also proposed detection methods, for the purpose of gait analysis but not for FES control. Accelerometers, gyroscopes and heel switches have been compared to establish the accuracy of heel strike detection [25]. In that study, the heel switches failed for 9 out of 32 subjects [25].

Tong and Granat [26],used a single gyroscope on the lower leg, for gait analysis. They also controlled FES of the peroneal nerve of SCI subjects [27,28] using neural network algorithms and various sensor combinations on the upper and lower legs, shoes and crutches. Others [29,30,31] also used gyroscopes in combination with other sensors, on various body segments, to control timing of FES.

Due to the clear unreliability of the heel switch and complexity of available FES control methods, a simple alternative control method is needed for control of push-off stimulation. As each control method must be suited to the function to be restored, distinct, quantifiable characteristics of the function must be known, in order to be properly exploited. During healthy gait, at push-off the centre of mass passes over the ankle. As this occurs, the triceps surae are activated to provide the force necessary for push-off. We propose to use the change in angle of the lower leg since the start of the stance phase as a control signal, because it relates to the progression of the body over the stance leg. It can be derived by integration of the angular velocity of the sagittal plane, measured using a rate gyroscope placed on lateral side of the lower leg. The advantage of measuring control signals from the lower leg is that stimulation of the triceps surae muscles will not greatly affect the pattern of the lower leg angular velocity pattern whereas, foot angular velocity is significantly altered due to FES of the plantarflexors [32] as the heel pivots over the forefoot. The other problems, associated with instability and unreliability of the

heel switches, are also solved by controlling the stimulation from the lower leg, based on orientations rather than on preset time delays.

The goal of this research is to demonstrate that FES of the triceps surae of stroke subjects can be reliably controlled using one gyroscope, measuring lower leg angular velocity perpendicular to the sagittal plane. In contrast to methods used in the past, with multiple sensor combinations, on more than one body segment, the method proposed here requires only one gyroscope on one body segment, close to the stimulation location, to control the stimulation timing. Furthermore, this is a new application involving FES of the triceps surae of stroke subjects for push-off. If the FES proves successful in facilitating push-off of stroke subjects, a completely implantable stimulator may be possible.

3.2 Methods

3.2.1 Design

During gait, the lower leg experiences a characteristic pattern that repeats every gait cycle. Figure 3-1A, shows a typical trace of the angular velocity of the lower leg ($\dot{\varphi}_{LL}$) of a healthy subject during gait. The lower leg experiences high angular velocity as it rotates around the knee joint, during swing. At around heel strike, $\dot{\varphi}_{LL}$ crosses negatively through zero as the lower leg rotation changes direction. During stance, the lower leg rotates relatively slowly around the ankle joint, over the foot. The proposed algorithm uses these distinctive features of the $\dot{\varphi}_{LL}$ over the gait cycle to control FES during gait.

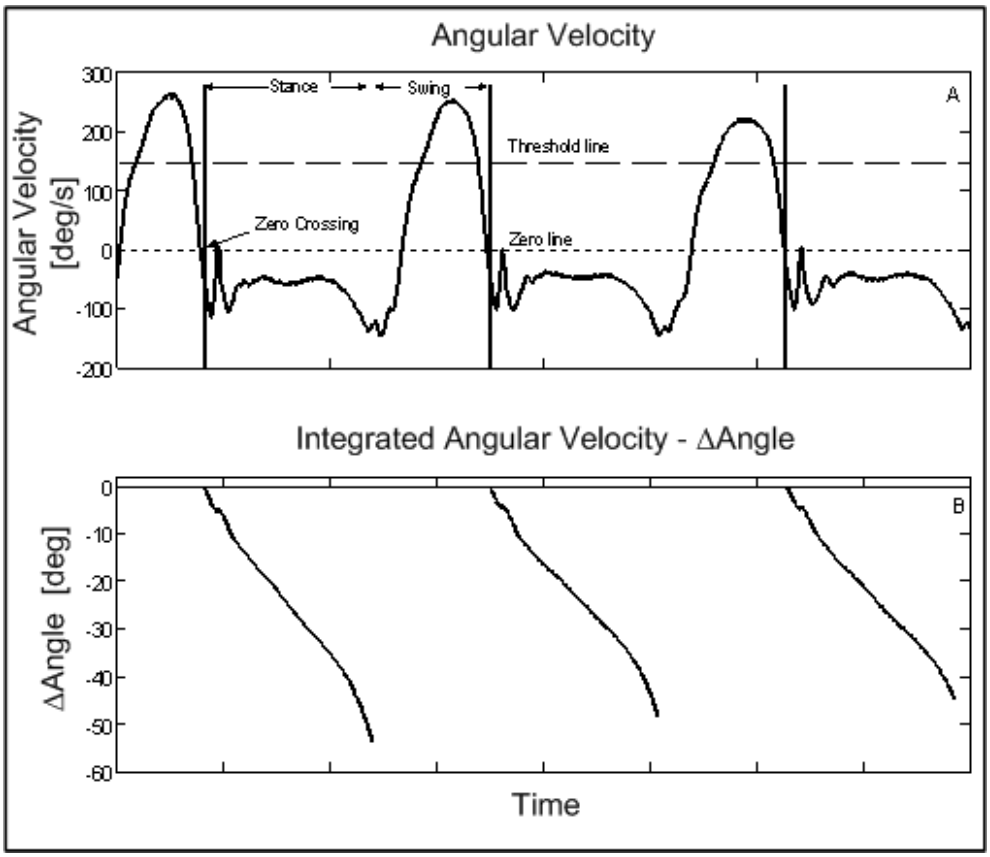

Figure 3-1: Healthy Subject data. A) Angular velocity of the lower leg. B) Integrated angular velocity (angle).

3.2.2 Algorithm

The control algorithm was intentionally kept simple and robust. The algorithm involves monitoring $\dot{\varphi}_{LL}$ during gait. When $\dot{\varphi}_{LL}$ exceeds a preset threshold during the swing phase, "Threshold Swing" (T_{sw}) the algorithm is triggered. See "Threshold Swing (T_{SW}) in Figure 3-1A. As the foot approaches, then strikes the ground, $\dot{\varphi}_{LL}$ changes direction, crossing negatively through zero. Zero Crossing is shown in Figure 3-1A, where the signal crosses the "zero line". At zero crossing, the integration of $\dot{\varphi}_{LL}$ is initiated. Integration of this angular velocity results in change of angle since zero crossing ($\Delta\varphi$); $\Delta\varphi$ is shown in Figure 3-1B. At a preset

$\Delta\varphi$, the stimulation burst is given. This sequence of events repeats when T_{SW} is again exceeded. T_{sw} crossing is an important feature of this stimulation control, which prevents unwanted stimulation bursts by waiting for the indication that gait is in progress. If this threshold is not crossed, the algorithm will not be initiated. It is also important to note that the integration resets at every step as this prevents integration drift. It is clear from Figure 3-1B that integration drift is successfully avoided.

The working algorithm can be summarised in the following flow chart, Figure 3-2:

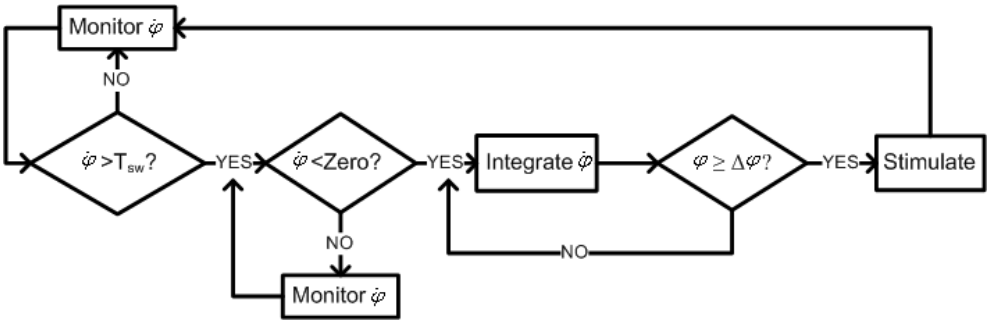

Figure 3-2: Flow chart depicting the main steps involved in the stimulation control algorithm.

3.2.3 Equipment

The algorithm operates in real-time on an embedded controller in a purpose-built symmetrical bi-phasic stimulator. Angular velocity can be measured using a gyroscope. The gyroscope used for this research is inside an inertial sensor unit, the MT9, from Xsens Technologies B.V. The gyroscope sensitive to angular velocity of the sagittal plane was selected. MT9 signals are converted to binary data in the Xsens bus master at a sample frequency of 100Hz. The stimulator is connected serially to the bus master. The digital signal is expressed in deg s^{-1} using calibration information inside the embedded controller.

3.2.4 Subjects

Five stroke subjects, recruited from the Roessingh Rehabilitation Centre, in Enschede, the Netherlands were included in this study. The medical ethical committee of The Roessingh Rehabilitation Centre approved the experiments.

The subjects were aged between 42 and 58 years old. All subjects had suffered a left hemispheric stroke. Testing was carried out, at least 6 months post-stroke. Subjects had no previous experience of FES facilitated gait. Subjects 2, 4 and 5 used a walking stick daily, therefore also used it during the gait trials. Subjects 2 and 5, who normally used an ankle foot orthosis removed this aid during the experiments to prevent masking of any mechanical effect of stimulation.
All subjects signed an informed consent form.

3.2.5 Experimental setup

Subject preparation

An MT9 inertial sensor, attached to a Perspex plate, which was made in-house, was fixed to the paretic leg. The MT9 was connected to the bus master, and in turn to the biphasic stimulator for stimulation control. Figure 3-3 shows a typical subject set up. The additional MT9 sensors were used to measure kinematics for purposes beyond the scope of this article. Only the MT9 on the lower leg was used to control stimulation onset. The stimulator was transported in a rucksack on the subject's back.

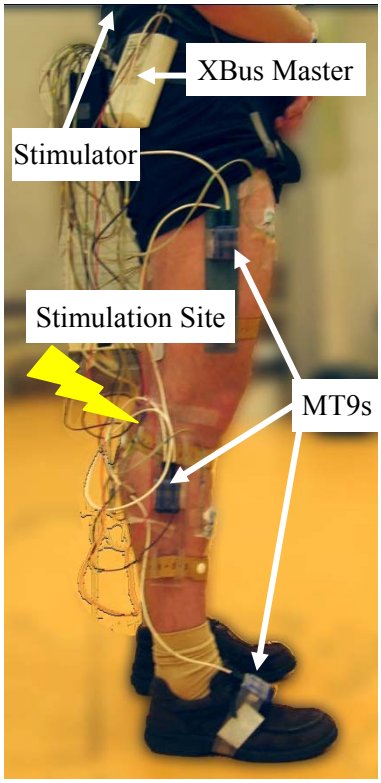

Figure 3-3: Subject donned with equipment for FES experiments.

3.2.6 Experimental Protocol

The experiment was comprised of a stimulation phase and a non-stimulation phase. During non-stimulation, the subject walked at a self-determined pace on a flat surface, in a gait laboratory. The $\dot{\varphi}_{LL}$ was analysed after the first non-stimulated trial in a custom-built program in Lab View. T_{SW} was estimated as approximately two-thirds of the maximum peaks of five sample steps.

The next stage of the Lab View program showed integrated values, in relation to angular velocity. The optimal $\Delta\varphi$ for stimulation was approximately mid-stance. This could be seen on the $\dot{\varphi}_{LL}$ data and correlated directly to the $\Delta\varphi$.. Both T_{SW} and $\Delta\varphi$ were determined for each subject and manually input to the controller. The other stimulation settings included 15 biphasic pulses, with a negative pulse width of 300μs applied at 50Hz for a burst duration of 300ms were the same for every

subject. This burst duration was in accordance with the work of Bajd et al.[21]. Stimulation amplitude was different for each subject. This value was determined while subjects stood in push-off posture, with the foot of their paretic side on a force plate. Stimulation amplitude was increased until a forceful movement was generated.

During the stimulation phase, as with the pre-stimulation trials, the subjects walked at a self-determined pace. Stimulation was applied at every step, when $\Delta\varphi$ reached the preset value.

3.2.7 Results Processing

In order to determine the reliability of the control method, a number of parameters were used. The number of steps taken were processed offline using gyroscope data. The number of stimulated steps could be found using stimulation artefact present in activation patterns of electromyography (EMG) data, which was recorded for purposes beyond the scope of this paper[32]. Data was manually checked to determine when stimulation was missing and when extra stimulation bursts (false positives) were delivered. Reliability was calculated using the number of steps taken and the number of stimulation bursts detected, excluding the missing first step, when present. Because of synchronisation between the two systems (EMG and MT9), some data had to be rejected as is reflected in the number of steps included from the two to three minutes measurement time.

3.3 Results

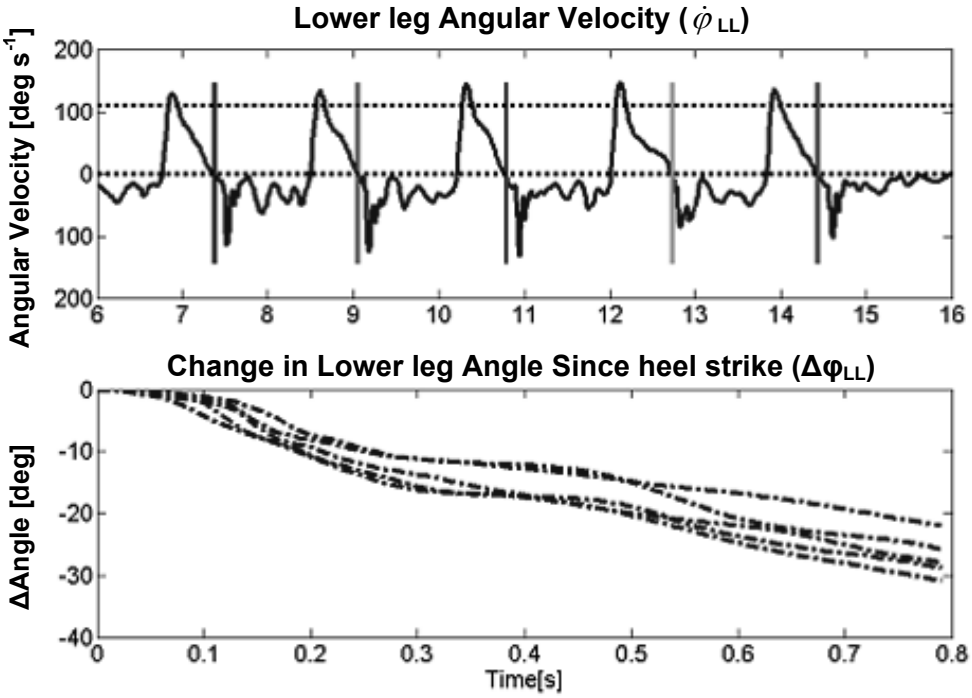

Figure 3-4: Patient Data. A) Angular velocity [deg s^{-1}] of stroke subject number 5 during gait. Uppermost, horizontal dashed line is T_{sw}, parallel to this, along zero is the zero line. The vertical lines indicate zero crossing. B) Integrated angular velocity (change in angle in [deg] versus time [s]) since negative crossing through zero.

Figure 3-4A shows an example of angular velocity results recorded from a stroke subject who was a poor walker. In the figure, the triceps surae of the subject was stimulated at the same Δφ in each gait cycle. The horizontal, dashed line, in Figure 3-4A at approximately 100 deg s^{-1} provides an example of the maximum value that can be chosen for T_{sw}. The horizontal dashed line at zero shows where the angular velocity crossed negatively through zero.

Figure 3-4B shows the repeatability of the integrated values, therefore the working of the algorithm for this subject. Note however, that the values are not on the same time scales as the angular velocity signal. It is clear from the figure, that the angle does not reach the desired change at exactly the same time instant. Therefore the algorithm is not dependent on gait speed, but stimulation time varies depending on

the time taken for the angle to change. This subject does not exhibit the exact angular velocity characteristics during gait as displayed in Figure 3-1 for a healthy subject. However, the relatively large amplitude of angular velocity during swing, followed by zero-crossing is sufficient for the algorithm to be meaningfully implemented. The angular velocity increases and decreases, in a cyclical manner during the stance periods shown in Figure 3-4, unlike the angular velocity of the healthy subjects, as shown in Figure 3-1. Had stimulation been controlled with a heel switch, this subject may have experienced limit cycling, since the heel may have been unloaded and loaded repeatedly.

Table 3-1: Results summary of gyroscope stimulation timing control.

	Sub 1	**Sub 2**	**Sub 3**	**Sub 4**	**Sub 5**
T_{SW} [deg/s]	110	85	56	56	42
$\Delta\varphi$ [deg]	25	25	20	25	17
No. steps taken	101	88	85	98	87
No. steps missed	1	1	3	6	45
First step missed	Y	Y	Y	Y	Y
Reliability excl. 1st step [%]	100	100	97.6	95	49.4
False positives after last step	Y	Y	Y	Y	N
False positives during gait	0	0	0	0	0

Table 3-1 gives an overview of the results of the stimulation repeatability using the gyroscope control algorithm. From the table it is clear that push-off of every first step is missed. This is because the leg to be stimulated must first provide the signal that gait is in progress and that stimulation is required. The angular velocity generated during swing, even if not preceded by stimulation is sufficient to trigger the algorithm in the subsequent steps. Also, one last stimulation burst always followed the final swing of the stimulated leg. This extra stimulation burst was undesired; however, this was limited to one extra burst per complete termination of gait. For two of the five subjects, stimulation was applied reliably for 100% of the steps taken. This was least 95% for two other subjects, while for Subject 5, this

was approximately 50%. However, offline post-processing revealed that use of different threshold levels increased reliability of Subject 5 to 99%.

3.4 Discussion

The results demonstrate that real-time triggering of stimulation for push-off during gait is possible using a uniaxial gyroscope signal. The algorithm used is sufficiently flexible to be utilised in stroke subjects. The primary condition for the operation of this algorithm is that angular velocity during swing has adequately high amplitude and is succeeded by zero-crossing, as angular velocity of the lower leg changes direction.

Not only is the gyroscope algorithm method independent of the method of foot-floor contact, it is also independent of gait speed. When the preset angle is reached, stimulation is applied regardless of the time taken to reach this angle. Furthermore, the gyroscope is very flexible in terms of location on the lower leg. The gyroscope used for this description was placed on the lateral side of the lower leg. The gyroscope sensitive to motion perpendicular to the sagittal plane was selected as the sensor to control the stimulation. Tong and Grant [26], used the gyroscope on the lower leg, close to the foot, revealing the same angular velocity pattern over the gait cycle.

A few drawbacks exist for the gyroscope method, namely, that the subjects' first push-off will never be stimulated, as the user must first trigger the algorithm with a relatively high angular velocity during swing. Furthermore, the final step taken by the user may initiate an undesired stimulation burst, even if the user wishes to stand still. Although these drawbacks exist, they do not pose serious detrimental effects to the gait of the users, as they affect only the first and last steps taken. Additionally, the missing first stimulation step is a feature of this algorithm as it is the main method of preventing unwanted stimulation, therefore is a small sacrifice for the potential benefits.

In their research, Skelly and Chizeck [23] stated that control of stimulation by preset timing is not optimal. This is supported by our initial experiments using heel switches. However, their solution to preset timing was to update timing parameters using data from a previous step. This solution may not be optimal when timing of subjects' gait events vary from step to step. While the timing of the stimulation in

our method was not preset, the burst duration was. However, it is possible to solve this by appending the algorithm to end the stimulation burst at toe-off, rather than 300ms after stimulation onset. At toe-off, push-off is complete. This is theoretically a positive crossing through zero, following the initial negative through zero crossing at the beginning of stance. To prevent over stimulation, such an algorithm should also include a maximum burst duration.

We have demonstrated that a single gyroscope can be used to control the timing of stimulation for a very precise action, such as push-off, during gait. There is potential to extend this application to combine push-off and drop foot stimulation, in an implantable drop foot stimulator. Currently implants rely on a cable between the heel switch and the stimulator. However, research is being directed towards creating a completely implantable system, including stimulation control [33].

Because only one sensor is required for our proposed controller, we expect that a minimal amount of energy will be required. Furthermore, there will be no need for cables from the controller to the stimulator, ensuring discretion for the user and increasing the chance of acceptability of this device as a daily support system. Additionally, there is no measurable processing delay. With a sample rate of 100Hz, processing takes place within the sample time of 10ms in the microcontroller, which is negligible compared to the time taken to reach the angle.

The stimulation controller described here, in combination with the implantable drop foot stimulator, could potentially be used to improve the gait of hemiparetic subjects, ranging from preventing knee hyperextension during early stance, to inducing push-off by calf muscle stimulation followed by lifting the toes during swing by subsequent stimulation of the dorsiflexor muscles.

We can conclude that a single gyroscope can be used to reliably control the timing of stimulation for a very precise action, such as push-off, during gait.

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Chapter 4 Healthy Subject Evaluation (I)

Interaction of Artificial and Physiological Activation of the Gastrocnemius During Gait

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Abstract

Objectives: The purpose of this research was to understand the effects of surface functional electrical stimulation (FES) of the tibial nerve on the activation of the gastrocnemius medialis (GM) of the stimulated side.

Methods: FES was carried out on six healthy subjects, initiated at three different times during gait: early, mid and late stance. Each stimulation burst consisted of 15 pulses, applied for 300 ms, at 50Hz stimulation frequency. Mixed model statistical analysis was carried out on the median on and offset times of the GM and the RMS of the inter-pulse interval responses.

Results: Results indicate that the EMG response to FES is dependent on the time of application. The most prominent effects found in the intervals between the stimulation pulses (inter-pulse intervals (IPI)) were found when stimulation was applied early in the stance phase. This study revealed that the only statistically significant effect on burst timing was a delay in offset timing due to mid-timed stimulation.

Conclusions: We concluded that additional activation may have been compensated, at least in part, by blocking of the physiological activation during the stimulation burst.

4.1 Introduction

Functional electrical stimulation (FES), the use of electrical stimulation to provide a functional improvement for the user, has been in use for decades. However, interactions between FES and the nervous system are not well understood. Neurophysiological studies are required to gain a better understanding of these interactions [1] to prevent undesired effects of FES, as well as enabling predictions of functional outcomes, which is important for progression of FES as a medical treatment. Stimulation in healthy subjects should provide insight into the outcomes of stimulation when applied to improve gait.

Frequently referenced work of Liberson [2] highlights that since the 1960's FES has been used as a medical treatment for subjects with stroke (CVA) to remove the drop-foot characteristic present in their gait pattern. However, research to date has focussed on biomechanical improvements due to stimulation, rather than measuring the interaction of the stimulation with muscle activation by the body's nervous system. This interaction can be studied by incorporating electromyography (EMG) measurements [3].

Studies since the late 70s [4,5,6,7,8,9,10] involving EMG and gait pattern measurements revealed that a CVA often results in a lack of push-off. These measurements of the muscle activity after a CVA confirmed that the triceps surae (TS) muscle's normal activity was altered.

The calf muscle, the triceps surae is made up of three muscles. The monoarticular soleus muscle is connected to the Achilles tendon, thus its primary role is ankle plantar flexion. The biarticular gastrocnemii are attached to the Achilles tendon and to the medial and lateral posterior condyles of the femur. Gastrocnemii activation induces ankle plantar flexion, together with the soleus, as well as knee flexion, with the hamstrings. The soleus is densely populated with slow-twitch, low force, output motor units, while the gastrocnemii contain a more equal variation of fast and slow units, enabling a larger range of force output [11].

Research shows that in healthy subjects, the TS is the primary muscle group required for push-off, performing positive work just prior to toe-off [12]. FES of plantar flexors of spinal cord injured (SCI) subjects has been carried out, with the researchers stating that stimulation of the plantar flexors alone could induce push-

off for these subjects, preparing the leg for swing [13,14]. It is believed that FES applied to the plantar flexors of stroke subjects can provide the same improved push-off observed with SCI subjects, enabling an improved gait pattern.
FES of the TS of CVA subjects has not been investigated in literature. For the purpose of push-off, FES should be given at a time when the TS is active, which is when the stimulated leg is loaded. Thus, interactions with the reflexive neural control of the TS, as well as, feed-forward responses are expected. This could be investigated with EMG as this gives insight into the activation of the muscles.
The work presented here describes FES in healthy subjects, during level walking, applied at three different times during the gait cycle. Under a given stimulation condition, a burst of stimulation was applied at each step. The question is, how does this FES affect the activation patterns of the gastrocnemius medialis (GM)? This question will be answered by applying FES to the tibial nerve, while simultaneously measuring the EMG of the GM, to evaluate muscle activity. The on and off times of physiological bursts will be investigated, to determine how timing is effected. It is expected that analysis of such data can provide an insight into the effect that stimulation has on the normal GM activity.

4.2 Methodology

A group of healthy subjects endured a series of trials, which involved walking around a set area of a gait lab, at their own selected walking speed. Each trial systematically involved gait, either with or without stimulation, while the EMG of the GM was measured.

4.2.1 Subjects

Data from six healthy subjects was used; four male and two female, mean age 25 (+/- 5) years old. Subjects had no history of neurological disorders. Each subject signed an informed consent form, which was approved of by the medical ethical committee of the Roessingh Rehabilitation Centre, as part of study for FES of CVA subjects.

4.2.2 Equipment

The experimental set up is schematically depicted in Figure 4-1.

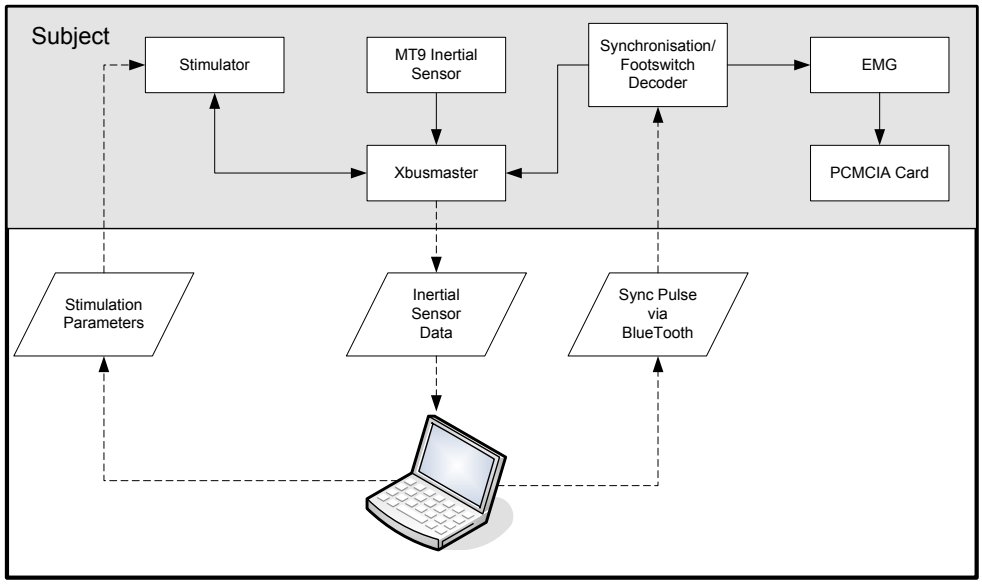

Figure 4-1: Experimental Setup, depicting equipment used during the experiment. White rectangles in the upper Grey box shows equipment that subjects donned. Information contained in the parallelograms represents data that has been transmitted. Dotted lines show signals that were transmitted via Bluetooth. Solid lines indicate the presence of a direct connection between two pieces of equipment.

EMG:

EMG system: Porti-5 16 channel/ASD unipolar EMG, from TMS International. Sample frequency: 2048Hz. Input Common mode range: -2V / +2V. Amplitude range: 22bit, resolution 71.9nV. Gain: 20x CMRR: > 90 dB. Input impedance: > 10^12 Ohm Noise: < 1.5µVpp. The EMG recording was performed using the ambulant-setup with a P CMCIA card to allow the subjects to walk freely. Solid gel Ag/AgCl EMG electrodes, oval shaped, 22mm x 35mm from Arbo were used.

Stimulation:

A custom-built, custom-programmed, biphasic electrical stimulator with an embedded controller to control stimulation timing was used. Stimulation

parameters were modified on a laptop and sent via Bluetooth. This enabled the stimulator and subject to remain physically disconnected from any mains power supply. The stimulator and Xbusmaster were connected serially to allow the sagittal plane gyroscope signal to be input to the stimulator in real-time for accurate control of the stimulation timing. Each stimulation burst comprised 15 pulses, which was equivalent to approximately 300ms. The burst time was in accordance with work of Bajd et al. [13].

Stimulation Timing Control:

Equipment: An MT9 inertial sensor was placed on the lateral side of the lower leg of the stimulated leg. Each MT9 unit, from Xsens Motion Technologies B.V., contains three accelerometers, rate gyroscopes and magnetometers, arranged orthogonally, such that 3D signals are measured. MT9 data was sampled at a frequency of 100Hz and baud-rate of 115k2bps by the Xbusmaster portable measurement system. A Bluetooth configuration was utilised during recording, this allowed the subjects to walk free of physical constraints.

Algorithm: The stimulation timing control only employed the angular velocity signal from the rate gyroscope, sensitive to motion in the sagittal plane, as illustrated in Figure 4-2.

Figure 4-2A reveals that angular velocity during swing is relatively high. An initial threshold (see line annotated "Threshold Line") is set, such that it will be crossed during swing; this is the trigger for the timing control algorithm to begin. At approximately foot floor contact, the angular velocity passes through zero (see annotation "Zero Crossing"). At this point, the algorithm begins to integrate the angular velocity (see Figure 4-2B), essentially calculating change in angle since foot floor contact. A threshold change in angle since zero crossing is preset into the stimulator. Stimulation was delivered consistently at this change in angle every step of the gait cycle [15].

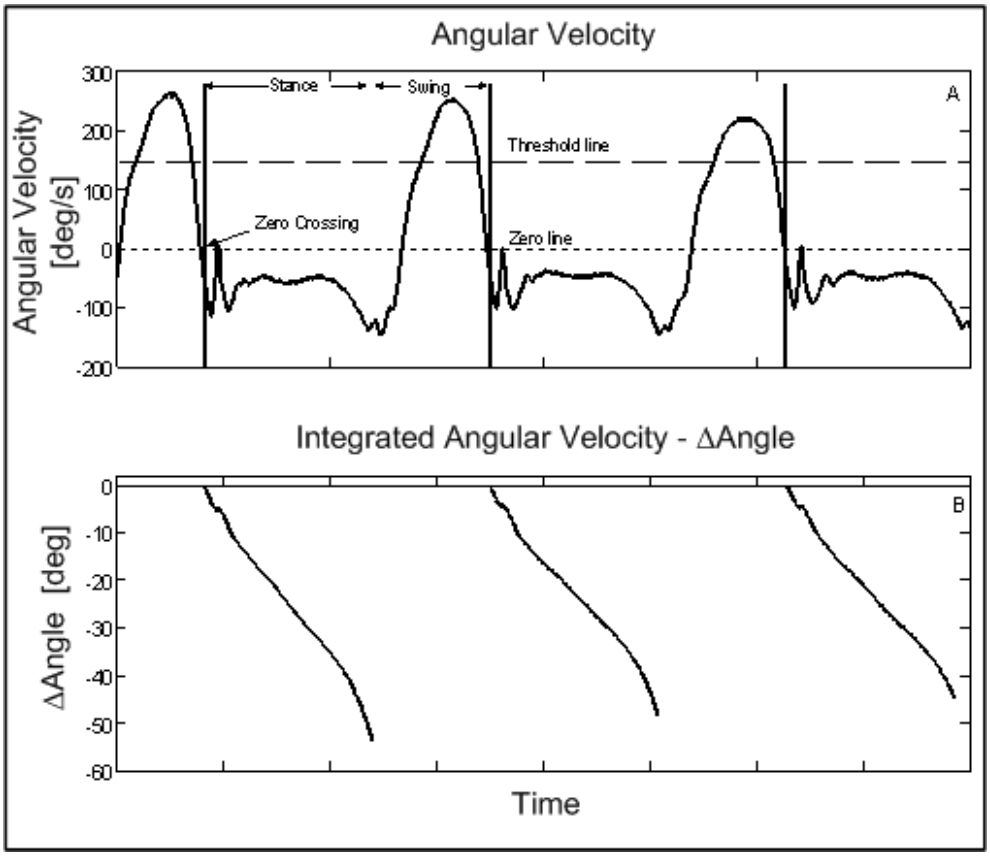

Figure 4-2: An example of gyroscope signals used to control stimulation timing. Stimulation displayed as degrees after heel strike. Figure 4-2A, gyroscope signal, in deg s^{-1}. Typical activity during stance and swing are highlighted. Figure 4-2B shows the integrated signal, the angle, in degrees, which was used to trigger the stimulation during gait.

4.2.3 Subject Preparation

The stimulation site was determined as the subject lay face down. The exact stimulation location was determined by moving a stimulation probe around the area of the popliteal fossa, the target was the tibial nerve. When a clear plantar flexion movement was generated, this site was marked. An EMG electrode, which was used as the cathode, to allow for a small stimulation area, was fixed to the skin. The stimulation site was rechecked with this new electrode in place, to ensure that

the same effect was generated. The electrode was immobilised and pressed as close to the nerve as possible, to achieve low-threshold activation. During the experiment, EMG was recorded from 8 muscles, however, only the stimulated gastrocnemius is discussed in this article. Measurement sites, inter-electrode distance, as well as skin preparation were carried out according to SENIAM [16] recommendations. The area to be measured was shaven, then cleaned abrasively with alcohol. When the skin dried, self-adhesive Arbo electrodes were fixed to the recording sites, 20 mm apart.

An MT9 inertial sensor attached to a Perspex strip, to avoid skin motion artefact, was fixed to the lateral side of the lower, stimulated leg for stimulation timing control.

4.3 Experimental Procedure

The experimental procedure was divided into stimulation and non-stimulation blocks.

A) Pre-Stimulation gait trials: the subjects walked for approximately 2-3 minutes in a loop. Physiological and inertial data were collected simultaneously. With the help of a pulse to each system, these signals were synchronised, during processing. Inertial data was analysed to determine adequate stimulation timing parameters. This is possible using custom-built software, which allows the recordings and integration values to be observed, per step.

B) Stance Trial The subject stood on a force plate while stimulation parameters were adjusted such that a noticeable forceful movement was generated.

C) Stimulation gait: Subjects walked, as in part A, but with stimulation applied at every step, triggered according to the change in angle of the lower leg, after heel strike.

Following part C, the subject again walked without stimulation for 2-3 minutes in order to determine if changes in EMG could be observed. The subject then rested, and part C was repeated with a different stimulation time. In total 3 stimulation times were applied, with a non-stimulated trial before and after. The order of stimulation, early, mid and late was randomised from subject to subject, to ensure that results were not influenced by time. A, B, C1, A 5 minute break C2, A, 5 minute break, C3, A.

Mid-timed stimulation was selected as the optimal stimulation time, this started half way through the stance phase, in order to support push-off. Early stimulation was applied 10 degrees before and late stimulation was applied 10 degrees after mid-timed stimulation. From this point on, the stimulation conditions will be referred to depending on when stimulation was applied: NSe = non-stimulated trial prior to early stimulation, Se = Early stimulation, NSm = non stimulated trial prior to mid stimulation, Sm = mid stimulation, NSl = non stimulated trial prior to late stimulation, Sl = late stimulation, NSf = the last non stimulated trial. Statistical analysis revealed that the results found during the non-stimulation (NS) conditions were not different from each other, thus a NS condition has been implemented as a combination of all non-stimulation results.

4.3.1 EMG Processing

The EMG data was recorded after applying a high-pass filter of 5Hz and a low-pass filter of 2kHz. Stimulated trials first underwent a stimulation artefact removal phase, based on work by O'Keefe et al. [17]. All stimulation artefact-free signals, including non-stimulation trial data were post-processed in Matlab, with a high-pass filter of 50Hz as this enabled removal of the filter response of the stimulus artefacts. The EMG was further processed utilising a program built in Matlab. This program used a standardised burst detection method, based on the approximated generalised likelihood ratio (AGLR) principle [18]. The program generated on and off times of the EMG burst; normalised to percentage gait cycle. The program also generated smooth rectified EMG (using a low-pass filter of 25Hz) signals of the muscles. For each subject, one set of thresholds, amplitude and variance, were used to determine the on and off times of the bursts, these parameters were determined in the very first non-stimulated trial. Additionally, if the results of a muscle showed that in the first non-stimulated trial, the muscle had one burst, but in another trial this same muscle had two bursts, split by the stimulation burst, the onset of burst one and offset of burst two were used.
As EMG is known to be affected by gait speed, this was also evaluated utilising the time interval between heel strikes.

4.3.2 Statistical Analysis

A mixed model analysis was carried out in SPSS to evaluate the statistical significance of the median on and off times of the GM of each subject due to stimulation. The level of significance was $p<0.05$, findings underwent a pairwise comparison using least significant difference method (LSD).

4.4 Results

The results that follow include EMG data, which is the activity between the stimulation pulses, followed by the on and offset times of the EMG bursts.

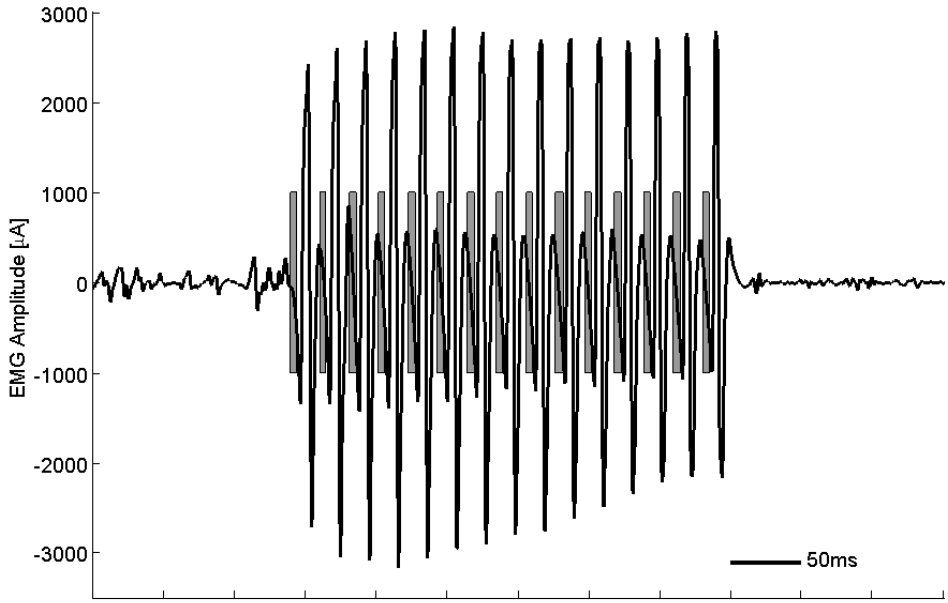

Figure 4-3: Represents EMG data of subject 1 during Se. Stimulation artefact has been removed and the signal then filtered at 50Hz (solid line). Grey shaded areas represent where the stimulation pulses were removed.

Figure 4-3 above shows that the artefact removal process and the filtering at 50Hz has been a successful method of processing the EMG data. The large amplitude waves, found between the removed stimulus pulses (grey boxes on Figure 4-3) are physiological responses to stimulation. These inter-pulse responses are plotted in Figure 4-4 and are discussed below.

4.4.1 Physiological Response: Motor Units

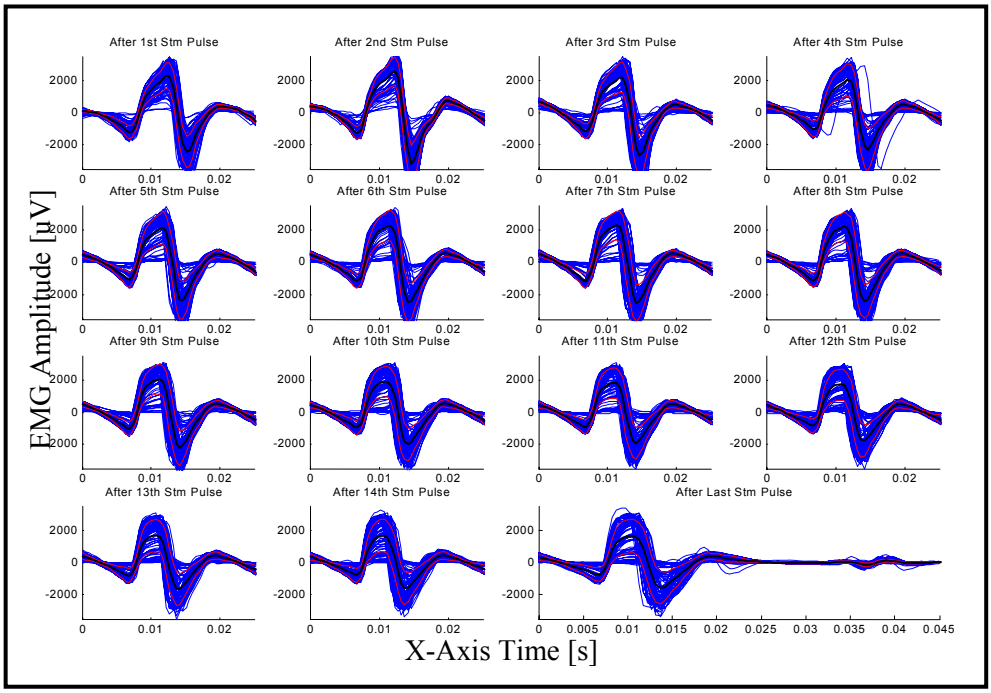

Figure 4-4: Patterns during inter-pulse intervals (IPI) for subject 4 for each step, during Se. The waveform between 8 and 15ms is the M-wave in response to each stimulation pulse. After pulse 15, two waves are noticeable, one at 5-15ms and another at 35-45ms, timing of this indicates a monosynaptic H-reflex.

Figure 4-4 shows the pattern of activity between pulses of the Se burst in subject 3, this was reproducible over all subjects. Between 8 and 15ms after each stimulation pulse, a clear response was generated; highlighting motor (M)-response, direct muscle activation due to stimulation. Figure 4-4 also shows that after the 15th (final) pulse of the burst, a second wave was generated. This second wave occurred at 35-40ms, the time expected for the generation of the monosynaptic Hoffman (H) reflex. Due to the stimulation frequency of 50Hz, the inter-pulse interval (IPI) was 20ms. This time interval allows the M-wave to be seen. If an H-reflex was generated due to this pulse, it will not be seen within this first inter-pulse interval; but may contribute to the signal during the inter-pulse interval of subsequent pulses (approximately 15ms after the preceding pulses).

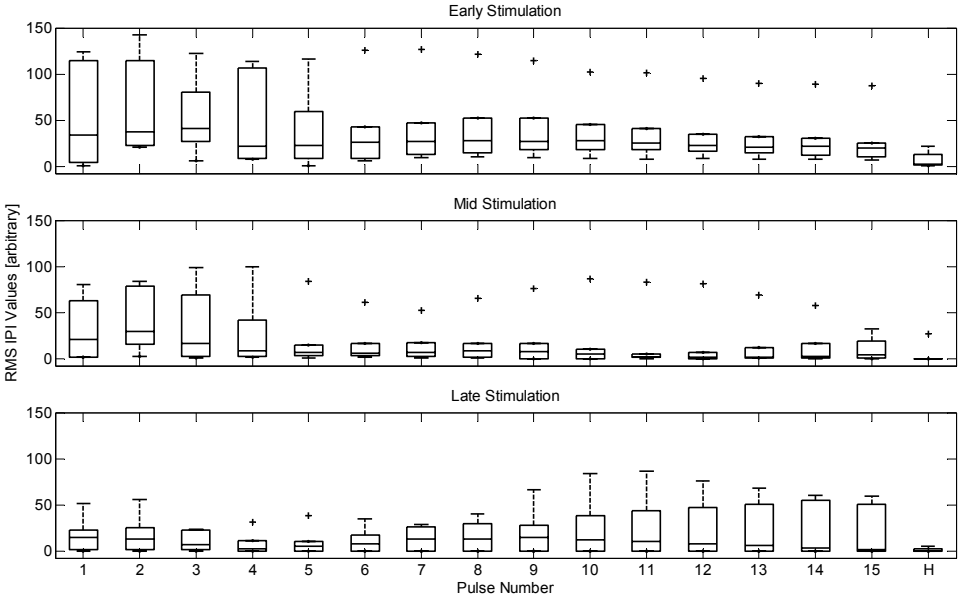

Figure 4-5: Boxplots of relative RMS values within the inter-pulse intervals for Se, Sm, Sl conditions.

The ensemble average of each IPI signal was calculated over the number of steps taken during the entire stimulation trial (minimum 55 steps). The root mean square (RMS) of this averaged value was calculated and divided by the mean RMS value over all gait cycles of the non-stimulated trial preceding the stimulated trial. The boxplots in Figure 4-5 show relative RMS values over all subjects, between each pulse, for each stimulation condition.

It is clear from Figure 4-5 that the muscle was activated due to the stimulation. Multi-level mixed model statistical analysis was carried out to investigate the significance of amplitude differences of these waves due to the stimulation conditions. This test revealed that the amplitudes of the responses due to Se were statistically significantly larger than the responses generated by the other two conditions (overall: $p < 0.001$ for condition and Se v Sm: $p < 0.001$, Se v Sl: $p < 0.001$). The differences were not statistically significant between Sm and Sl. This analysis also revealed that the pulse number had a significant effect on the amplitudes of responses (overall: $p = 0.001$).

Finally, a paired t-test revealed that the amplitudes of the final H-reflexes were not significantly different for the three stimulation timing conditions.

4.4.2 Results: Burst Times

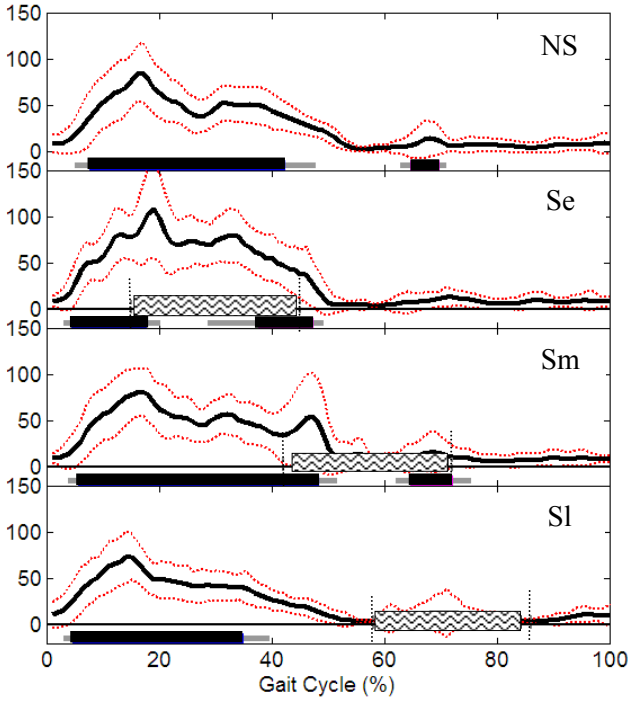

Figure 4-6: Output from AGLR burst detection program for the GM from subject 5.

The solid curves are smooth rectified EMG traces. The dotted lines to either side of the solid line are the standard deviations. Black horizontal bars below the curves indicate the median time that the muscle is active; the grey bars protruding from these are the 25 and 75 percentiles. The patterned bars shown in the stimulated trials indicate stimulation on time. The vertical lines outside of this represent the 25 and percentile of the on time and 75 percentile of the off time.

Figure 4-6 shows a typical graphical result from the AGLR program used to determine gastrocnemius activity. Stimulation artefact was removed prior to application of the program as described in methods section above; it is clear from Figure 4-6 and Figure 4-3 that this was done adequately.

During non-stimulation trials one burst of gastrocnemius activity per gait cycle is observed, this is with the exception of subject 5 during NSl. Due to stimulation, some circumstances lead to an extra burst manifesting (this effect can be seen in Figure 4-6). Only subject 1 generated an extra burst with every stimulation condition, while subject 2 did not show this phenomenon at all. Generally, during early stimulation, physiological bursts began before stimulation was initiated and ended after stimulation was terminated. The only exception to this was Subject 2.

The EMG bursts during Sm condition began before stimulation was initiated. The off times of all subjects occurred later due to Sm. These EMG bursts ended during the stimulation burst, or the offset times of the EMG bursts occurred before the onset of stimulation. The only exception was subject 4, whose EMG bursts ended later in the gait cycle than the stimulation.

All on-times of bursts during the Sl condition began before stimulation was initiated. The off times of the physiological bursts occurred inside the stimulation burst for two of the subjects. For the subjects whose off time did occur within the burst, this value was later in the gait cycle compared to without stimulation.

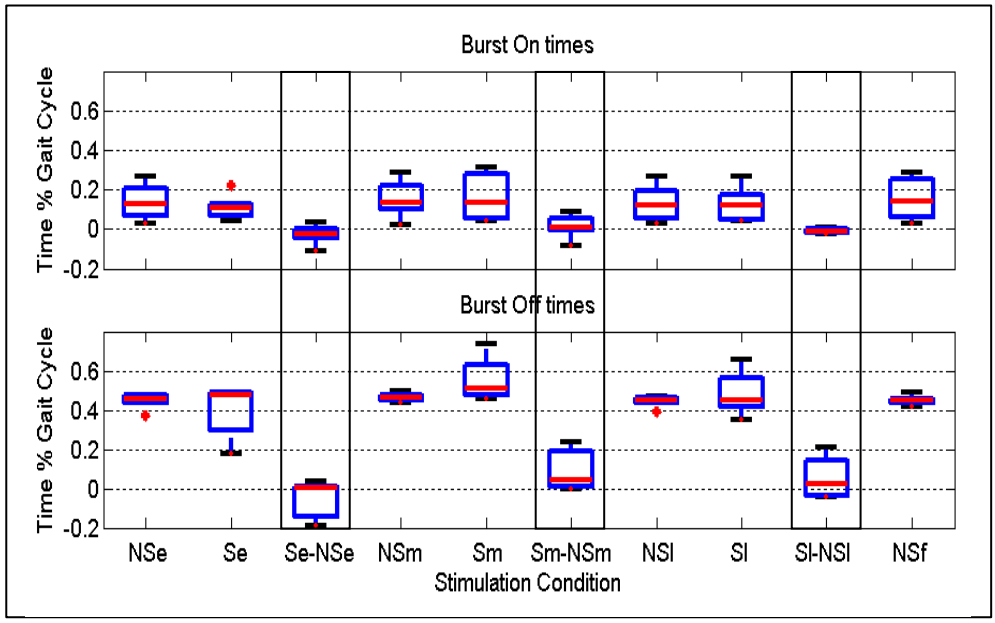

Figure 4-7: Boxplot of relative on and off times of the GM under all 7 stimulation conditions, including the differences between with and without consecutive stimulation conditions.

Figure 4-7 is a display of boxplots, used to represent the median on and off times of each subject per stimulation condition. Initially mixed model analysis was carried out on the non-stimulated trial timings. This resulted in no statistically significant effects. Therefore, the non-stimulated trials were amalgamated as one non-stimulation (NS) condition. Mixed model statistical analysis was carried out on the median on and offset times of NS and each individual stimulation condition (Se, Sm, Sl), to determine if the stimulation caused a statistically significant effect on the physiological timing with respect to NS. No significant effects were caused to the onset times. Offset times were statistically significantly affected by the stimulation condition, $p = 0.018$. Pairwise comparisons, utilising the least significant differences (LSD) method revealed that Sm was the cause of this effect, with Sm v NS: $p = 0.003$, Sm v Se: $p = 0.043$ and Sm v Sl: $p = 0.017$.

It should also be mentioned that statistical analysis was carried out on the time interval between heel strikes – thus effectively a measurement of gait speed. These tests revealed that gait speed was not significantly altered due to the application of FES.

4.5 Discussion

The results demonstrate that stimulation was clearly able to induce muscle contractions. This was observed in the M-waves and H-reflexes during and after each stimulation burst. Se induced the largest IPI responses, to a statistically significant level. The amplitude of the IPI responses varied across the stimulation bursts. The results also show that the Sm condition induced the largest change in burst timing, specifically offset times, which was statistically significant. These offsets occurred while the stimulation was still active.

The signals between the stimulation pulses consist of a direct M-wave as a response to the preceding stimulus, associated with direct efferent activation of the muscle. The first response cannot contain reflexive components this can thus only be an M-wave. The subsequent responses may also include a monosynaptic H-reflex. Due to the similar latencies of the H-reflex and F-wave responses, it was believed that an F-wave may also be present, however, it is unlikely that F-waves would occur here as they have been reported to occur only at supramaximal levels [11]. The H-reflexes were visible only after the last stimulation pulse, around

35-40ms. Due to the relatively short IPI, the reflex responses during the IPIs are masked by the stimulation pulse and/or the M-wave.

The fact that the waves in between stimuli reach relatively high amplitudes in comparison to maximum RMS EMG during physiological activity means that the gastrocnemius muscle was recruited to a significant level in response to stimulation. It should be noted that the actual level of recruitment remains unclear. To compensate for this increased activation of the muscle, it was expected that the central nervous system would reduce the physiological activation of the triceps surae muscle, resulting in a functionally adequate total activation of the muscle. Our findings, however, show that burst on- and offsets did not change, except in response to the Sm condition, for which the offset occurred significantly later. In contrast to the other two conditions, the late offset for the Sm condition may have been influenced by interference with the stimulation burst, because it occurred during stimulation. At the beginning of stimulation, relatively high M-wave responses were generated (as Figure 4-5 shows). This may have effectively contributed to extending the activation of the muscle in this phase. It would seem thus that Sm was the most effective stimulation condition for extending the burst at the time of push-off, which was the intention of the stimulation.

The reason for not finding reduced physiological burst durations in the presence of stimulation may be found in blocking of the physiological activation during the stimulation burst, which can be seen in Figure 4-3 and Figure 4-4. This blocking is a well-known phenomenon [19,20], which can be explained by the generation of antidromic activity in the α-motor neuron fibres in response to stimulation, colliding with orthodromic physiological and reflex activity for several tens of milliseconds. This also explains why the H-wave is reduced at higher levels of stimulation, when a larger part of the α-motor neuron fibre population is activated, associated with a higher M-wave, while a larger part of the incoming H-reflex activity [11,20,21] is blocked. Because of this phenomenon, stimulation of physiologically active muscles, like the triceps surae during the stance phase of gait in healthy subjects, not only results in added activation by direct muscle stimulation, but may also result in reduced activation by blocking physiological and reflex activity generated by the α-motor neurons. The net effect is a lower activation than expected from the added stimulation, which may be the same or less

than the physiological activation without stimulation. Part of the stroke population, has reduced physiological activation of the triceps surae during the stance phase of gait [4,5,6,7,8,9] as well as low spasticity. We hypothesise that stimulation may result in increased total activation of the muscle with this particular group of subjects, if stimulation is at a sufficiently high level, since little or no physiological activity is present that can be blocked. This must be investigated further.

It should be noted that we have only evaluated EMG, providing information about the response of CNS to neuromuscular stimulation at the level of muscle activation. Evaluation of force and movement would be required to evaluate the net kinetic and kinematic impact of stimulation and CNS response, which can only be speculated about on the basis of EMG.

The M-wave RMS values, described in the results were normalised to the RMS physiological activation level of the preceding non-stimulation trials during gait. Determination of the maximal M-wave (M_{max}) level would require stimulation above the tolerance level of the subjects. It should be noted that a normalised level of 1, does not mean that the activation was at the same level, since synchronised EMG of the M-wave signals of many motor units is a linear summation, whereas the RMS EMG during physiological activation increases proportionally to the square root of the number of independently activated motor units [16].

Another methodological issue concerns the 50Hz high pass filtering of the raw EMG. Despite the fact that some signal power is filtered out, the majority of the signal is passed, since the bandwidth of raw EMG is approximately 10 to 500Hz [16]. The resulting filtered EMG still provides a good indication of the activation level of the muscle, assuming that the power below 50Hz relative to the total power does not change with activation level. During EMG measurement as described in the methods section, a 5Hz HPF was used. This resulted in the presence of filter responses to the stimulation. The advantage of using the 50Hz HPF is that these filter responses were removed from the signal.

The variability of the M-waves over the three stimulation conditions shown in Figure 4-5 indicates that the recruitment of nerve fibres of the tibial nerve may not have been very stable. As stimulation was applied transcutaneously to the tibial nerve at the popliteal fossa, the position of the electrode relative to the nerve may have varied during knee movements. Had supramaximal stimulation been applied,

the transfer between stimulation and recruitment may have been less sensitive to these variations. However, such stimulation levels were not tolerable by the healthy subjects for the 50Hz stimulation bursts given. An alternative partial cause of the variability of the M-waves may have been differences in M_{max}, which have been reported to vary depending on limb position and contraction level of the muscle [22,23,11,20]. Tucker et al. were able to induce M_{max}, using single stimuli in contrast to the 50Hz stimulation bursts given in the current study. In addition, the stimulus bursts in this study were given during functional movement (gait), while Tucker et al. applied the stimuli while the subjects were lying prone on a physiotherapy table [22].

Concluding, our study demonstrates that physiological activation timing of the triceps surae of healthy persons does not change significantly when the muscle is activated with electrical stimulation of the tibial nerve, except for a change of offset time for Sm. The additional activation may have been compensated, at least in part, by blocking of the physiological activation during the stimulation burst. Therefore, it is not self-evident that physiologically active muscles produce extra force when stimulated.

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Chapter 5 Healthy Subject Evaluation (II)

The Effect of FES of the Tibial Nerve on Physiological Activation of Leg Muscles During Gait

Monaghan CC, Hermens HJ, Nene AV, Tenniglo MJB, Veltink PH.

Submitted.

Abstract

Objectives: The purpose of the experiments was to understand the resulting effects of stimulation of the tibial nerve on the activation of leg muscles from both legs. Eventually, the experimental protocol will be transferred to subjects such as the stroke population, who could benefit from improved push-off during gait.

Methods: Surface functional electrical stimulation of the tibial nerve of a group of six healthy subjects was carried out at three different times during gait: early, mid and late stance. Changes to activation patterns of muscles were investigated using EMG. Changes to angular velocity of leg segments were measured using inertial sensors.

Results: Results show that FES of the tibial nerve at the popliteal fossa changes control of physiological activation of both sides; yielding modified control of the on and off times of the tibialis anterior of both legs and the gastrocnemius medialis of the stimulated side. Additionally, activation level of the tibialis anterior and semitendinosus of the leg contralateral to stimulation was significantly decreased.

Conclusions: This information is important for future applications of stimulation as it means that stimulation not only affects the stimulated muscle but also the physiological motor control by the CNS.

5.1 Introduction

Functional electrical stimulation (FES) involves electrical stimulation of a muscle or nerve to provide functional improvement. Applications of FES include restoration of upper limb functions such as reaching and grasping and lower limb functions such as standing, balance, posture and gait.

Reports show that the Physiological Cost Index (PCI) and walking speed improve in response to stimulation of the tibialis anterior muscle/peroneus nerve to minimise drop foot [1,2]. Studies also show that activities of daily living, quality of life and range of motion are improved due to use of FES [3]. Additionally, physiological activity, measured using electromyography (EMG) of the upper limbs is improved in response to upper limb FES [4]. However, to our knowledge, no studies to date have investigated the effect on neuromuscular control of leg muscles, while applying FES during gait. The most similar research is the measurement of reflexes and joint kinematics, following randomised, non-functional electrical stimulation [5-7] of lower leg cutaneous nerves during gait.

It is necessary to study the effect of FES in healthy and patient populations, in order to fully understand the consequences of functional stimulation [4], not only on the stimulated muscles, but also on the neuromuscular control of other muscle groups.

Results from EMG studies [8-15] show that calf muscle activation and as a consequence, push-off during gait are adversely affected as a result of a stroke. Muscle activation patterns of both sides are affected and muscles from both sides change during the recovery period [14-17]. Research shows that the plantar flexors provide a major contribution to push-off [18] and swing initiation [19]. Reinforcing this, Bajd et al. found a 40% increase in force from rest to push-off, as well as a decrease in the time duration of push-off during FES of the plantar flexors of SCI subjects. Bajd et al. found that FES of ankle plantar flexors causes the heel to rise, in preparation for swing, providing forward and upward propulsion to the swinging leg; as well as knee flexion, which is important for effective shortening of the swinging leg. They concluded that stimulation of calf muscles alone can provoke swing [19]. This was also confirmed by Ichie et al. [20], who added that stimulation elicits the flexion withdrawal response, through activation of afferent fibres. This

implies that FES of the calf muscles of stroke subjects could improve push-off and alter the activation patterns not only of the affected side, but also the non-paretic side.

We previously reported that FES of the tibial nerve affects the activation patterns of the gastrocnemius medialis (GM) of healthy subjects during gait [21]. Direct and/or reflexive motor responses were generated in this muscle. It was expected that the stimulation would decrease the amplitude and possibly duration of physiological activation bursts of the GM. However, this was not the case. The reason may be attributed to the presence of antidromic stimulation, which would block the physiological activation of the gastrocnemius during the stimulation burst. As FES of the tibial nerve affects the response of the GM, the stimulation interacts with the physiological motor system. As such, it can be expected that FES of the tibial nerve will, directly or indirectly, influence activation patterns of other leg muscles.

The aim of the research presented here was to determine if muscle activation patterns of upper and lower leg muscles and angular velocity of both legs change due to the unilateral application of FES to the tibial nerve during gait in healthy subjects. This study has been performed in preparation for similar testing in stroke subjects who could benefit from improved push-off during gait.

5.2 Methodology

Data was collected from six healthy subjects, four male and two female, mean age 25 (±5) years old. The subjects had no history of neurological disorders. Each subject signed an informed consent form, which was approved of by the medical ethical committee, of the Roessingh, Rehabilitation Centre, as part of a study for FES of stroke subjects.

A detailed methodology has already been presented [21], the following is a summary of this protocol, with relevant additions where needed. The results presented are from the same group of subjects and protocol.

EMG data was recorded, using the ambulant set up of the Porti-5 from TMSI, Enschede, NL at a frequency of 2048Hz, and filtered using a 5Hz-2kHz band-pass filter during gait. Muscles measured included the gastrocnemius medialis (ipsilateral: iGM, contralateral: cGM), tibialis anterior (iTA, cTA), semitendinosus

(iST, cST) and rectus femoris (iRF, cRF). EMG electrodes were applied according to SENIAM guidelines [22].

Kinematic data was recorded from the lateral side of the thigh and lower leg of the side ipsilateral as well as the lower leg contralateral to stimulation and the bridge of the foot of the stimulated side. Kinematics were recorded using inertial sensors from Xsens Technologies B.V., Enschede, NL. Each inertial sensor contains three uniaxial gyroscopes, accelerometers and magnetometers. Gyroscopes measure angular velocity. Sample rate was 100Hz. In this study, only angular velocity recorded from the gyroscopes of sagittal plane movement is reported. The inertial sensor on the ipsilateral lower leg was connected directly to a biphasic stimulator to allow control of stimulation. The control principle has been previously detailed [21,23]. When angular velocity of the lower leg changed direction, at the beginning of stance, the angular velocity signal was integrated, resulting in angle change since this instant. Stimulation began at a preset change in angle of the lower leg.

An EMG electrode was utilised as the stimulation electrode. The optimal stimulation site for tibial nerve stimulation, at the popliteal fossa, was determined using a hand held stimulation probe. The anode was fixed to the lower leg, under the gastrocnemii. Stimulation was applied at 50Hz. Burst duration was 300ms, consistent with the work of Bajd et al. [19].

The experimental procedure was divided into stimulation and non-stimulation blocks, as shown in Figure 5-1. To prevent the influence of the order of stimulation timing on the results, timing was randomised between subjects.

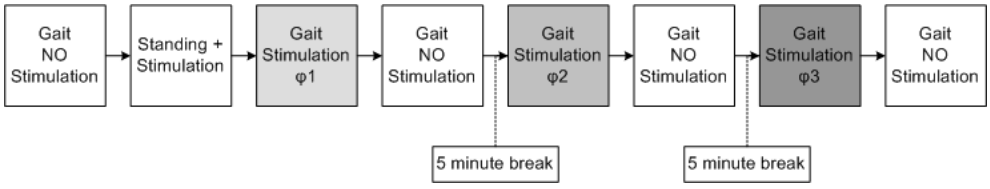

Figure 5-1: Block diagram of the experimental protocol. φ1, φ2 and φ3 represent a different change in angle since heel strike. The order of the three stimulation conditions (early, mid and late) was randomly chosen per subject.

During gait trials, subjects walked continuously for three minutes around the gait lab at a self-determined pace while data was recorded. Following the first non-stimulation trial, subjects stood with the foot of the stimulated leg on a force plate, mimicking posture at push-off. Stimulation amplitude was increased until a satisfactory force and movement were generated.

Mid-stimulation (Sm) started approximately half-way through the stance phase; we hypothesised that this angle coincided with normal contraction time of the gastrocnemii. Early stimulation (Se) was applied 10 degrees before and late stimulation (Sl) was applied 10 degrees after Sm. Sl may have continued into the swing phase, depending on the Sm angle. Statistical analysis revealed that the non-stimulation (NS) conditions did not produce significantly different results, thus NS denotes results from all non stimulation trials, which have been combined, mainly for statistical purposes.

5.2.1 Data Processing

The EMG data was processed offline in Matlab. Stimulated trials underwent stimulation artefact removal [24]. A 50Hz high pass filter was applied to artefact-free signals to remove any remaining filter response to the stimulus artefacts. The EMG was further processed in two manners. One was to determine the EMG activity between the stimulation pulses (IPI). The other utilised a standardised burst detection method, based on the approximated generalised likelihood ratio (AGLR) principle [25]. The AGLR generated on and off times of the physiological EMG burst; normalised to percentage gait cycle and smooth rectified EMG (low-pass filtered to 25Hz) enabling determination of the magnitude of bursts [25]. The analysis of the inter-pulse intervals (IPI) of all muscles, to investigate the direct effect of stimulation during the stimulation burst involved the following sequence:

For each stimulation trial of each subject, the ensemble average of all inter-pulse interval signals following corresponding stimuli of the bursts were calculated. The minimum number of steps per person, for each stimulation condition was 55. A root mean squared value (RMS) of each averaged signal was calculated. The RMS signals were then normalised against the RMS value found over all gait cycles for that muscle during the previous non-stimulated trial. The resulting values are thus dimensionless.

Segment angular velocities, recorded utilising the rate gyroscopes, were used to assess the impact of stimulation on kinematics. For segmental angular velocity to be used, each sensor underwent a sensor to segment calibration before the gait trials began. Calibration trials involved rotation of the segments with attached sensors in the sagittal plane, to facilitate a coordinate transformation procedure in Matlab [26]. The time course of the angular velocity signal was normalised to percentage gait cycle. The start of a gait cycle was determined using the impact response of the accelerometer of the foot sensor.

5.2.2 Statistical Analysis

In addition to the mixed model statistical analysis previously detailed [21], mixed model analysis was also performed on the maximum angular velocities in the sagittal plane and timing of these maxima, for each segment measured with the inertial sensors. The minimum number of steps analysed, therefore over which a median value was taken, was 55. This minimum value represents simply the number of heel strikes that could be reconstructed, from the 3 minute walk. The level of significance was $p<0.05$. Mixed Model Analysis works on the same principle as ANOVA, but handles missing samples more effectively.

5.3 Results

5.3.1 Inter-pulse Interval Responses

Across each stimulation burst, 15 pulses were delivered; the space between the pulses is called the inter-pulse intervals (IPI). The signals during each IPI, and up to 50ms after the final pulse of each burst were investigated for each muscle. In some muscles, synchronised responses to the stimulation pulses were generated. Figure 5-2 is an example of synchronised activity observed in the IPI of the iTA.

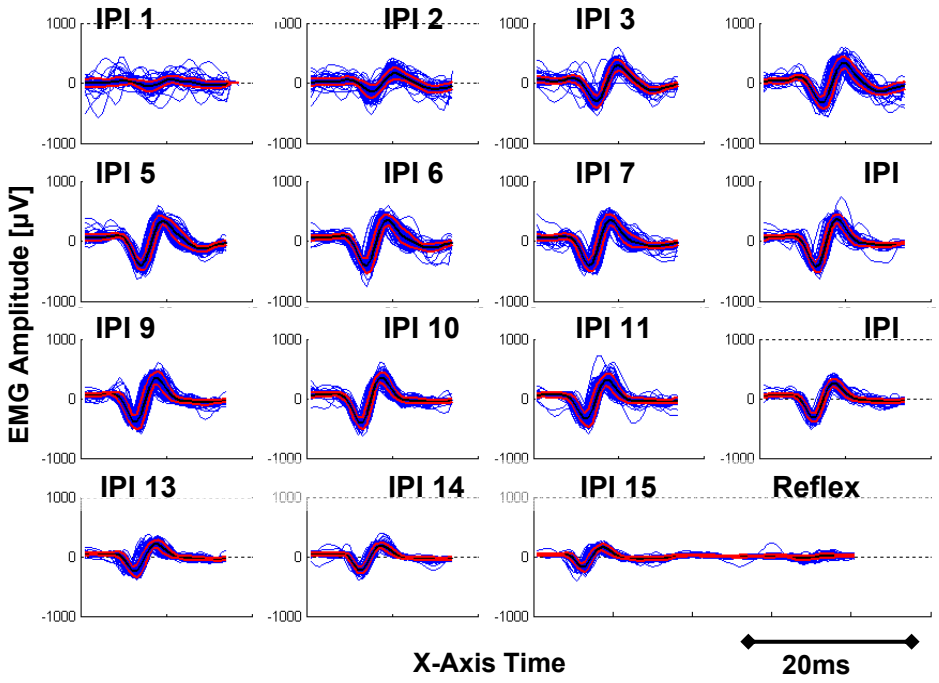

Figure 5-2: An example of synchronised activity during inter-pulse intervals (IPI) of the iTA, in response to FES of the tibial nerve during Se. The signal after the first pulse does not show synchronised activity in this example. The IPIs during successive pulses reveal clear waveforms between 8 and 15ms; the timing of which may indicate a reflex.

Synchronised responses were observed on all muscles of the stimulated leg, although less frequently on the iRF. On the contralateral side, the cRF revealed synchronous activity in two subjects, during each stimulation condition. The only other muscle on the contralateral leg to show this activity was the semitendinosus. However, this occurred only in one subject, during one stimulation condition. Figure 5-2 shows that the response to the first pulse is not synchronous; therefore, as expected, a motor response was not generated in this muscle. However, the successive responses are clearly synchronous. Each IPI is approximately 20ms, the peak in the second IPI (IPI 2) occurs at around 10ms, which is around 30ms after the first stimulation pulse (SP 1). Therefore the peak, observed in IPI 2 may be a reflex, in response to SP 1, etc. No synchronised activity is observed during IPI 1, in Figure 5-2; this shows that no motor response was generated after SP 1. This

indicates that we did not stimulate the peroneal nerve. However, there is no signal 35ms after SP 15, where the final reflex is expected, if the signals observed in the IPIs are purely reflexive.

Figure 5-3 shows box plots of the mean, normalised RMS values calculated during each IPI for the iGM, iTA and iST. The values for the stimulated muscle are excessively larger than the other values. Note that the scale of the y-axis of the iGM is ten times larger than for the other two muscles. Figure 5-3 highlights that the IPI responses of the iTA and iGM are different, in terms of the size and variation of size across the stimulation burst. This confirms that the iTA responses are not measurements of crosstalk.

Apart from the responses observed in the iGM (details discussed in Monaghan et al. [21]), the magnitudes of responses measured from iTA were always larger than in other muscles. In the iTA, this magnitude increased between the first and second pulse for every stimulation condition, as Figure 5-3 shows. Approximately 35ms after the final pulse, an additional reflexive response is expected. In Figure 5-3, "R" indicates the amplitude of the signal at this time. To prove our hypothesis that the synchronised pulses in the IPIs are only reflexive, in response to two stimulations pulses prior to a given IPI, the amplitude of this "R" is expected to be of comparable amplitude to the others in the plot. This was not the case, according to Figure 5-3. Furthermore, although no synchronised responses were seen in IPI 1 of Figure 5-2, no visible reflex peak was observed after the final stimulation pulse either; the reason for this is observation unclear.

The synchronised activity observed in the iST in response to the stimulation were very low in value as demonstrated on Figure 5-3.

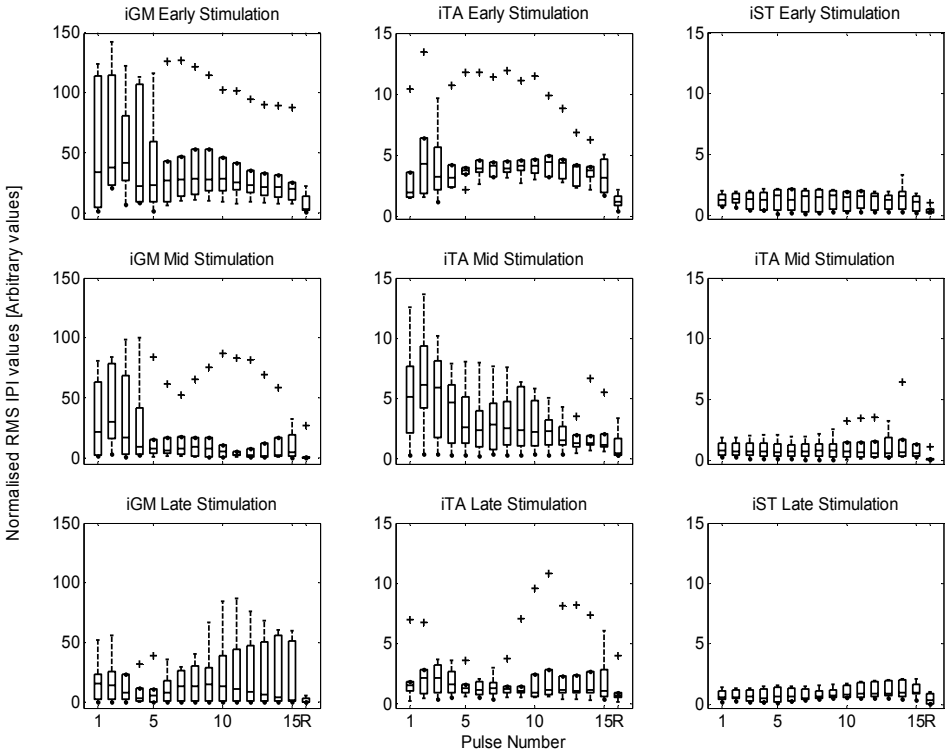

Figure 5-3: Relative normalised IPI RMS values of muscles, which revealed synchronous activity in response to FES of the tibial nerve. From left to right these are the iGM (stimulated muscle), the iTA, and the iST. Note the different scales used, to highlight the differences in magnitude.

5.3.2 Physiological On and Offset Timing

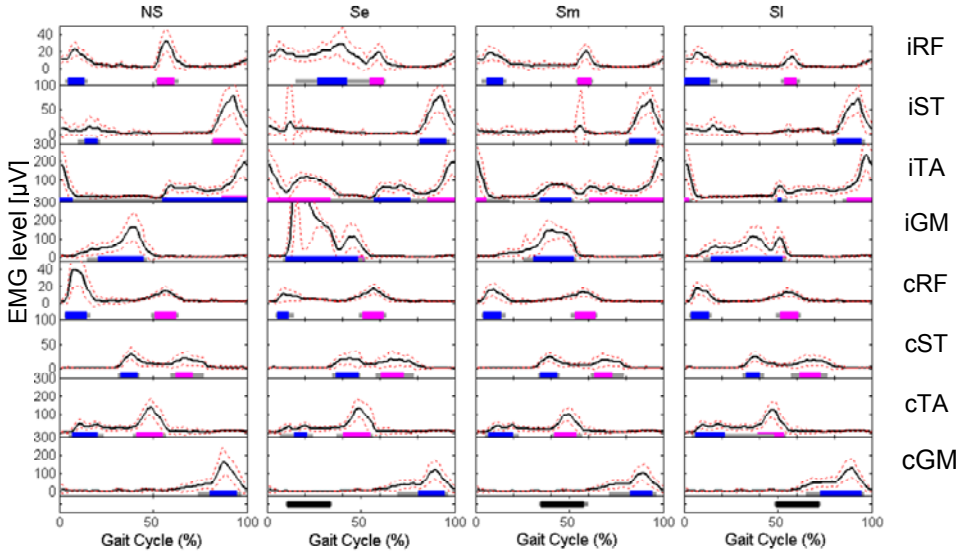

Figure 5-4: Muscle Activation patterns for Subject 5. Each column represents a stimulation condition, from left to right, NS, Se, Sm, Sl. Each row represents a muscle, from top to bottom: iRF, iST, iTA, iGM, cRF, cST, cTA, cGM. Solid bars represent muscle activation on. Grey bars represent the 25 and 75 percentiles of the timing. The bottom row, solid black bar highlights where stimulation occurred in the gait cycle.

Figure 5-4 shows an example of the results from the AGLR burst detection program, which was used to process the EMG bursts. Results consisted of median on and off times for each muscle per subject, per stimulation condition, normalised to percentage gait cycle [21,25]. Each column represents a given stimulation condition, NS, Se, Sm, and Sl, from left to right. The bars under each muscle burst represents the median on to offset times of the muscles. The timing of stimulation are shown in the bottom rows, represented by the black bar. The faint grey bars protruding from the black bars represent the 25 and 75 percentiles of respective timing.

Statistical analysis revealed that the stimulation of the tibial nerve during gait affects the physiological activation timing of muscles from the same and contralateral leg muscles. These muscles included the iGM, iTA and cTA. The

significant effects on the iGM have already been reported[21]. Table 5-1 summarises the remaining effects of the stimulation on the individual muscles, where a significant change was observed.

Table 5-1: Summarising the significant effects of stimulation on burst timing of leg muscles

	iTA_2 Off	**cTA_1 Off**	**cTA_2 On**	**cTA_2 Off**
Overall (p)	0.013	0.01	0.015	0.009
NS - Se (Δ%)	21%	5%	1%	-
NS - Sm (Δ%)	-	-	-	-
NS - Sl (Δ%)	-	-	2%	3%
Se - Sm (Δ%)	21%	-7%	-2%	-
Se - Sl (Δ%)	22%	-5%	-	-
Sm - Sl (Δ%)	-	-	3%	-

Table 5-1 provides an overview of the results that had statistically significant findings. The differences in timing are provided for those that produced a statistically significant pairwise result. No significant effects were observed on the onset times of the ipsilateral muscles. Offset times of the iTA and cTA were statistically significantly affected by stimulation. Although statistically significant, these changes were relatively small, with the exception of the delay in iTA offset time. This is due to activity, in the IPI, giving the impression that the muscle continued activity throughout stance.

5.3.3 Activation Level

The activation level of each burst was determined, utilising the AGLR method. A mixed model analysis revealed that apart from the iGM, only in the iST and the cTA muscles was the overall change in amplitude of bursts due to stimulation statistically significant.

Table 5-2: Table summarising the significant effects of stimulation on muscle amplitude of activation

Muscle / Effect	***iST*** **Decreased**	***cTA*** ***Decreased***
Overall Significance	$p < 0.05$	$p = 0.000$
Pairwise comparisons	NS – Sm = 6μV: p = 0.05	NS – Sm = 15μV: p = 0.000
	NS – Sl = 7 μV: p = 0.03	NS – Sl = 7μV: p = 0.04
		Sm – Se =-16μV: p = 0.000
		Sm – Sl = -9μV: p = 0.03

From these results, it is clear that the cTA was the most effected by stimulation. This was mainly during Sl or Sm. Se did not cause any significant changes to the activity level of the cTA, even though the cTA was physiologically active, and in the swing phase of gait at the time of stimulation.

Kinematic changes

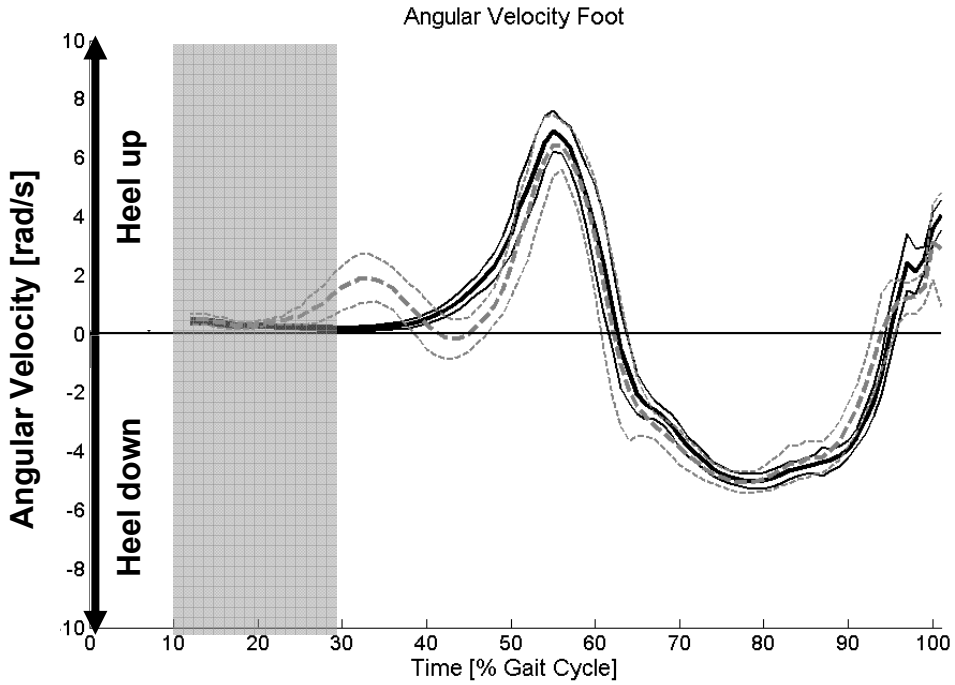

Figure 5-5: Mean angular velocity of the foot, of Subject 1, in the sagittal plane during gait. Solid black line: NS. Grey dashed line: Se. Thin lines at each side of the heavy lines represent the standard deviations of the signals. The grey box indicates where stimulation was active.

Statistical analysis of angular velocity revealed that the most clearly defined kinematic changes occurred at the foot, during stance in response to Se; causing a large increase in angular velocity. This has been highlighted Figure 5-5. The overall statistical significance of this change was $p = 0.001$. This peak, occurring during each stance phase is the heel rising prematurely during stance in response to Se, at 2.3 rad/s ±0.6 compare to no stimulation, 1.2 rad/s ±0.4. This occurrence highlights the strength of the stimulation, as the whole body weight was on the foot. However, this foot lift did not facilitate functional push-off since it was too early for the push-off peak.

The only other change was that the timing of peak of angular velocity of the lower leg during swing occurred significantly earlier. This marginally significant change was due to Se compared to NS ($p = 0.04$) and Sm ($p = 0.05$).

5.4 Discussion

Stimulation of the tibial nerve of healthy subjects influences not only the stimulated muscle, but the muscle activation patterns of muscles from both legs. Synchronised activity was observed in the iTA and marginally in the iST. On and offset times of the cTA and the offset time of the iTA were significantly altered. EMG levels of the cTA and iST were significantly decreased, in response to Sm and Sl. A significant increase of angular velocity of the foot during stance was observed, during Se. Stimulation did not affect the magnitude of the angular velocity of the larger segments, such as the lower legs or the thigh.

Synchronised responses were observed following individual stimulus pulses, mainly in leg muscles ipsilateral to stimulation. Results from other studies showed that reflexive changes occurred in upper leg muscles and in muscles contralateral to stimulation [5-7,18]. We found synchronised responses in the cRF, in only two subjects, and in the cST of one subject during one stimulation condition. The magnitudes of these responses were very small; therefore we cannot rule out that they may have been remainders of the removed stimulus artefacts.

Apart from the iGM, clear synchronised responses were also visible in the iTA. Figure 5-2 shows that no synchronised activity occurred during the first IPI of Se, for this subject, but did occur in subsequent IPIs. Had a direct motor response been induced, it would have been seen in the first IPI. This was not the case. The synchronised activity appeared in the second IPI. This implies that a reflex response to the first stimulation pulse was visible during the second IPI; and not a direct motor response to stimulation. If the synchronised activity measured at the iTA was a motor response to the stimulation, this suggests that the peroneal nerve, which innervates the tibialis anterior muscle was stimulated, along with the tibial nerve, as we measured synchronised activity in the iGM [21]. Direct stimulation of the peroneal nerve did not occur in the example provided in Figure 5-2, as no motor response is present in the first IPI. However, due to the close proximity of the tibial and peroneal nerve, the possibility that the peroneal nerve was unintentionally stimulated in other cases cannot be ruled out.

The possibility that the synchronous activity is cross talk is not likely, because the amplitudes and patterns of amplitudes are very different, as shown in Figure 5-3.

Previous studies reveal that bilateral reflex responses were generated in response to cutaneous stimulation [5-7,18]. We did not observe these reflexive changes, as the lack of bilateral synchronised signals showed. This may be attributed to different stimulation conditions used [5-7,18] as the impact of stimulation depends on stimulation parameters [6,7]. In our study, 300ms bursts of 15 pulses, at 50Hz were applied. Zehr et al. [7] applied three to six pulses at 200Hz to the sural and tibial nerves, Tax et al. [6] gave five pulses at 200Hz. Berger et al. [27] applied a single pulse to the tibial nerve during gait. Due to the differing parameters, it is difficult to compare the activation levels achieved during each stimulation study. The other studies mentioned randomised stimulation time between gait cycles, whereas we applied a stimulation burst at the same predictable time for each stimulation condition tested. Because of this, adaptation of the physiological activation patterns may have occurred. Thus a centrally controlled, non-reflexive response may have been involved, particularly on the cTA, where synchronous activity was not detected, but a change in burst timing or amplitude was reported.

Random stimulation of the tibial nerve at the foot, [5-7,18] is effectively an electrical perturbation. Tax et al. [6] reported that the reflexive response to perturbation in the cat serves to minimise stumbling and ensure that balance and cadence is maintained. Based on other studies, relating the similar nature of cat and human reflexes, it is possible that human reactions serve the same purpose as those of the cat.

The optimal timing of the FES applied during our experiments was not expected to cause strong deflections from an optimal gait pattern. Our aim was to support push-off; therefore, particularly with Sm, push-off characteristics were expected to have appeared more pronounced. This was not the case, with Sm; we have previously attributed this to the occurrence of antidromic activation [21], colliding with the physiological activation at push-off. This collision would block physiological activity and prevent a net increase in muscle activity. Blockage due to antidromic firing would be less prevalent in early stance, where the unwanted heel rise was observed, because physiological calf muscle activity was still low; not reaching maximum activation level, until terminal stance.

The FES caused shorter bursts and decreased amplitude of the cTA. Tax et al. [6] stated that the response to stimulation is not necessarily related to the phase that the

stimulated limb is in, but is dependent on the phase of the leg in which the responses occur. They found that the cTA of healthy subjects showed a suppression of activity in response to stimulation during contralateral end swing [6]. The decreased activation levels that we observed, may also be attributed to inhibition of activity, as the changes occurred during Sm and Sl; corresponding to contralateral terminal swing and early stance. During this time, the cTA is actively decelerating the limb, in preparation for heel strike, and stance, while the side ipsilateral to stimulation enters into push-off. Therefore these subjects experienced both shorter bursts and decreased amplitude of the cTA due to sensory input from antidromic firing or from cutaneous activation, indicating active triceps surae. This caused the cTA to adapt its activation pattern. Sensing that the opposite limb was ready for push-off, it had to terminate activation earlier than normal. It would be expected that as a consequence, the triceps surae would onset earlier in order to provide balance and posture control during stance. However, this is more the role of the soleus [28], which was not measured in these experiments. This would be an interesting addition for a future study.

The stimulation applied caused significant changes to the foot during early stance, actually causing the ankle to lift, with full body weight. We found less kinematic effects of stimulation on the larger segments. Zehr et al. also noted that their cutaneous perturbation had a larger effect on the kinematics of more distal limb segments [7]. It was additionally unexpected that during the stimulation time that we considered to be optimal, no significant changes occurred to the kinematics. However, as we described [21] this could be due to collisions of physiological activation with antidromic firing. With no net change in activation, no change in the mechanical effect of the stimulated muscle can be expected.

It was expected that the results would provide a more clear indication of the effects of FES on the tibial nerve of healthy subjects. It would be beneficial to continue these tests on a larger healthy population, as well as to incorporate other measurements such as changes in kinetics, to provide more information about the change to push-off, including ankle moment, and power, however this was beyond the scope of the results presented here. The present study shows that the stimulation interacts with the CNS, yielding modified control of the on and off set times of muscles at both sides. This is important for future applications of

stimulation, for patient groups who can benefit from this, as it means that stimulation not only affects the stimulated muscle but also the physiological motor control by the CNS. For optimal utilisation of FES for rehabilitation purposes, better understanding of the physiological effects of FES is required.

The aim of the present research was to investigate how FES of the tibial nerve affects the muscle activation patterns of upper and lower leg muscles in healthy subjects, with the intention of applying the technique, in the future, to improve push-off of the post-stroke population who show a clear lack of this function during gait [8-13]. The results show that changes occur in healthy subject gait. In particular, unwanted early heel rise occurred in response to Se. Although the Sm did not induce the exaggerated push-off movements we had expected in these healthy subjects, we hypothesise that tibial nerve stimulation will benefit those with low calf muscle activation [8-13]. The antidromic activation, which we believe blocked physiological activation in this healthy group [21] is not expected in subjects with low activation, as this did not manifest during Se when the calf muscle activity was relatively low. Furthermore, Bajd et al. were able to induce push-off in SCI subjects [19,29,30], and the drop foot stimulator has proven to be successful in carefully selected subject groups since the 1960s [2,3,31].

The next step is to repeat the experiments performed in this study on the stroke population, with a primary goal of restoring lost push-off function in these subjects as well as to investigate changes in muscle activation patterns. As well as decreased amplitude of muscle activation, stroke subjects also exhibit co-contractions [14], and extra bursts [15] of the muscles on the non-paretic side. Therefore, further to the goals stated, it is hypothesised that FES of the paretic calf muscles will reduce the need for compensatory activity of the non-paretic side.

5.5 References

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Chapter 6 Patient Evaluation

Effects of FES of CVA Subjects on Stimulated and Non-Stimulated Muscles and Kinematics

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Submitted.

Abstract

Objectives: The purpose of this research was to understand the interactions between FES of the paretic tibial nerve and the activation patterns of the stimulated muscle group, and those of the non-stimulated muscles of the paretic and non-paretic sides, during gait. The triceps surae were chosen because these are the primary muscles needed for push-off, which is lost due to a CVA.

Methods: FES was carried out on the tibial nerve of five CVA subjects during gait, at a stimulation timing assumed to be optimal to generate push-off. Each stimulation burst consisted of 15 pulses, applied for 300 ms, at 50Hz stimulation frequency. The median on and offset times of all measured muscles, the signals measured during the inter-pulse intervals of the stimulation burst and the angular velocity, of the foot, lower leg and thigh of the paretic side as well as the lower leg of the non-paretic side were investigated.

Results: Results indicate that FES interacts with the activation patterns of the paretic and non-paretic leg muscles of stroke subjects. In the majority of subjects, muscle onset and offset timing changed for the gastrocnemius medialis, the tibialis anterior and semitendinosus of the stimulated side, and the gastrocnemius of the non-stimulated side. Additionally, activation bursts of the gastrocnemius medialis, semitendinosus and non-paretic gastrocnemius had increased amplitudes. Furthermore, the angular velocity of the foot was altered due to the FES.

Conclusions: In most subjects, changes were measured in both stimulated and non-stimulated sides of the subjects. This shows that FES is interacting with physiological activation. However, these results were not clinically or functionally relevant for the subjects, meaning that further efforts are needed to improve the gait of these subjects and the results obtained.

6.1 Introduction

Post-stroke gait has been investigated for decades. The benefits of the drop foot stimulator [1] on stroke gait, were already shown in the 1960s. Activation, timing and amplitude of paretic leg muscles, investigated using electromyography (EMG) [2,3,4,5,6,7] show that as well as drop foot, push-off is also severely diminished in part of the stroke patient population. Decreased activation levels, or co-contractions of leg muscle activity cause diminished push-off. All leg muscles of the affected side of stroke subjects have decreased EMG activation levels (paresis) [8]. In some subjects, there is premature activation of calf muscles, in others, complete or diminished activation of this muscle group on the paretic side. This can result in knee hyperextension, which diminishes the possibility to plantar flex and therefore push-off adequately [2,3,4,5,6,7]. The other type of post-stroke gait is characterised by co-contractions of leg muscles resulting in a gait pattern that appears more like cerebral palsy than stroke gait [9].

More recently, changes in muscle activation patterns of both paretic and non-paretic legs of stroke subjects have been assessed [10,11,12]. Further studies have involved analysing the development of these changes over the recovery period [10]. These research findings show that the activation patterns of the non-paretic muscles are also changed and that these patterns, for a select group of subjects, may change over time [11]. However, in the research carried out by Buurke [10], it was noted that although the walking pattern clearly improved over the recovery period, the coordination patterns did not.

During normal gait, the soleus and gastrocnemii, collectively known as the triceps surae, or more commonly, the calf muscles, have peak activation coinciding with push-off. Calf muscles are the primary plantar flexors [13], providing forward and upward propulsion to the leg as it enters swing at terminal stance [14,15,16]. According to Neptune et al. [17], only the gastrocnemius contributes to swing initiation, this is reinforced by Goldberg et al. [18] who state that the gastrocnemius makes a large contribution to knee flexion at the end of stance.

Due to spasticity of the calf muscles of the stroke population [19], there appears to be a general reluctance to stimulate these muscles. However, for the sub-population described above, with diminished activation levels, calf muscle

stimulation is a logical approach to restore the push-off that these subjects have lost. Furthermore, Knutsson and Richards [6,7] stated that this type of subject would respond well to FES treatment.

Because drop foot is one of the most commonly treated problems using FES, there is a lot of literature surrounding the clinical success of this method [19,20,21] and although there are many success stories, there are also many problems associated with it. Researchers [19] have stated that good patient selection is crucial to increase the chances of this technique. When comparing the relative ease of implementing drop foot and push-off correction using FES, a basic consideration is that the swing phase of gait lasts from approximately 60 to 100% gait cycle. During swing, the dorsiflexors for drop foot stimulation are stimulated. This period is comparatively longer than the event of push-off, which lasts approximately 20% of the gait cycle. Additionally, during swing, no body weight is on the foot. This has two advantages: drop foot FES can (relatively) easily be triggered using lack of pressure on a heel switch; and body mass will not conceal movement, due to the effect of FES. To induce push-off, body weight must be on this stimulated leg, complicating the triggering mechanism and the effect of stimulation is potentially disguised due to this weight. Stimulation levels should therefore be quite high to generate substantial force to raise and push the body forward, using electrical stimulation. These technical considerations, in combination with the potential of spasticity may shed some light on why push-off problems are comparatively less treated than drop foot, in stroke, using FES. An additional reason is that researchers find that by stimulating the peroneal nerve, a withdrawal reflex can be generated, effectively raising the leg, as well as dorsiflexing the ankle.

Bajd et al. [14,15,22] found improved push-off of SCI subjects using FES of the plantar flexors. Burridge [19,23] recommended that stroke subjects, unable to activate calf muscles during push-off may benefit from stimulation of this muscle group in combination with or instead of, the drop foot stimulator. However, no further data has been published based on this recommendation. Motivated by the above, we applied FES to the plantar flexors of healthy subjects [24]. These results showed that while we did activate the calf muscles, we did not significantly alter gait patterns of these subjects, particularly when stimulation was applied at the optimal stimulation time. Our interpretation is that we blocked the physiological activation and

replaced it with artificial, synchronous activation such that no net increase in activation occurred.

Furthermore, a pilot study that we carried out on one stroke subject showed that biomechanics were influenced and that push-off was improved; determined by increased knee flexion and ankle plantar flexion [25]. Based on the results of this pilot study and isometric evaluations (unpublished), we found that tibial nerve stimulation could generate more forceful movements at lower amplitudes than direct calf muscle stimulation.

The questions to address are: does FES of the tibial nerve influence the activation patterns of leg muscles of stroke subjects; and does this stimulation restore the push-off function?

We hypothesise that FES of the paretic plantar flexors of stroke subjects, with reduced activation of the calf muscles, will produce a net increase in activation. Over the recovery period, following a stroke, changes are seen in muscle activation patterns of both legs [11]. We hypothesise that the muscle activation patterns of non-paretic leg muscles will be affected by stimulation, in addition to changes in the activation patterns of the paretic side; either reflexively or compensatory. Therefore, changes in muscle activation patterns (timing and amplitude) from both legs were measured using EMG. Measurements were made with and without FES, during gait in order to facilitate understanding of the physiological responses as they occurred.

6.2 Methods

An experimental protocol has been previously described in detail [24] for healthy subjects. The following is a summary of this protocol, with relevant additions, where needed.

6.2.1 Subjects

Five stroke subjects, recruited from the Roessingh Rehabilitation Centre, in Enschede, the Netherlands were included in this study. The subjects were aged between 50 and 60 years old. All subjects had suffered a left hemispheric stroke. Testing was carried out, at least 6 months after the stroke. Inclusion criteria: relatively good walkers; little or no increase in calf muscle spasticity; and would

clearly benefit from improved push-off. Exclusion criteria: leg contractures; restricted range of motion of the knee or ankle; high calf muscle tone; non-walkers; and "normal" walkers. Subjects 2, 4 and 5 used a walking stick daily, therefore also used it during the gait trials. Subjects 2 and 5, who normally used an ankle foot orthosis removed this aid during the experiments to prevent masking of any mechanical effect of stimulation. All subjects signed an informed consent form. The medical ethical committee of The Roessingh Rehabilitation Centre approved the experiments.

6.2.1.1 Subject Intake Trials

Prior to inclusion in the experiments, all subjects underwent an intake test. During intake, a medical professional evaluated the subjects. Spasticity was assessed using the Modified Ashworth Scale [26]. Stiffness of the ankle and knee was measured according to the Perry-Silver Scored Procedure. This included measuring the possible range of motion (RoM) of the ankle and knee. For the ankle this was measured during knee flexion and during knee extension. The Motricity Indices of the hip, knee and ankle [27] were evaluated. A sensation test was carried out, testing skin sensation and proprioception. Stimulation tests of the tibial nerve were also carried out, to ensure that stimulation could generate movement.

6.2.2 Equipment

Stimulator:

A custom-built, custom-programmed current-controlled symmetrical bi-phasic stimulator was used. This had a current range of 0-100mA and a pulse width range of 50-500μs.

EMG system:

Porti-5, 16 channel/ASD unipolar EMG, from TMS International, Enschede, NL. Sample frequency: 2048Hz. Input Common mode range: -2V / +2V. Amplitude range: 22bit, resolution 71.9nV. Gain: 20x. CMRR: > 90 dB. Input impedance: >

10^{12} Ohm. Noise: < 1.5μVpp. EMG recording was performed using the ambulant setup. This allowed subjects to walk freely, without restrictions due to cables.

Inertial Movement Sensing

Inertial sensor data was recorded using the Xbusmaster and MT9 sensors from Xsens Technologies B.V., Enschede, NL. The MT9 module contains (3x) accelerometers, gyroscopes and magnetometers, arranged orthogonally to obtain 3D inertial and magnetic sensor information. Only sagittal plane angular velocity, measured from the gyroscopes will be detailed in this paper.
Stimulation during the gait cycle was controlled using the angular velocity of the lower leg ipsilateral to stimulation [28].

Electrodes

EMG electrodes used were solid gel Ag/AgCl EMG electrodes, oval shaped, 22mm x 35mm from Arbo.
An EMG electrode was used as the stimulating cathode, to allow greater precision of the stimulation area. The anodes were 50x90mm and were positioned on the lower leg of stimulated side.

6.2.3 Experimental Design

6.2.3.1 Subject Preparation

The optimal location for the stimulation of the tibial nerve was determined while the subject lay face down on a bed. A stimulation probe was moved around the area of the popliteal fossa, through which the tibial nerve can be stimulated. The position with the lowest stimulation threshold was established. An EMG electrode, used as the stimulation cathode, was then secured and stimulation was tested to ensure that the same effects were observed. Except for Subject 2 who (described later) was influenced by a Phenol injection at the time of the experiment, preventing activation of the tibial nerve. Therefore the stimulation was applied directly to the muscle bulk for this subject.
For EMG measurements skin preparation, measurement sites and inter-electrode distances were carried out according to SENIAM [29] recommendations. The EMG

was recorded from the gastrocnemius medialis (ipsilateral: iGM, contralateral: cGM), tibialis anterior (iTA, cTA), semitendinosus (iST, cST) and rectus femoris (iRF, cRF).

Inertial sensors were attached to Perspex strips, which were fixed to the lateral thigh and lower leg of the paretic side, (ipsilateral to stimulation) as well as the lateral side of the lower leg of the non-paretic side (contralateral to stimulation). One additional sensor was placed on the bridge of the paretic foot. See Figure 6-1 for a photograph of a subject donned with the equipment for the gait trials.

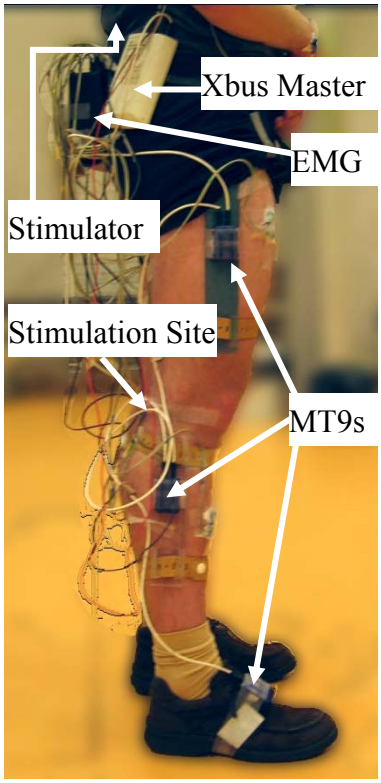

Figure 6-1: Subject donned with equipment for FES experiments.

6.2.3.2 Experimental Protocol

Stimulation frequency was 50Hz, with a burst duration of 300ms; this burst duration was in accordance with work of Bajd et al. [14]. The experimental protocol is presented briefly in Figure 6-2.

Figure 6-2: Block Diagram of the experimental protocol

Gait Pre-Stimulation

For a continuous three minute duration, subjects walked at their own pace around the gait lab. EMG and inertial sensor data were recorded over this entire period.

Standing and Stimulation

Subjects stood, in a push-off posture, with the stance leg, the leg preparing to push-off, on an AMTI force plate. The other leg was not on a force plate. Subjects were requested to load their push-off leg on the force plate as much as possible. Test stimulation bursts were remotely delivered while forces were measured.
Stimulation amplitude was increased gradually until a forceful movement was observed. The minimum stimulation current needed for maximum force was termed optimal and was used throughout the experiment.

Rest period

Subjects rested for approximately 5 minutes, to reduce the possibility of fatigue.

Gait Stimulation

For a continuous three minute duration, subjects walked at their own pace around the gait lab. Stimulation was applied to the tibial nerve at each stride. The timing of stimulation was controlled using the change in orientation of the lower leg since heel strike. For convenience, this event will be referred to as “stimulation time”. EMG and inertial sensor data were recorded over this entire period.

Gait Post-Stimulation

As with Gait Pre-Stimulation Trial, subjects walked for 3 minutes, continuously, at their own pace around the gait lab. EMG and inertial sensor data were recorded over this entire period.

6.2.4 Results Processing

6.2.4.1 Stance Trial Processing

Vertical ground reaction force (F_z) was directly recorded from force plate information. Change in centre of pressure in the horizontal direction (CoP_x) in response to stimulation was calculated. The change in torque was calculated as the product of the change in CoP and the body weight on the force plate. Maximal values of the responses during the 300 ms after the first stimulation pulse were evaluated.

Dimensionless force was calculated in accordance with Hof[30], by dividing the generated force by the subject's body weight (product of body mass and gravity).

Dimensionless torque was calculated in accordance with Hof[30], by dividing the torque by the product of body mass, acceleration due to gravity (9.98), and leg length.

6.2.4.2 EMG Processing

The EMG data was recorded at 2048Hz, after applying a high-pass filter of 5Hz and a low-pass filter of 2kHz. Further processing was carried out in Matlab. Data from stimulation trials first underwent stimulation artefact removal, based on work by O'Keefe et al.[31]. Following artefact removal, two types of processing was carried out. One analysis was performed to determine if the motor or reflexive responses were present. These were analysed over the period between each pulse, the inter pulse intervals (IPIs). The timing of the IPIs were based on the results from the artefact removal process. The means and standard deviations of the maxima were found, when motor responses (after ~10 ms) or reflexes (H-reflex after about 35ms) are expected.

The second analysis involved determination of the burst amplitudes and timings. All signals free from stimulation-artefact, including non-stimulation trial data were high-pass filtered at 50Hz. This removed filter responses from the stimulus artefacts. A standardised burst detection method, based on the approximated generalised likelihood ratio (AGLR) principle[32] was used to generated on and off times of the EMG bursts, normalised to percentage gait cycle. Smooth rectified EMG (SRE) using a low-pass filter of 25Hz was also generated. For each subject,

one set of thresholds, amplitude and variance, were used to determine the on and off times of the bursts. These parameters were determined using data from the pre-stimulation gait. If muscles had one burst, during pre-stimulation, but this same muscle had two bursts in the stimulated trial, split by the stimulation burst, the onset of burst one and offset of burst two were used.

6.2.4.3 Inertial Sensor Data Processing

Segment angular velocities were obtained from the rate gyroscopes inside the inertial sensor units. Each sensor underwent a sensor to segment calibration prior to the gait trials. Calibration involved rotation of the segments with attached sensors in the sagittal plane. These calibration procedures facilitated a coordinate transformation procedure in Matlab [33] to ensure that the angular velocity around the axis perpendicular to the sagittal plane could be estimated.

The time course of the angular velocity signal was normalised to percentage gait cycle. The start of a gait cycle was determined using data from the impact response of the accelerometer of the foot sensor.

6.2.4.4 Statistical Analysis

Because only five subjects were measured and due to large variability among these subjects, statistical analysis between subjects was not possible. Statistical results reported will therefore be on the individual subjects involved.

Mixed Model statistical analysis used was carried out in SPSS. Mixed Model is comparable to ANOVA, but handles the missing values better.

6.3 Results

6.3.1 Subject Intake Results

Subject intake tests were carried out on a number of patients, as described in the methodology. Eight subjects were included and three subjects dropped out. The five subjects presented here are the remaining subjects who participated in the research. During intake, Subject 2 had a pseudo clonus (clonus with irregular and variable amplitude) at the ankle. During the experiment, but not during intake, this subject was also affected by a Phenol injection. During intake, Subject 5 had a

clonus at the ankle, as well as a Modified Ashworth Score of 2-3 on the quadriceps. Other aspects of the intake were relatively normal, for all subjects, except that Subject 5 did show stiffness in the soleus and gastrocnemius, during testing of range of motion. These results also manifest as the results continue.

6.3.2 Stance Force Plate measurements

The torque results, measured during stance stimulation were carried out to determine if the stimulation induced a forceful movement. Figure 6-3 shows the mean change in centre of pressure, ground reaction force, and calculated torque generated in response to the FES of the tibial nerve, during stance. The results presented are from Subject 1, and are typical of results generated in each patient.

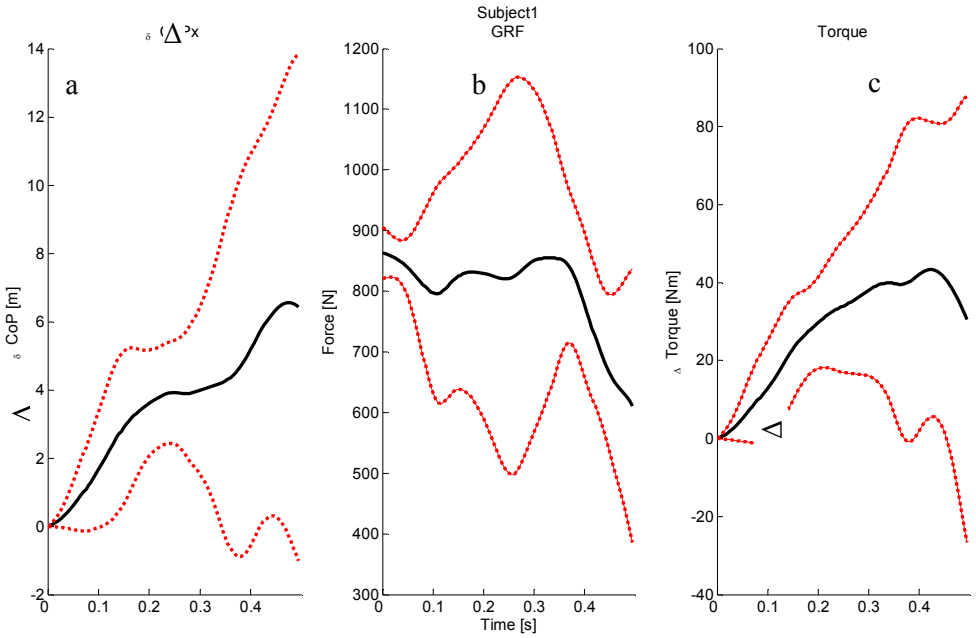

Figure 6-3: Mean responses and associated standard deviations, following stimulation during stance of Subject 1. Figure 6-3(a) is the change in Centre of Pressure (ΔCoP), given in centimetres. Figure 6-3(b) is the ground reaction force (GRF), measured in Newtons, Figure 6-3(c) is the calculated change in torque resulting from the product of ΔCoP and GRF, [Nm].

The results in Table 6-1 show that Subject 2 and Subject 5 displayed the lowest torques, forces and CoPs generated in response to the stimulation during stance

trials. The changes are largest in Subject 1. Subject 1 and Subject 3 were the most independent walkers of this group.

Table 6-1: Mean and standard deviation of Peak: vertical ground reaction force (Max. F_z), Normalised Max. F_z, Torques, Normalised Torque and maximum change of centre of pressure movement in the X direction (CoP_x), between 0 and 300ms after stimulation, per subject during stance stimulation.

	Sub 1	Sub 2	Sub 3	Sub 4	Sub 5
Mean Max. F_z [N]	991±63	761±71	774±20	761±347	520±40
Normalised Mean Max. F_z [-]	1.19	0.89	1.01	0.97	0.69
Mean Max ΔCoP_x [cm]	9±3	2±1	7±2	5±3	4±2
Mean Max. Torque [Nm]	57±19	12±5	44±11	57±52	17±9
Normalised Mean Max. Torque [-]	0.07	0.02	0.06	0.08	0.02

6.3.3 Evoked EMG Responses in the Inter-Pulse Intervals

Figure 6-4 shows that motor responses (M-waves) were generated in the IPI of the stimulus pulses, of the iGM. However, unlike the healthy subject data, this does not cause a response in the other leg muscles. In healthy subject tests, results showed a reflexive response from the iTA [24], this may have been expected from these stroke subjects. However, it is also possible that these subjects could not voluntarily contract the iTA. The EMG traces of Figure 6-5 show that the iTA was active during gait, but with a lower peak amplitude than the cTA. It is known that the EMG activity of the paretic legs of CVA subjects are less [2,3,4,5,6,7] than the non-paretic side and less than normal EMG amplitudes. This may explain why no responses were observed in the iTA, or other paretic muscles.

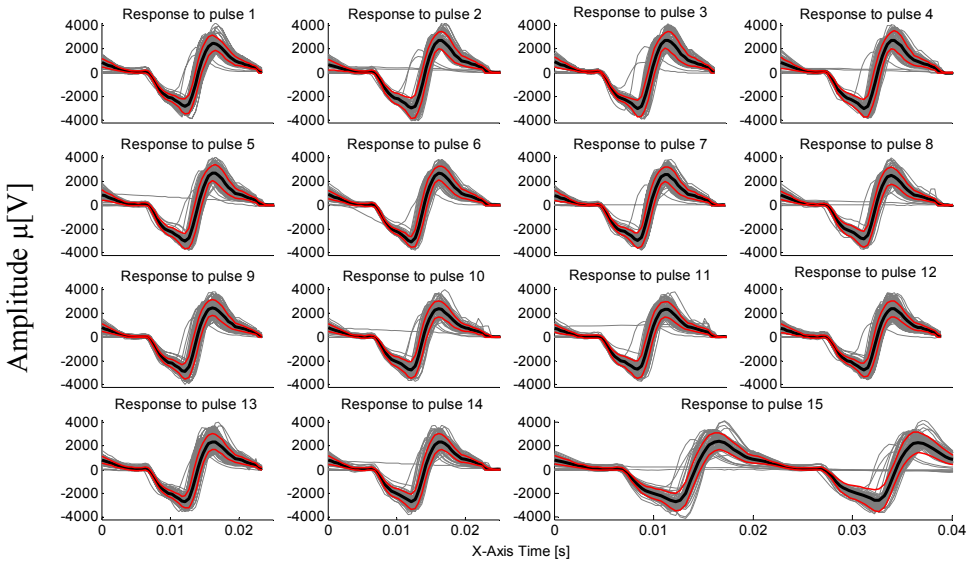

Figure 6-4: Subject 4 Inter-pulse interval response to stimulation, of the iGM. Each individual line represents the response during a given IPI, measured during each step. The thick black line represents the mean IPI response over all steps for a given IPI.

The inter pulse interval (IPI) responses of the iGM are shown in Figure 6-4. It can be seen that these responses are synchronous, with the timing of the peaks indicating that these are motor responses. However, 30-40ms after the last stimulation pulse, this subject exhibited an extra response. This suggests that the response is reflexive, the timing indicates that it is monosynaptic, therefore possibly the Hoffman Reflex (H-reflex). It is also possible that the responses seen in the pulses 2-14 also contain reflex components. This second wave after the last stimulation pulse is observed in Subjects 1, 4 and 5. Subject 4 displays the largest amplitude response. The IPI plots clearly demonstrate that responses to stimulation are present during the stimulated gait in these stroke subjects.

6.3.4 Activation Timing Changes

During the analysis of the change in burst patterns of the stroke patients, Subject 5 displayed characteristics of clonus in the iGM in the stimulation trial.

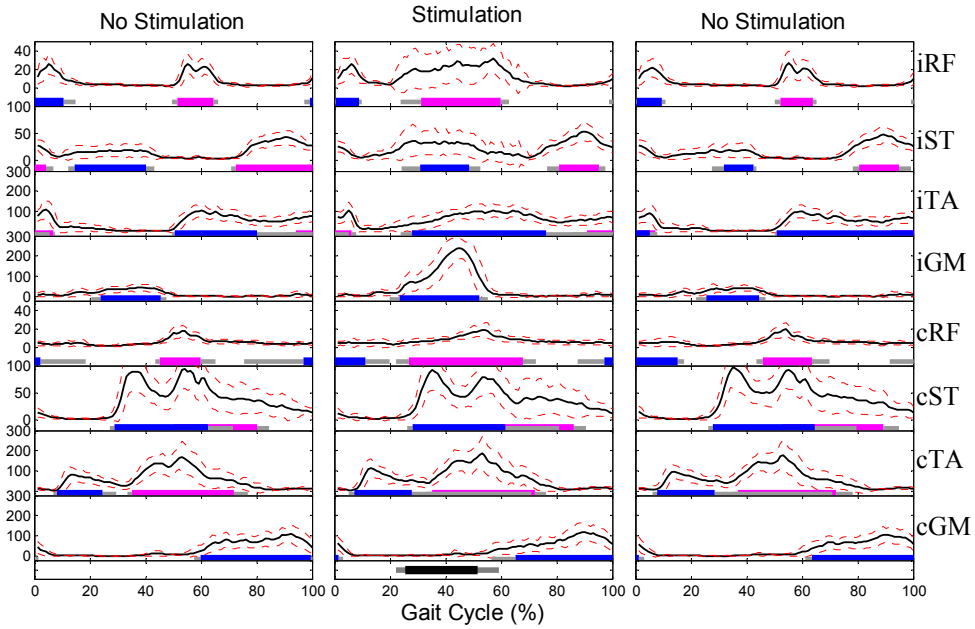

Figure 6-5: Muscle activation patterns for Subject 1, measured during gait. Each column represents a stimulation condition, from left to right, Pre-Stimulation, Stimulation, Post-Stimulation. Each row represents a muscle, from top to bottom: iRF, iST, iTA, iGM, cRF, cST, cTA, cGM. Solid bars represent muscle activity. Grey bars represent the 25 and 75 percentiles of the timing. The solid black bar on the bottom row, indicates when stimulation occurred in the gait cycle. The gait cycle represents that of the paretic side.

Figure 6-5 shows a typical output of the AGLR programme, showing a series of SRE traces, as well as the on and offset timing of muscle activation. Under each plot is a solid bar, this represents the median duration of the physiological burst, the thinner bars protruding represent the 25 and 75 percentile of the burst timing. The plots on the left hand column shows the mean SREs of each muscle, prior to any intervention. The middle column shows the mean SREs of the muscles during stimulated gait trials. The solid black bar in the bottom row of the middle column indicates when median stimulation time, the grey protruding bars represent the 25 and 75 percentiles of stimulation timing. The right hand column contains the SREs of the same muscles without stimulation, during the post-stimulation trials, subsequent to the stimulation trials. Figure 6-5 shows that prior to stimulation, the

iGM activity is very low and due to stimulation, the activity increases dramatically. It is also clear from Figure 6-5 that both the onset and offset time of the iGM have been altered due to stimulation. In the middle column, the iGM onsets earlier and offsets later than the non-stimulation trials. However, in this subject's data, the iTA is also onset earlier, due to stimulation. On and offset times will be discussed in more detail below.

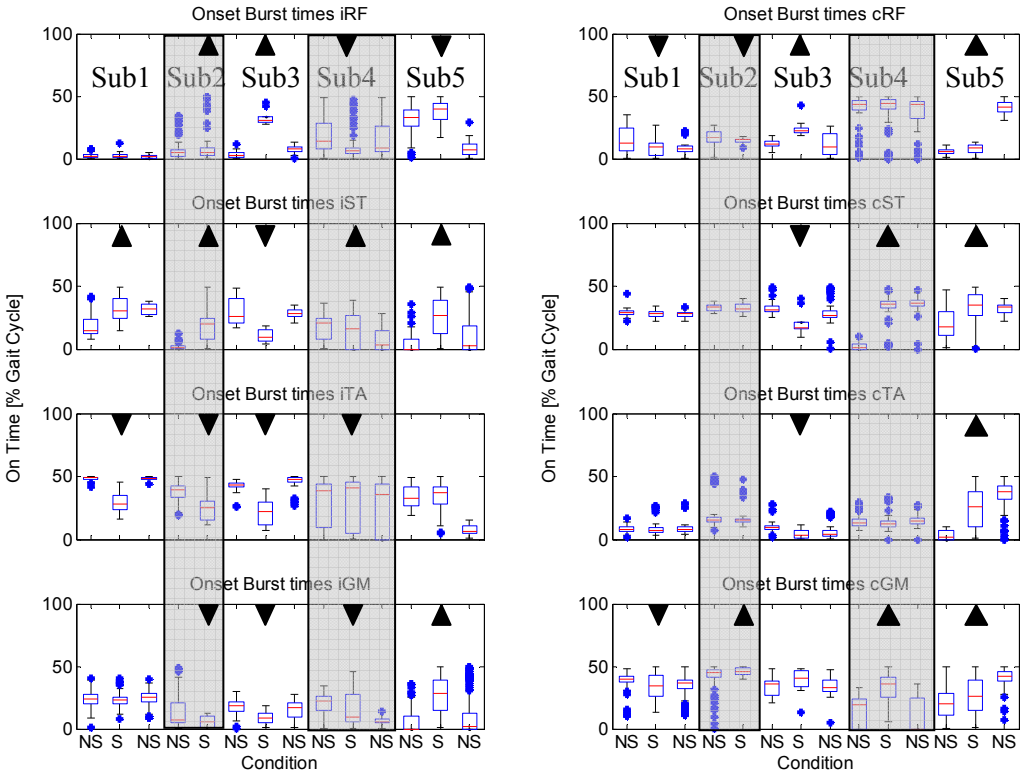

Figure 6-6: Boxplots of the median onset times of all muscles measured, with and without stimulation, during gait for all subjects. S = Stimulation NS = No Stimulation. ▼ Statistically Significantly earlier ▲ Statistically Significantly Later.

Figure 6-6 shows the onset times of each muscle, for each subject. The boxplots of the left-hand-side show the timing of the muscles ipsilateral to stimulation, which are the muscles on the paretic side. The boxplots on the right-hand-side, show the muscles contralateral to stimulation, the non-paretic muscles. For each set of muscles, the alternating columns represent each subject (1-5), from left to right per stimulation condition, NS = no stimulation and S = stimulation trials. (Note that

for Subject 2, there was no second NS result.). The solid triangles represent a statistically significant change between the first non stimulation trial and the stimulation trial. ▲ indicates an increase, therefore significantly later onset time, and ▼ indicates an earlier onset time. Earlier onset due to stimulation occurs in the iTA of four subjects (Subjects 1-4, $p = 0$) and iGM of three subjects (Subjects 2-4, $p \leq 0.0001$). The iST (Subjects 1,2,5, $p = 0$) and cGM (Subjects 2,4,5, $p \leq 0.007$) onset later in the gait cycle as a result of stimulation.

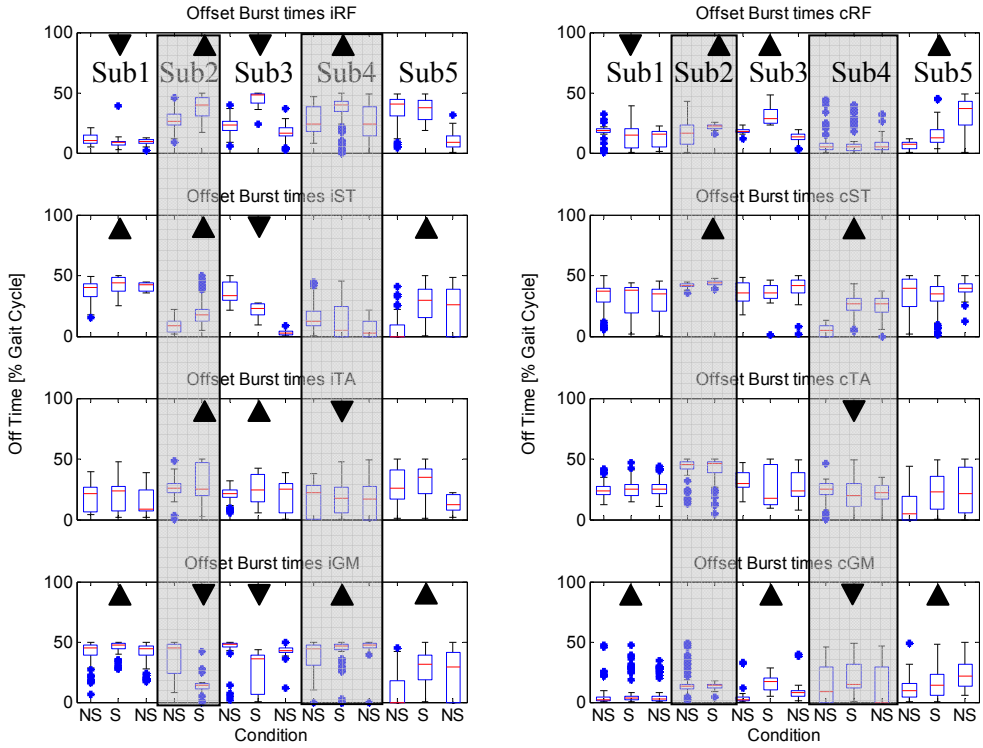

Figure 6-7: Boxplots of the median offset times of all muscles measured, with and without stimulation, during gait for all subjects. ▼ Statistically Significantly earlier ▲ Statistically Significantly Later

Figure 6-7 represents the effect of stimulation on the offset times of muscles during gait. The layout is the same as Figure 6-6. From Figure 6-7, the main significant difference found in offset timing includes the later offset of the iGM muscle in three of the five subjects (Subjects 1, 4 and 5, $p \leq 0.023$). This effect is also seen

in healthy subject results [24]. However, it was also earlier in the remaining subjects (Subject 2 and 3, $p = 0$). The iST (Subjects 1, 3 and 5, $p = 0$), cGM (Subjects 1, 3 and 5, $p \leq 0.044$) and cRF (Subjects 2, 3, 5, $p \leq 0.002$) also offset later due to stimulation.

6.3.5 Activation Amplitude Changes

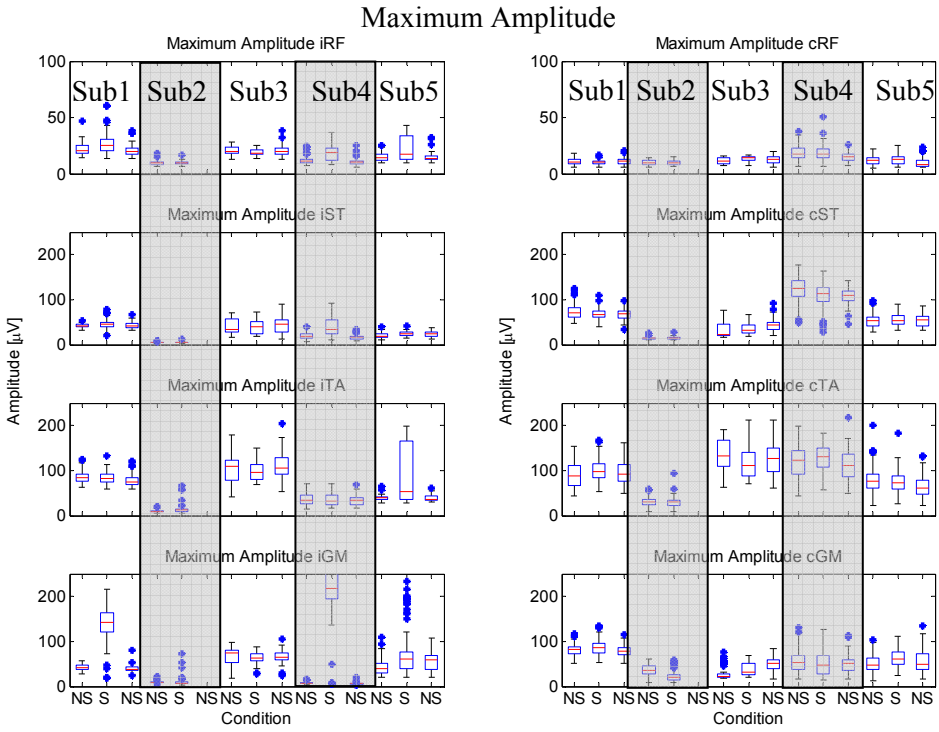

Figure 6-8: Amplitudes of muscle activation, per subject, during gait, with and without stimulation.

Figure 6-8 shows the change in amplitude due to the stimulation condition, with or without stimulation, for each subject, for a given muscle. As with Figure 6-6 and Figure 6-7, the graphs on the left-hand-side represent amplitudes of the muscles ipsilateral to stimulation. The right-hand-side, represents the muscles contralateral to stimulation. The clearest changes in amplitude due to stimulation are seen, as expected, in the iGM. The bottom left plot of Figure 6-8 shows this. Statistically significant changes were seen in Subjects 1, 4 and 5 for the iGM during the

stimulation trials. Subject 2 amplitude increased, but not statistically significantly. The amplitude of the iGM of Subject 3 decreased, although not statistically significantly. This result is contra to the expected result.

The iST also increased its activation level considerably, which can be seen in Figure 6-8, for Subjects 1, 2, 4 and 5. Overall less effects are seen on the contralateral side, except for the cGM, which has increased the amplitude of activation in Subjects 1, 3 and 5, and decreased its activation in Subject 2.

6.3.6 Kinematic Changes

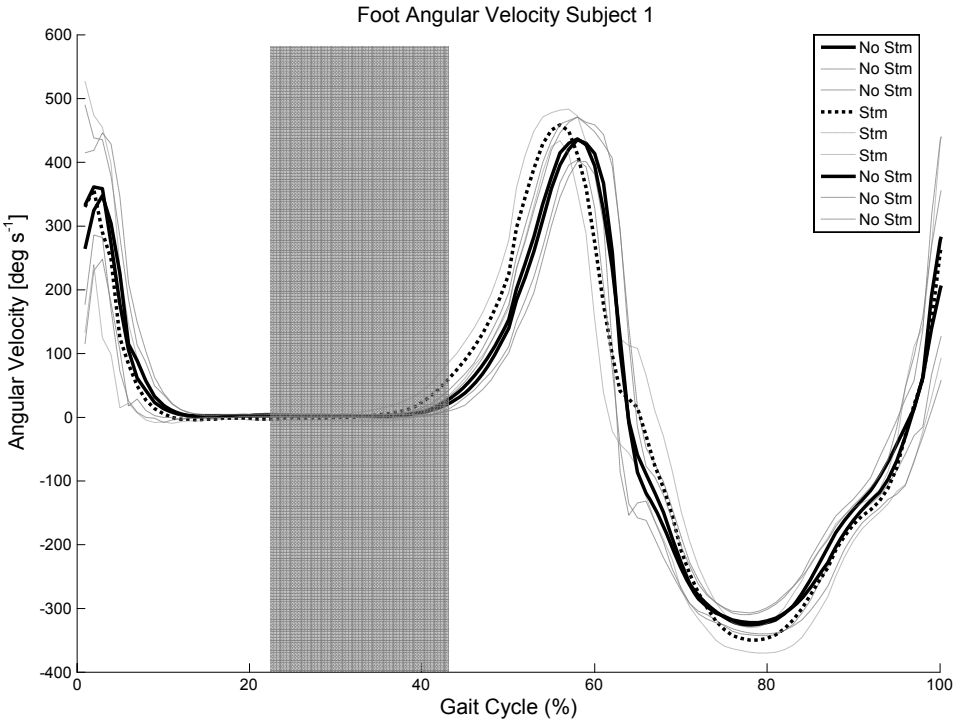

Figure 6-9: Typical angular velocity [deg s^{-1}] trace of the foot, with and without stimulation during gait, for Subject 1. The faint grey area represents the presences of stimulation.

Figure 6-9 shows a typical trace of foot angular velocity ($\dot{\varphi}$ foot) during gait. The maximum angular velocity, at the push-off phase increased, and this maximum

occurred earlier in the gait cycle at push-off, as a result of the stimulation. The result was determined to be significant, as shown in Table 6-2.

Table 6-2: Summary of results of foot angular velocity at push-off ($\dot{\varphi}_{foot\_PO}$) and the time of this maximum ($T\dot{\varphi}_{foot\_PO}$), with reference to the peak IPI values.

	$\dot{\varphi}_{foot\_PO}$			$T\dot{\varphi}_{foot\_PO}$		
	NS1	**S**	**NS2**	**NS1**	**S**	**NS2**
1	435 *	458*+	447 +	60 *$	57 *+	59 +$
2	201 *	286*	0	65	65	
3	378 *	355*	361	60 $	61 +	59 +$
4	229 *	286*	229	61 *	59 *+	60+
5	74 *	126*	86	62 $	59	60 $

In Table 6-2, the * indicates a statistically significant difference between NS1 and S. The + sign indicates a statistically significant difference between NS2 and S, and the $, a statistically significant difference between NS1 and NS2. It can be seen, from Table 6-2 that all subjects, except for Subject 3, show a statistically significant increase in the angular velocity of the foot at push-off. This increase was by at least 23 deg s^{-1} (Subject 1). The maximal increase of 85 deg s^{-1} was seen in Subject 2. This peak occurred slightly (and significantly) earlier in the gait cycle for Subjects 1 and 4.

The changes of the angular velocities of the other segments measured were not statistically significant. This was also the case with healthy subjects. However, it was expected that the increase in foot angular velocity would have an effect on the angular velocity of the lower leg.

6.4 Discussion

Results Summary

During stance, the stimulation changed F_z, CoP and torque. During gait, the large responses measured in the IPI of the stimulation bursts show that stimulation was

large enough to generate a motor response. Additionally, a reflexive response succeeded the last pulse of the stimulation burst. These physiological interactions also influenced the timing of physiological bursts of the iGM as well as other leg muscles. The kinematics, the foot angular velocity, was also significantly altered.

Stance / Force Plate Results

The stance trial results show that the change in torque reached up to 42Nm. Considering that an average foot is 10-15 cm and average body weight is 70-100kg, a maximum torque between approximately 70 and 150Nm can be expected during gait. Therefore, the torque measured during stance is approximately half of the minimum expected torque experienced during healthy gait. Direct reactions to stimulation are expected to occur between 0 and 300ms, this is shown in Figure 6-3. After the direct effect of stimulation, body weight is likely to shift to the opposite foot and corrective actions take place to correct posture. These results are provided to support the claim that the stimulation was applied at an adequate level to induce a forceful push-off for the subjects during gait. This is particularly true for Subjects 1, 3 and 4, however, Subject 2 and 5 showed less impressive changes during stance. The reasons will be discussed below.

Muscle Activation Patterns During the IPIs

During gait, the IPI signals during and immediately after the stimulation burst revealed synchronised responses in the iGM. The timing of these signals indicate that these were either direct motor responses and/or reflex responses. The timing of the burst succeeding each stimulation burst indicates that these are monosynaptic H-reflexes. As with healthy subject results, it is possible that the signals in the IPIs after the second pulse may actually be reflex responses from the stimulation pulse prior to the pulse where the IPI was measured. That is, the signal measured in the second IPI may fully or in part, be a monosynaptic reflex in response to the first stimulation pulse, and so on. While this is a possibility, it is not likely in this case, as the signal measured in the first IPI is also synchronous and of comparable amplitude to those of the other responses. These IPI results prove that stimulation resulted in muscle activation during gait. Furthermore, they imply that the stimulation level remained at a high and functional level during this time. All

subjects, except Subject 2, showed clear synchronous activity, and only Subjects 2 and 3 did not show an H-reflex after the stimulation burst. The synchronous activity levels of healthy subjects was in the range of 600 to 4000μV [24]. This shows that the physiological response in these stroke subjects is comparable to those of healthy subjects.

Burst Amplitude

The large amplitude IPI responses greatly affect the amplitude of the burst of the iGM (see Figure 6-8). Even though it is likely that burst amplitude is actually a measure of synchronous activity within the stimulation bursts, this may be considered increased activity. We hypothesised that FES can replace the lack of physiological activity, to create adequate calf muscle contraction and push-off. Increased activation was measured in the iGM, iST and the cGM. The magnitudes of the EMG bursts of other leg muscles did not change due to stimulation. The iGM amplitude increase implies that the stimulation fulfilled the goal of increasing the activation levels of the iGM. However, synchronous activity, generated by electrical stimulation, is less effective in creating output force than natural, asynchronous activity. Therefore, although we stimulated at a high level, this stimulation may not have created a force large enough to induce push-off, as is generated by, for example healthy subjects.

Burst Timing

During gait, the stimulation of the tibial nerve has some influence on muscle activation timing. The onset of the iGM is significantly delayed in three subjects. The offset of the same muscle, is significantly delayed in three subjects; although, in two subjects the offset is significantly earlier. The iTA onset earlier in four subjects, while the iST and the cGM onset later due to stimulation. The iST, cGM and cRF offset later due to stimulation. Overall, muscles did not tend to deactivate earlier in response to stimulation; this happened sparingly across the group for a few muscles.

Kinematics

Significant changes of angular velocity of the foot were observed during push-off, in the range of 23 to 85 deg s^{-1}. This range appears to be not only statistically significant, but also functionally beneficial. Of note, the largest change in angular velocity occurred in Subject 2, who had the phenol injection. This subject did not show large changes in the stance measurements, nor did this subjects have synchronous activity in the IPI signals. Therefore was not expected to show patent changes in other aspects measured.

Explanations

Subject 2 had a pseudo clonus at the ankle. Additionally, at the time of the experiment, this subject had a Phenol injection to relax the calf muscles. This injection would prevent the FES from generating adequate contraction of the triceps surae muscles, even though for this subject we stimulated directly over the muscle bulk. Notably, this subject generated the lowest torque during stance stimulation. Even though Subject 2 had the Phenol injection, this would not have prevented effects of cutaneous stimulation. Additionally, while afferent stimulation may generate reflexes, these signals cannot reach the muscle due to the blockage caused by the Phenol injection. This Phenol injection would not prevent the manifestation of reflex responses, nor detection of these signals in other muscles. Therefore, changes could still be expected in the activation patterns of other muscles. Subject 5 had a clonus at the ankle and increased spasticity of the hamstrings, which was measured during intake. These intake results may account for the lack of responses seen in both subjects, particularly the force plate measurements.

The testing of subjects in this group is comparable to previous tests carried out on healthy subjects [24]. Strikingly, the results are also comparable, which was not expected as the groups are not age matched controls. With healthy subject experiments, three stimulation angles were used, relating to too early, too late and an optimal stimulation time, to provoke push-off. As with the healthy subjects [24] high amplitude IPI signals and iGM amplitude, as well as kinematic changes were observed with these stroke subjects at this optimal stimulation time. In the healthy subject tests, when stimulation was applied too early, the stimulation caused the

heel to rise prematurely, when the entire body weight was on the foot. This shows that the stimulation parameters caused forceful movements, noticeably altering the gait pattern. With the same stimulation parameters, applied later in the gait cycle (as described), the effect was less visible. Under loaded conditions, small but significant increase in angular velocity, may correspond to a relatively large increase in ankle plantar flexion torque. As torque was not measured during gait, this cannot be verified. However, this concept provides scope for further research.

Three of the five stroke subjects exhibited delayed offset time of the iGM, this trend was also observed in healthy subjects [24]. However, other subjects also show earlier onset of iGM, due to stimulation. The reason for this is likely to be the very low amplitude iGM signal without stimulation, therefore stimulation is detected as earlier onset and later offset due to the presence of an actual burst, thus this can be considered a functional improvement.

We hypothesised that FES would provide functional support, compensating for the lack of push-off on the paretic side. Furthermore, past research has shown that as well as the paretic side, timing of physiological bursts of the non-paretic side of stroke subjects changes over time [10,11]. For this reason, we expected that the FES would influence the activation patterns of the non-paretic side, reducing the need to compensate for the diminished activity on the paretic side. A select number of muscles, did exhibit alteration of activation patterns. In four subjects, the stimulation induced later onset of the iST. The semitendinosus muscle is a hip extensor as well as a knee flexor during swing. The gastrocnemii flex the knee, in preparation for swing. It is therefore possible that the iST activation pattern adapted in response to changed iGM activation. However, if this was the case, it would be attributed to earlier onset of the iGM, providing the knee flexion needed, in preparation for swing. But, of the four subjects showing delayed iST onset, only two also had earlier onset of the iGM. We cannot rule out other factors, which were not measured, causing the delay in the iST. Therefore, further research is needed to test this effect and whether or not it is functionally beneficial in the greater stroke population.

The iTA onset was earlier in four subjects. Two of these subjects (Subjects 2 and 3) had earlier offset of the iGM, this may mean that push-off raised the foot earlier; therefore the need for the iTA action was required earlier. However, for the

remaining subjects (Subjects 1 and 4), the iGM was delayed, even though the iTA onset earlier. This does not appear to be functional and may even mean that co-contraction occurred.

Buurke et al. [10] observed that in stroke subjects the cGM onsets earlier in the gait cycle than in healthy subjects. Early cGM onset also manifested in this subject group. Interestingly the stimulation delayed cGM onset in three subjects, providing signs of a more a normal activation pattern.

Although many significant changes have been presented, in the muscle activation patterns' on and offset timing, there has not been a clear trend over all of the subjects, nor is there always a clear system of change within the subjects to indicate that stimulation was either functionally beneficial or detrimental for the subjects. With healthy subjects, there was a lack of significant changes, during "optimal" stimulation. The possible reason is antidromic activation [24] blocking physiological iGM activity. The FES replacing the physiological activity would ensure that no net change in activity occurred. However, as mentioned, the stroke subjects chosen for this research were selected due to decreased activity of the calf muscles. Therefore, it is expected that the net activity of the iGM would increase, causing a uniform effect to all subjects. The amplitude did increase in three subjects, as Figure 6-8 shows. However no uniform effects could be interpreted in terms of temporal activation patterns. This may be due to a number of reasons.

Subjects used for this research were at least 6 months post-stroke, to ensure that recovery was complete and that any changes observed could only be attributed to stimulation, and not to the natural recovery process. Six months post stroke, with a need for improved gait implied that these subjects are less mobile [34] than younger healthy subjects or an age matched control group. Inactivity can lead to muscle atrophy. Atrophied muscles are difficult to artificially contract using stimulation; higher amplitudes are needed, and the resulting force may not be adequate. Additionally, the non-stimulated, atrophied muscles will compensate for changes less readily than healthy muscles.

Timing of stimulation to improve push-off is critical. The healthy subject results show that early stimulation caused heel rise during stance; however at an undesired time of the gait cycle [24]. It is possible that between this early stimulation time and what we considered optimal timing for push-off, there lies a more optimal time to

generate adequate push-off for these subjects. For improved control, further research is needed.

Other factors must also be considered, for example the use of walking aids may prevent or mask potential changes. AFOs were removed during the gait trials to prevent any masking of the effect of stimulation. However, it is possible that the muscles relying on this support could not compensate for the lack of AFO support, and additionally compensate for the presence of the stimulation, in the relatively short time of the experiment. Three of the subjects (Subjects 2, 3 and 5) used a walking stick during the experiment. While some studies report that walking sticks do not alter the activation timing [35], others report otherwise [10]. Therefore, if subjects already have a tendency to bear weight on their walking aids, the aid would continue to take this weight should subjects need to suddenly lean on it, for support during the increased force generated at push-off. If this did occur, it may have masked any significant changes to the kinematic results. This concept ties with our results, as stimulation clearly interacted with physiological activation, as shown in the IPI motor and reflexive responses; while overall, the burst timing and limb angular velocities were not consistently impacted upon.

Contra to the citations mentioned here, other researchers [36] have found that normalisation of muscle activation timing is not a requirement for functional gait improvement, as gait speed may influence the improvements observed. Furthermore, they state that the aim of normalising the temporal coordination of muscle activity may not necessarily be a clinical goal when improving stroke gait. This is strengthened by the work of Buurke et al. [10] who observed the recovering activation patterns of stroke subjects, and found that although gait clearly improved, muscle coordination did not necessarily change. We had assumed that a change in temporal pattern would indicate some form of adaptation to the stimulation.

As the FES of SCI plantar flexion was functionally successful [14,22,15], and because of the success of the drop-foot stimulator on stroke gait, our hypothesis was that stroke subjects would show improvement in push-off due to FES of the tibial nerve. The group of stroke subjects selected for this research has diminished physiological calf muscle activation. However, pain sensation, as measured during the intake tests, possibly limited the amplitude of the stimulation. Pain, due to high

amplitude levels would not manifest in the SCI subjects as they often exhibit complete lack of sensation below the lesion. Therefore Bajd et al. may have used much higher stimulation levels, creating stronger calf muscle contractions and providing very noticeable differences to the gait pattern.

Problems in drop foot stimulation have been overcome through the use of the implantable device. An implantable push-off stimulator would be useful, in order to improve the specificity of the stimulation location, maintenance of this stimulation location, over the entire gait cycle and reduction of stimulation amplitude needed to obtain a desirable contraction level. The stimulation location chosen for this research was selected due to the ability to obtain a good contraction, while minimising the stimulation level. However, at the popliteal fossa, there are tendons and skin which, if stimulated may feel painful. Additionally, as described in the methodology, in order to minimise electrode movement, the electrode was fixed firmly in place, this could not prevent movement such as the unavoidable increased distance from the stimulation electrode to the tibial nerve, which is inevitable during knee flexion, at terminal stance. Implantable electrodes would solve each of these problems. However, it is first necessary to prove this concept externally, or possibly through use of needle electrodes.

Based on the results, future work is needed to further investigate the possibility of improving push-off function of stroke subjects. In the small patient population selected for this research, some subjects did show signs of possible benefits. However, more subjects should be tested. A more stringent selection criteria should be created, to ensure that stimulation will lead to improvement. The criteria of diminished calf muscle activity will help prevent the onset of spasticity due to stimulation.

In their studies, Bajd et al. [14] found improved activation in the SCI subjects after a period of training. Therefore, future work involving FES of the plantar flexors of stroke subjects to improve push-off should involve similar muscle strengthening and FES-assisted gait training.

6.5 References

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Chapter 7

Final Discussion and Recommendations for Future Work

7.1 General Discussion

This research was carried out to understand the interactions between FES and the activation patterns of stimulated and non-stimulated muscles during gait. The triceps surae (TS) were chosen because these are the primary muscles needed for forward and upward propulsion [1,2,3] during push-off, which can be lost due to a CVA. Electrical stimulation of the TS muscles should restore the lost function of push-off.

Overall, the presented results show that it is possible to activate the calf muscles of healthy and CVA subjects using FES. Furthermore, interaction occurs between the stimulation and physiological activation. This interaction was shown in Chapters 4-6, in the IPIs of the iGM of both healthy and CVA subjects, as well as the iTA and mildly in the iST of the healthy subjects, revealing motor and/or reflexive responses. Additionally, changes of the on and offset times of the stimulated muscle, as well as other muscles of both limbs were observed in both the CVA and healthy subjects. This shows that the stimulation of the tibial nerve influenced the normal activation patterns of these muscles. Furthermore, the stimulation was strong enough to raise the foot of healthy subjects during mid-stance, in response to early stimulation (Se) (Chapter 5).

However, notably throughout the thesis, the results were considerably variable and inconclusive regarding the clinical and functional relevance to CVA subjects. Variability of results from CVA subjects may be expected [4], however more consistent findings were expected in the healthy population – particularly in the well-defined isometric tests. There are a few explanations for this variability, which relate to recruitment properties of the gastrocnemii, electrode-nerve distance influencing the recruitment properties as well as the stimulation levels possible, which was considerably lower during gait than during isometric measurements.

7.1.1 Recruitment and Plantar Flexion Torque

The results from Chapter 2 show that even in a healthy subject population and in a very well-defined experimental setup, maximum torque and the shapes of the inter and intra-subject recruitment curves are variable. Variability was also found by another research group, when isometrically testing the plantar flexor group, in

response to FES [5]. The variability of plantar flexion torque production [6] found in the isometric recruitment curves may be explained by the mixture of fast and slow muscle fibres [6,7] found in the gastrocnemius. Even when the muscle fibres of a given muscle are the same type, their optimal length for force production can be different. Therefore, as the gastrocnemius contains both muscle fibre types, their optimal length and threshold for activation can vary considerably even in the same subject. Additionally, variability of recruitment of nerve fibres that activate these different muscle fibres may contribute to torque production variability.

Large-force producing and fast-fatiguing muscle fibres, activated by large diameter nerve fibres, and slow-fatiguing, low-force muscle fibres, activated by small nerve fibres are recruited according to the size principal [8,9,10]. The size principle states that muscle fibres are recruited incrementally, according to their size and amount of force they can produce, beginning with small nerve fibres, activating small motor units. However, when activated using artificial electrical stimulation, the recruitment order was found to be reversed compared to size principle [8,9,10]. Recruitment variability may also explain the variability of changes to the physiological activation patterns, measured in both subject groups during the gait trials (Chapters 4, 5 and 6).

The isometric results of Chapter 2 show that even at stimulation levels reaching up to 120mA and generating torques up to 80Nm, saturation was generally not attained. This has implications for the stimulated gait trials, when considerably lower stimulation levels were applied. These implications include a decreased chance of reaching saturation due to lower stimulation levels and knee flexion increasing the nerve to electrode distance, reducing the chance of full recruitment of the nerve.

7.1.2 Limitations to Stimulation Level

During gait, healthy and CVA subjects had similar tolerance levels for stimulation, ranging between 27 and 55mA in healthy subjects, and between 32 and 44mA in CVA subjects, compared to a tolerance of up to 120mA during isometric testing. Threshold stimulation levels during isometric stimulation ranged between 26 and 46mA, producing torques less than 20Nm and often negligible. While comparable to threshold stimulation levels during isometric tests torques up to 57Nm in CVA

subjects were generated while standing on force plates (see Table 2-2 and Table 6-1 for comparison).

As maximum stimulation levels were limited by subject tolerance to the stimulation, the difference in posture, seated versus stance, is likely to be the cause of this difference in tolerance. It is possible that subjects did not accept higher stimulation levels during gait knowing that the stimulation would be delivered at every step taken throughout the experiment. Faist et al. [11] reported that load on the limb can cause different reactions because of the activation of various receptors. They found differences in the inhibition and facilitation of Ib reflexes during gait, fictive gait, loaded and unloaded conditions. Therefore, it may be possible that these factors also influence stimulation sensation felt by the subjects.

7.1.3 Variability of Interaction with Physiological Activation

During gait and stance trials, the stimulation contracts the plantar flexors and causes knee flexion. This desired result would dynamically increase the distance between the stimulation electrode and the nerve, decreasing the current density reaching the nerve [10] while also possibly changing the orientation of the current field. While all precautions were taken to minimise electrode movement, and the electrode was pressed tightly against the skin, a change in distance between electrode and nerve cannot be completely prevented, therefore its effect cannot be ignored. The variability of chance and order of recruitment [10] may subsequently induce variability of the physiological responses. A more stable recruitment may provide a more predictable physiological response.

The dynamic nature of gait adds the factor of background physiological activation, which influences the effect of FES. Any physiological activity of the stimulated muscle during isometric and stance testing would be comparably less than during gait. The results of Chapters 5 and 6 reveal that although the same stimulation level was used throughout the stimulation gait trials, early stimulation (Se), generated larger amplitude M-waves than mid-stimulation (Sm) or late stimulation (Sl). Furthermore, the stimulation level was large enough to force the heel to rise during Se when the body weight was on the stimulated foot, but such a clear difference was not observed with the other stimulation conditions. A possible explanation is that at initial stance, when Se is applied, the physiological activation

of the iGM is still relatively low. However, physiological activation of the iGM increases during stance, Sm and Sl correspond to this time of increased physiological activation. At this time, antidromic firing, which blocks physiological activation, may have occurred, preventing a net increase of activation level. During stimulation of the cutaneous tibial nerve, at the foot, Duysens et al. [12] also found facilitation of extension responses in the early phase of stance, which decreased during late stance and swing. They also attributed this to suppression of activity [12] of the triceps surae.

Reduced physiological activation of muscles of CVA subjects would mean that less physiological activation is present to be blocked by the stimulation. Therefore, the FES should increase the net activation of the stimulated iGM. For this reason, we had expected greater changes than those observed in Chapter 6. M-waves were generated in this CVA subject group, proving that FES activated the muscles. However, in general the results from this set of experiments were considerably variable and inconclusive. This may be due to muscle atrophy, in particular of the weakened paretic side due to relative inactivity [13] of stroke subjects.

Due to the timing of the stimulation pulses, the signals measured during the IPIs of the stimulation burst may have been either motor or reflexive responses. Many studies have involved generation of the motor response and H-reflex in the calf muscles, mainly in the soleus. Zehr [9] found that in older subjects, the H-reflex was lower in amplitude. Furthermore Zehr [9] and Duysens [14] found that in all subjects the H-reflex was lower in amplitude during gait compared to lying prone. Tucker et al. [15] found variability in the maximum M-wave of the gastrocnemius, depending on the orientation of the foot and background activation. They also found that bipolar electrode setups, as was used in our study, influences M-wave magnitudes because of signal cancellation [15,16] and muscles contracting under the skin, which may change the inter-electrode distance during a contraction.

The work presented here focussed on the hypothesis that alteration of the temporal physiological activation patterns is a reflection of a change to the gait pattern. However, other studies have shown that although the gait pattern, particularly of CVA subjects improves over the recovery period, the temporal activation and coordination patterns do not [17,18].

7.2 Recommendations for Future Work

A number of factors should be taken into account when continuing research to restore the push-off of CVA subjects. A much larger subject group is needed, patient criteria must be more strictly defined and adhered to, and stimulation methods could be improved to reduced the sensation of pain and ensure full and stable recruitment. Furthermore, to benefit the subjects undergoing the FES gait, they should undergo a training program to facilitate gait while using FES.

7.2.1 Patient Population

The lack of subjects included in these tests have probably contributed to the variation of results found. Furthermore, the experiments were tiresome for the subjects and as described, they did not like the sensation of stimulation, which restricted the permitted stimulation levels. Four CVA subjects left after the preliminary set of experiments, which have not been reported in this thesis.

7.2.2 Patient Inclusion Criteria

Early intervention and improved patient selection are advantageous for the post-stroke individuals [19]. It was mentioned in Chapter 6 that two participating subjects should probably have been rejected at the intake stage. These subjects were on the boundaries of inclusion and were included mainly due to the lack of patients available. However, they could walk independently and did show a lack of push-off, which in the defined inclusion criteria meant that they could be included, as restored push-off would benefit their gait pattern. Therefore, the inclusion criteria should have been better defined to realise a more homogenous and optimal subject population.

In the intake tests executed for these trials, the range of motion, spasticity, sensation and ability to contract the gastrocnemius using FES were tested. More quantitative selection is needed for future trials. Intake tests should involve EMG measurements and isometric stimulation as described in Chapter 2, followed by stance trials as described in Chapter 6. Patients should be included when they satisfy all of the following conditions:

1. activation of the gastrocnemius is significantly reduced (measure using EMG);

2. the spasticity of the gastrocnemii and soleus are less than 2 on the Modified Ashworth scale;
3. isometric stimulation can generate torques greater than a defined level;
4. FES can generate equivalently large ankle torques when standing on a force plate.

It is not feasible to expect patient classification according to the recommendations of Knutsson and Richards [20,21] in daily clinical practice. Therefore, researchers should quantitatively assess the abilities of participating subjects before including them in FES studies. Furthermore, classifications such as those developed by Knutsson and Richards [20,21] should be further developed and used as standards for future investigations.

7.2.3 Improve Recruitment and Reduce Painful Stimulation

Other issues mentioned throughout this thesis involve the change of distance between the electrode and nerve due to knee movement, during gait. Faist et al. [11] also reported difficulties of ensuring stability of recruitment when stimulating during gait.

Another problem was the pain threshold of subjects, which prevented elevated stimulation levels. As described, the technology for preventing drop-foot in CVA subjects is quite advanced; with an implantable two-channel drop-foot stimulator now available [22,23].

Implantation of the electrodes needed to stimulate the tibial nerve for push-off would eradicate the problem of movement between the electrode and the nerve during gait. Additionally, pain receptors in the skin would be completely by-passed, removing the problem of painful cutaneous stimulation. Furthermore, with implantable systems, stimulation levels can be significantly reduced, as the nerve and electrode are in direct contact.

7.2.4 Stimulation Method

Preliminary tests should be conducted using percutaneous stimulation electrodes to target the nerve directly and if benefits are apparent, a complete implant can be considered. An implantable stimulator to restore push-off would not solve the drop foot problem. Therefore, the addition of a third channel, to the current two-channel

implantable stimulator (Figure 7-1a) would create a three-channel lower leg stimulator to restore push-off and reduce drop-foot [24] see Figure 7-1b for a sketch of this concept.

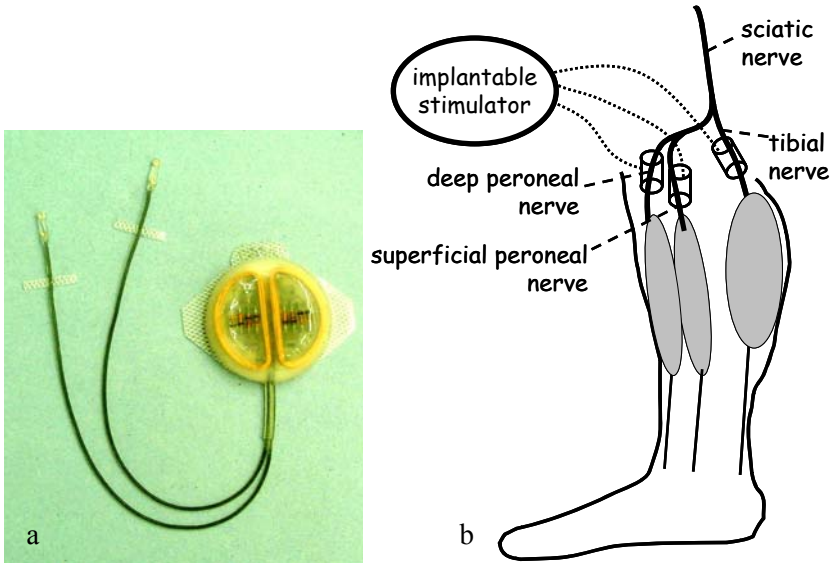

Figure 7-1a: Current two-channel implantable stimulator and Figure 7-1b: Concept of three-channel implantable stimulator to restore push-off and reduce drop-foot [24].

7.2.5 Training

Finally, and importantly, to improve the push-off of the CVA subjects, a training regime should be implemented. Alone, FES may hinder gait re-learning that the subjects undergo following a CVA. Therefore, use of FES should be part of a gait re-learning program. To improve push-off, subjects should be provided with a stimulator for home use, to increase the muscle strength. Additionally, subjects should undergo regular training at the rehabilitation facility, to improve FES-facilitated gait.

Activation patterns and gait abilities should be monitored before and after the FES training to determine how push-off improves over time, in a longitudinal study. While costing more time and resources, the gait-FES training method will be of greater benefit to the CVA subjects, as they will train their gait, in combination with FES, benefitting from the advantages of gait training and the extra help provided by muscle contraction provided by the FES.

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Summary

Every year stroke affects approximately 15 million people worldwide. It is the leading cause of disability in the western world. For those who survive a stroke, rehabilitation can be an arduous process. Gait relearning has high priority for stroke survivors. A number of aspects of gait are affected due to stroke. One of the most commonly treated is drop-foot, this is the inability to raise the toes during the swing phase of gait. To reduce the effects of drop-foot, an ankle foot orthosis is often prescribed. However, these mechanical supports are not often discreet, do not serve to improve muscle function and keep the ankle at 90^{o}, as opposed to enabling the toes to lift. In the 1960's Liberson first published work on the use of functional electrical stimulation (FES) on the peroneal nerve, which innervates the tibialis anterior muscle. The contraction of the tibialis anterior muscle, raises the toes and reduces drop-foot. Because the muscle becomes physically able to contract, improvements are seen in the gait of subjects, while using the stimulator. Reports also state that benefits remain visible even when the stimulator has been switched off or removed. This is known as carry-over and may be due to strengthening of the muscles, or possibly due to neuroplasticity – or both.

In the late 1970s, other researchers measured the electrical activity of leg muscles of stroke survivors, using electromyography (EMG) and found that not all subjects suffer from drop-foot. The EMG results showed that all muscles had decreased physiological activation. With reduction of activation of calf muscle activity as well as other factors such as premature activation of this muscle group, stroke subjects have the inability to push-off during gait. Instead, subjects have a tendency to hike their hips upwards, pulling the leg forward. Other researchers also found that muscle activation patterns of both the paretic and non-paretic legs show changes over the recovery period.

Our goal was to stimulate the calf muscles of stroke subjects, while measuring the activation patterns of the stimulated and non-stimulated leg muscles, with the intention of improving push-off, while gaining new insights into the effects of stimulation on the activation patterns of the muscles measured. The thesis describes the steps that we took in order to reach our goal.

Prior to experimentation on CVA subjects, tests were carried out on healthy subjects to optimise the methodology in terms of stimulation location, and control of stimulation.

Chapter 2 describes the isometric study that was carried out on healthy subjects, to determine if FES generated larger plantar flexion torques when stimulating the muscle directly or when stimulating the tibial nerve, which innervates the calf muscles. The results showed that neither method generated significantly larger torques. However, in most subjects it was possible to apply higher levels of stimulation directly to the muscle than the nerve. This is probably due to the lower current density, since larger electrodes were used for muscle stimulation. When muscle stimulation protocol was transferred to the first stroke subject, even at very high stimulation levels, no movement could be generated. When the stimulation protocol location was transferred to the tibial nerve, a forceful contraction was observed at a comparatively lower stimulation level. Based on this, for experimentation consistency, we decided to apply nerve stimulation to all subjects. Furthermore, as will be discussed below, if the stimulation proves to improve push-off it is possible to consider implanting the push-off stimulator, in which case the tibial nerve will be stimulated.

Chapter 3 presents a new method of controlling the timing of stimulation during gait, using a single gyroscope on the lower leg instead of a heel switch in the shoe. Heel switch control for stimulation of the calf muscles is unreliable in stroke subjects because they often make irregular foot floor contact involving heel strike, or mid-foot or toe strike, from step to step. The result is an irregular time interval between foot floor contact and push-off, meaning that stimulation control cannot rely on absolute time delays for this purpose. Furthermore, a phenomenon that we call “limit cycling” occurred, where subjects did not progress forwards when stimulated. Instead their weight fell back onto the heel, reactivating the heel switch and triggering stimulation again. For this reason we searched for an alternative control method and found that even during stimulation, the angular velocity of the lower leg maintained a regular pattern and a stimulation control method could be used, without relying on time delays. Chapter 3 describes the experimentation and the results of the gyroscope as a control method. Again, since the stimulator and the stimulation control signal can be placed in close proximity on the lower leg. If

the stimulation improves push-off, the stimulator and timing controller can be completely implanted, removing the need for external cables and improving the chances that FES users will accept this technology.

Chapter 4 is the first presentation of the healthy subject experiments during FES gait. The effect of FES on the EMG patterns of the medial gastrocnemius are detailed, showing that a motor response and possibly an H-reflex were induced in this muscle during gait. This shows that FES interacts with physiological activation patterns of the stimulated muscle. While clear waves were seen in the inter-pulse intervals of the stimulation burst, less clear changes were seen in the physiological on and offset timing of this muscle. The reason may be attributed to the stimulation: unlike physiological activation, which sends signals in one direction, the FES would cause efferent and afferent activation, generating antidromic stimulation, which can block physiological activation during the stimulation burst.

Chapter 5 expands on the results of Chapter 4, detailing the effect of FES on the tibialis anterior (TA), gastrocnemius medialis (GM), semitendinosus (ST) and rectus femoris (RF) muscles of both legs, with and without stimulation during gait. Kinematics of the thigh, lower leg and foot of the stimulated side and the lower leg of the non-stimulated side show that only the angular velocity of the foot was significantly changed due to FES. Activation patterns, in terms of M-waves and H-reflexes were observed in the iTA and iST and changes to the timing of a number muscles on both sides were altered due to stimulation in this healthy population.

Finally the tests were carried out on five stroke subjects (Chapter 6). FES was applied to the paretic tibial nerve of these subjects, while the activation patterns of the GM, TA, ST and RF muscles on the sides ipsilateral and contralateral to stimulation were measured, as well as the kinematics from the thigh, lower leg and foot of the ipsilateral side and lower leg of the contralateral side. Since stroke subjects have low activation of all muscles, antidromic activation was not expected to play a role in this subject group, thus the activation patterns, at least of the stimulated muscle was expected to increase greatly, resulting in improved push-off. Furthermore, since, during recovery from a stroke, activation patterns on both the paretic and non-paretic sides change, it was expected that the activation patterns of other leg muscles would also change. Some change was observed, but the results

were variable, thus it was unclear if the stimulation improved the activation patterns and could be clinically recommended as a treatment or not. This is addressed in Chapter 7, where the results of all tests are taken into account and a number of recommendations are suggested. These recommendations focussed on the problem of variability of results, which may be accounted for in the small and variable patient group tested. Future studies should involve a larger test group with more strictly defined patient criteria. Furthermore, the method of stimulation could be further improved, since issues arose due to the sensation of pain due to elevated stimulation levels. At times, these stimulation levels may not have been enough to generate forceful contractions, particularly, during gait, while the nerve may have moved away from the stimulating electrode as the knee flexed, at push-off. One solution is to use percutaneous or implantable stimulation electrodes, which would enable reduced stimulation levels, by-pass cutaneous sensation and prevent recruitment instability, since the electrode would be in direct contact with the nerve. Finally, I suggested that to benefit the subjects should undergo a training program to further facilitate gait while using FES.

Samenvatting

Elk jaar worden wereldwijd ongeveer 15 miljoen mensen getroffen door een beroerte. Het is de belangrijkste oorzaak van invaliditeit in de Westerse wereld. Voor overlevenden van een beroerte kan revalidatie een moeizaam proces zijn. Het opnieuw aanleren van het lopen is erg belangrijk voor hen. Door een beroerte worden verschillende aspecten van het lopen beïnvloed. Een van de meest behandelde is de sleepvoet, dit is het niet kunnen optillen van de tenen tijdens de zwaaifase van het lopen. Om het effect van de sleepvoet te verkleinen wordt vaak een enkel-voetorthese verstreken. Echter, deze mechanische ondersteuning is erg zichtbaar, de spierfunctie wordt niet verbeterd en in plaats van het mogelijk maken van het optillen van de tenen blijft de enkelhoek in 90°. In jaren 1960 publiseerde Liberson voor het eerst over het gebruik van functionele elektrische stimulatie (FES) van de peroneus zenuw, welke de tibialis anterior spier innerveert. Samentrekking van de tibialis anterior tilt de tenen op en verminderd de sleepvoet. Bij mensen die de stimulator gebruiken wordt de spier door de stimulatie gecontracteerd en is een verbetering in het lopen te zien. Uit literatuur blijkt dat de voordelen ook zichtbaar blijven wanneer de stimulator uitgeschakeld of verwijderd is. Dit staat bekend als “carry-over” en kan het effect zijn van versteviging van de spieren, misschien van neuroplasticiteit of van beide.

Eind jaren 1970 maten andere onderzoekers met behulp van electromyografie (EMG) de elektrische activiteit van beenspieren van overlevenden van een beroerte en vonden dat niet alle personen last hadden van een sleepvoet. Het EMG liet zien dat alle spieren verminderde fysiologische activatie hadden. Door een verminderde activatie in de kuitspier maar ook door andere factoren zoals vroegtijdige acitvatie van deze spiergroep kunnen mensen met een beroerte niet afzetten tijdens het lopen. In plaats daarvan hebben ze de neiging om hun heup op te trekken terwijl ze hun been naar voren stoten. Andere onderzoekers vonden bovendien dat de spieractivatiepatronen van de gedeeltelijk verlamde en niet verlamde benen verschillen laten zien tijdens de herstelfase.

Ons doel was om de kuitspieren te stimuleren bij overlevenden van een beroerte terwijl de activatiepatronen van zowel de gestimuleerde als de niet gestimuleerd beenspieren worden gemeten, met de bedoeling om het afzetten te verbeteren en nieuwe inzichten te verkrijgen in de effecten van stimulatie op de activatiepatronen van de gemeten spieren. Dit proefschrift beschrijft de stappen die we hebben genomen om dit doel te bereiken.

Om de methodologie in termen van stimulatielocatie en stimulatiebesturing te optimaliseren zijn er vooraf aan de experimenten met mensen met een beroerte testen gedaan met gezonde proefpersonen. Hoofdstuk 2 beschrijft het isometrische onderzoek, uitgevoerd met gezonde proefpersonen, om te bepalen of FES grotere plantaire flexie moment genereerd wanneer de spieren direct worden gestimuleerd of de zenuw die de kuitspieren activeerd, de tibiale zenuw. De resultaten laten zien dat geen van beide methoden een significant groter moment genereerde. Echter, in de meeste proefpersonen was het mogelijk om de spier met hogere stimulatieniveaus te stimuleren dan de zenuw. Omdat grotere elektroden zijn gebruikt voor spierstimulatie is dit waarschijnlijk toe te schrijven aan een lagere stroomdichtheid. Wanneer spierstimulatie werd gedaan met de eerste proefpersoon met een beroerte kon zelfs op het hoogste stimulatieniveau geen beweging worden gegenereerd. Wanneer vervolgens de stimulatie werd verplaatst naar de tibiale zenuw werd bij een relatief laag stimulatieniveau een sterke samentrekking geobserveerd. Voor experimentconsistentie hebben we gebaseerd hierop besloten om bij alle proefpersonen de zenuw te stimuleren. Verder, zoals beneden zal worden behandeld, wanneer blijkt dat stimulatie de afzet verbeterd is het mogelijk om implantatie van de afzetstimulator te overwegen waardoor de tibiale zenuw wordt gestimuleerd.

Hoofstuk 3 laat een nieuwe methode zien om de timing van stimulatie tijdens het lopen te controleren waarbij een enkele gyroscoop op het been is gebruikt in plaats van een hakschakelaar in de schoen. Omdat, na een beroerte, mensen maken vaak een onregelmatige voet-vloer contact van stap tot stap, waarbij hiel-, middenvoet- of teencontact betrokken is, is gebruik van hakschakelaar onbetrouwbaar voor de controle van de stimulatie van de kuitspier. Dit resulteerd in een onregelmatig

tijdsinterval tussen voet-vloer contact en afzet, dit betekend dat de tijdsintervallen niet gebruikt konden worden. Verder kwam een fenomeen voor dat we “limit cycling” noemen, hierbij gingen proefpersonen niet vooruit wanneer ze werden gestimuleerd. In plaats daarvan verplaatste hun gewicht zich op de hiel, waardoor de hakschakelaar weer werd geactiveerd en dit resulteerde in nogmaals stimulatie. Daarom hebben we gezocht naar een alternatieve besturingsmethode en vonden we dat zelfs tijdens stimulatie de hoeksnelheid van het been een regelmatig patroon hield en dat een stimulatiebesturingsmethode kon worden gebruikt zonder te rekenen op de tijdsintervallen. Hoofdstuk 3 beschrijft de experimenten en de resultaten van de gyroscoop als besturingsmethode. Als de stimulatie de afzet verbeterd kunnen de stimulator en de timingbesturing in zijn geheel worden geïmplanteerd op het onderbeen waardoor de behoefte aan externe kabels verdwijnt en de kans dat FES-gebruikers deze technologie accepteren wordt vergroot.

Hoofdstuk 4 worden de stimulatie-experimenten met gezonde proefpersonen tijdens het lopen voor het eerst gepresenteerd. Het effect op het EMG patroon van de gastronemius medialis wordt gedetailleerd beschreven, het laat zien dat tijdens het lopen een motor respons (M-golven) en mogelijk een H-reflex werden opgewekt in deze spier. Dit toont aan dat FES de fysiologische activatiepatronen van spieren door de gestimuleerde zenuw beïnvloed. Terwijl duidelijke golven waren te zien in de periode tussen twee stimulatiepulsen van de stimulatieburst waren er minder duidelijke veranderingen in de fysiologische begin en eind timing van deze spier. Dit zou kunnen worden toegeschreven aan de stimulatie: anders dan fysiologische activatie welke een signaal in één richting stuurt zou FES zowel efferente als afferente activatie veroorzaken, dus zorgen voor antidromische stimulatie welke de fysiologische activatie kan blokeren tijdens een stimulatieburst.

Hoofdstuk 5 gaat verder in op de resultaten van de hoofdstuk 4, het effect van FES op de tibilias anterior (TA), gastrocnemicus (GM) medialis, semiendinosus (ST), en de rectus femoris (RF) spieren van beide benen met en zonder stimulatie tijdens het lopen wordt verder onderzocht. Kinematica van de dij, onderbeen en voet van de gestimuleerde zijde en het onderbeen van de niet gestimuleerde zijde laten zien dat alleen de hoeksnelheid van de voet significant veranderde ten gevolge van FES.

In deze gezonde proefpersonen werden activatiepatronen, in termen van de M-golven en de H-reflexen, waargenomen in de iTA en de iST en veranderingen in timing van een aantal spieren in beide zijden door de stimulatie.
Ten slotte, zijn de testen uitgevoerd met vijf mensen met een beroerte (hoofdstuk 6). FES werd toegediend op de verlamde tibialis zenuw van deze proefpersonen terwijl de activatiepatronen van de GM, TA, ST en RF spieren werden gemeten aan de ipsi- en contralaterale kant ten op zichte van de stimulatie, en ook de kinematica van dij, onderbeen en voet aan de ipsilaterale kant en het onderbeen aan de contralaterale kant werd gemeten. Omdat mensen met een beroerte lage activatie hebben van alle spieren werd niet verwacht dat antidromische activatie een rol speelt in deze groep met proefpersonen, dus het werd verwacht dat activatiepatronen, van op zijn minst de gestimuleerde spiergroep, zeer groot zouden worden resulterend in een verbeterde afzet. Verder omdat tijdens het herstel van de beroerte activatiepatronen aan zowel de niet verlamde als de wel verlamde zijde veranderen werd het verwacht dat het activatiepatroon van andere spieren ook zou veranderen. Wat verandering werd waargenomen maar de resultaten waren variabel, dus het was onduidelijk of de stimulatie de activatiepatronen verbeterde en of het wel of niet klinisch zou kunnen worden aanbevolen als een behandeling. Dit wordt behandeld in het laatste hoofdstuk waar de resultaten van alle experimenten in ogenschouw worden genomen en worden enkele aanbevelingen gegeven. Deze aanbevelingen richten zich op het probleem van de variabiliteit in de resultaten, welke mogelijk kan worden toegeschreven aan de kleine en variabele patiëntengroep die is gebruikt. Toekomstige onderzoeken zouden een grotere testgroep met strenger gedefineerde patiënt criteria. Daarnaast, aangezien problemen zich voordeden door pijnsensaties als gevolg van hoge stimulatieniveaus kan de stimulatiemethode verder worden verbeterd. Soms waren deze stimulatieniveaus misschien niet genoeg om krachtige contracties te genereren, vooral tijdens het lopen terwijl tijdens kniebuiging bij de afzet de zenuw misschien verplaatst was ten op zichte van de stimulatieelectrode. Een oplossing is om een percutaneous of implanteerbare stimulatieelectrode te gebruiken die, omdat de elektrode rechtstreeks in contact is met de zenuw, lagere stimulatieniveas mogelijk maakt, cutane sensatie vermijdt en instabiliteit van

rekrutering voorkomt. Tot slot, een trainingsprogramma ter bevordering van het lopen gebruik makend van FES kan een voordeel zijn voor de patiënt.

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Thanks also to my colleagues who participated in my experiments. Thanks for your time and thanks for enduring the stimulation. I know it was not pleasant. I think that my experiments were more painful than Esther's pain experiments, at times. Anything for science, eh! Sorry Ralf for the carpet tape. Sorry Michael for the carpet tape and the placemats.

Thomas, if you ever get to read this, thanks for being a great masters student and helping me with the experiments. I 'ope you are doing well.

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Curriculum Vitae

Colleen Monaghan was born in Belfast, in the north of Ireland on 13th June 1979.

She studied Biomedical Engineering at the University of Ulster, Jordanstown from 1997 to 2001, obtaining a first class honours degree. As part of this four year course, she spent 12 months (1999-2000) on a work placement at Medtronic-AVE (now called Medtronic Vascular) in Galway, in the West of Ireland.

She started a PhD at the University of Twente, Enschede, The Netherlands, in 2001. The research goal was to measure the interaction between functional electrical stimulation and the activation patterns of stimulated and non-stimulated muscles during gait.

In 2006, she worked as part-time consultant, writing research proposals for Pro Support, in Hengelo, The Netherlands. At Pro Support, she successfully received funding from the European Commission in the programme "Research for the Benefit of SMEs". The project was HEELLESS "Development of a heelless shoe to reduce injury during running", project number: 222468.

She has been product specialist at Xsens Technologies, experts in miniature inertial sensor technology, since January 2009.

Publications

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