THE POTENTIAL OF ISOMETRIC ELECTRICAL STIMULATION EXERCISE FOR MUSCLE AND AEROBIC FITNESS

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A thesis submitted in fulfillment of the requirements for the degree of Doctor of Philosophy

Faculty of Medicine and Health
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CANDIDATE STATEMENT OF ORIGINALITY

I, Prakash Dhopte, hereby declare that to the best of my knowledge, the content of this thesis is my own work. This thesis has not been submitted for any degree or other purposes.

I, Prakash Dhopte, certify that the intellectual content of this thesis is the product of my own work, and that all assistance received in preparing this thesis and sources have been acknowledged.

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Prakash Dhopte
29 May 2025

SUPERVISORS' STATEMENT

This is to certify that the thesis titled **The Potential of Isometric Electrical Stimulation Exercise for Muscle and Aerobic Fitness** submitted by Prakash Dhopte in fulfilment of the requirements for the degree of Doctor of Philosophy is in a form ready for examination.

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ABSTRACT

Functional Electrical Stimulation (FES) has emerged as a key intervention for individuals with limited voluntary movement, improving aerobic capacity, cardiorespiratory fitness, and muscle health. It remains unclear, however, whether isometric FES is superior to FES cycling when it comes to regulating oxygen consumption, activating muscle, and transforming long-term physiological adaptation. Furthermore, the optimal contractions per minute (CPM) and Duty Cycle settings required to maximize the benefits of FES exercise remain unexplored. This thesis aimed to systematically evaluate the existing literature on FES exercise modalities while conducting a series of experimental studies to determine the relative efficacy of isometric FES and FES cycling in promoting aerobic and peripheral adaptations.

A systematic review and meta-analysis were performed to examine the immediate and long-term cardiorespiratory effects of FES exercise in patients with lower limb paralysis. The findings indicated that both isometric FES and FES cycling yield substantial advantages for aerobic capacity and peripheral health. Although FES cycling seems to be more efficacious in generating immediate aerobic responses and enhancing long-term cardiovascular results, isometric FES also provides equivalent advantages in oxygen consumption and muscle health. Despite some evidence, the long-term benefits of isometric FES remain unclear, highlighting the need for further research to determine its effectiveness and optimize clinical application. To further elucidate the physiological mechanisms underlying these responses and to refine stimulation parameters, a series of three controlled experiments was conducted in able-bodied participants.

The first experiment compared the acute oxygen consumption and cardiorespiratory response between isometric FES and FES cycling, revealing that both modalities elicited a similar

overall aerobic response, with FES cycling producing a transiently higher oxygen uptake. The second experiment examined the influence of CPM settings (5, 10, 20, 40 CPM) on muscle force, fatigue resistance, and aerobic demand, demonstrating that lower CPM settings (5-10 CPM) maximized peak muscle force and minimized fatigue, whereas higher CPM (20-40 CPM) resulted in greater aerobic responses but accelerated fatigue onset. The third experiment investigated the effect of Duty Cycle variations (10-40%) on oxygen uptake, revealing that higher Duty Cycles enhanced muscle force retention but increased participant discomfort, while lower Duty Cycles facilitated a more consistent and sustainable aerobic response. Collectively, the systematic review and meta-analysis, and experimental studies provide compelling evidence that isometric FES confer comparable aerobic and peripheral benefits, and that parameter optimization, particularly in terms of CPM and Duty Cycle, plays an important role in determining exercise efficacy.

These findings substantiate the clinical viability of isometric FES as an alternative to FES cycling, particularly for individuals unable to perform dynamic exercise due to lower limb paralysis. By integrating meta-analytic insights with experimental validation, this research advances our understanding of FES-induced physiological adaptations and supports the development of evidence-based rehabilitation protocols for individuals with neuromuscular impairments. Future investigations should focus on long-term training adaptations in clinical populations to further refine FES applications and establish standardized exercise guidelines.

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AUTHORSHIP ATTRIBUTION STATEMENT

Chapter 2 of this thesis is:
Prakash Dhopte, Claire E. Hiller, Suzanne Mate, Che Fornusek. A Systematic Review and Meta-analysis of the Aerobic and Musculoskeletal Benefits of Functional Electrical Stimulation in Individuals with Lower Limb Paralysis.

Contribution: Dr Ché Fornusek, Dr Claire Hiller, and I conceptualized and designed the systematic review and meta-analysis. I led the search and selection of studies, data extraction, interpretation of statistical analyses, and writing the first and subsequent drafts of the manuscript with contributions and recommendations from all reviewers. All reviewers reviewed and revised the manuscript.

Chapter 3 of this thesis is:
Prakash Dhopte, Claire E. Hiller, Che Fornusek. Acute Cardiorespiratory Responses to Functional Electrical Stimulation Cycling Versus Isometric Exercise in Able-Bodied Adults: A Randomized Crossover Trial.

Contribution: Dr. Ché Fornusek and I conceptualized and designed the study, and recruited and screened participants. I collected the data, led the analysis and interpretation of data with input from all reviewers. I wrote the first and subsequent drafts of the manuscript, and all reviewers reviewed and revised the manuscript.

Chapter 4 of this thesis is:
Prakash Dhopte, Claire E. Hiller, Alexis Brierty, Che Fornusek. Optimizing Functional Electrical Stimulation Parameters to Enhance Aerobic Fitness and Muscle Health.

Contribution: Dr. Ché Fornusek and I conceptualized and designed the study, and recruited and screened participants. I collected the data, and led the analysis and interpretation of data. I wrote the first and subsequent drafts of the manuscript with input from my supervisors.

Chapter 5 of this thesis is:
Prakash Dhopte, Claire E. Hiller, Alexis Brierty, Che Fornusek. Differential Muscle and Cardiovascular Responses to Duty Cycle Modulation During Isometric Functional Electrical Stimulation Exercise

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I, Prakash Dhopte, hereby declare that I was the principal researcher for all the work contained in this thesis, where contribution to the research has been acknowledged. The contributions of each author are acknowledged
in the authorship attribution statement.

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This is to certify that the contributions of multiple authors to the thesis titled **The Potential of Isometric Electrical Stimulation Exercise for Muscle and Aerobic Fitness** submitted by Prakash Dhopte are accurately acknowledged in the authorship contributions for manuscripts.

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OUTLINE OF THESIS

This thesis comprises six chapters, consisting of three experimental chapters

Chapter 1: Literature review introduces functional electrical stimulation (FES) exercise modalities and their cardiorespiratory and peripheral health effects. It reviews current evidence on FES cycling and isometric FES applications for improving cardiovascular fitness and peripheral muscle function and identifies knowledge gaps regarding optimal stimulation parameters.

Chapter 2: Systematic review and meta-analysis

Systematically reviews the literature on and summarizes the effects of different FES exercise modalities (including FES cycling, isometric FES, and other FES exercise) for improving cardiorespiratory fitness and peripheral health in people with lower limb paralysis.

Chapter 3 (Study 1): Comparative Analysis of Isometric FES and FES Cycling

The first experiment compared the acute cardiorespiratory responses elicited by isometric FES and FES cycling.

A cohort of 20 able-bodied participants were recruited and randomized to perform both FES cycling and isometric FES. Identical stimulation parameters were employed in both modalities to isolate the effects of static and dynamic muscle contractions. Key physiological outcomes, including heart rate, and oxygen consumption (VO_2), were recorded during each session. The study hypothesized that isometric FES would demonstrate measurable cardiorespiratory responses comparable in magnitude to FES cycling under identical stimulation conditions.

Chapter 4 (Study 2): Determining Optimal contractions per minute (CPM)

The second experiment explored the influence of varying CPM, on muscle force generation and aerobic responses during isometric FES. The CPM is a critical parameter that determines the balance between force production and metabolic demand. The goal of this experiment was to examine the relationship between CPM and both force production and cardiorespiratory responses during isometric FES.

A cohort of 12 able-bodied participants participated in randomized trials with CPM conditions of 5, 10, 20, and 40. Muscle torque output was measured using a dynamometer, and oxygen consumption and heart rate were recorded to assess aerobic responses. Participants rated their

discomfort using a numeric scale to provide insight into tolerability. This study was exploratory, examining the effects of different CPM settings on muscle torque production and cardiorespiratory responses during isometric FES. Participants also rated perceived exertion using RPE to evaluate subjective exercise intensity during the FES sessions.

Chapter 5 (Study 3): Optimizing Duty Cycle Configurations

The third experiment investigated how duty cycle can affected muscle force output, aerobic responses, and perceived exertion during isometric FES. This experiment aimed to examine how different duty cycles affected these physiological measures.

Twelve able-bodied participants completed trials with four duty-cycle configurations (10%, 20%, 30%, and 40%) under consistent stimulation parameters. Primary outcomes included heart rate, oxygen consumption, muscle torque output, and RPE. While comfort was discussed, it was not formally quantified beyond participant reports. The goal was to evaluate how increasing on-off ratios affects cardiorespiratory and mechanical outcomes in an isometric FES exercise protocol.

Chapter 6 presents a discussion of the main findings and limitations of the thesis, as well as implications for exercise prescription and clinical practice, and suggestions for future research.

Each chapter contains its own reference list. Appendices are presented at the end of the relevant chapter. Ethics approval from The University of Sydney was granted for **Studies 1, 2**, **and 3,** which involved human participants, prior to data collection commencing.

ABBREVIATIONS

The following list of abbreviations were adopted and used in this thesis. These included:

Abbreviation	Meaning
AB	Able-bodied
ANOVA	Analysis of Variance
BMD	Bone Mineral Density
CNS	Central nervous system
CO	Cardiac Output (L.min-1)
CPM	Contraction Per Minute
CSA	Cross-Sectional Area
CT	Computed Tomography
FES	Functional electrical stimulation
HR	Heart Rate (b·min-1)
LMN	Lower motor neuron
mA	Milliamperes
MD	Mean difference
MeSH	Medical Subject Headings
MS	Multiple Sclerosis
N.m	Newton-meter
PNS	Peripheral Nervous System
RQ	Respiratory Quotient
RPE	Rating of perceived exertion
RPM	Revolutions per minute (rev·min-1)
SCI	Spinal Cord Injury
SD	Standard Deviation

UMN	Upper Motor Neuron
μs	micro-second
VCO_2	Carbon Dioxide Output (l·min-1)
V_E	Minute Ventilation
VO_2	Oxygen Uptake (l·min-1)

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No content produced by generative AI tools has been used in the preparation of this thesis.

Background

Functional electrical stimulation (FES) is increasingly used to facilitate exercise in individuals with impaired voluntary muscle control, including those with paralysis caused by central nervous system disorders such as spinal cord injury (SCI), multiple sclerosis (MS), and stroke.

FES is applied clinically to induce muscle contractions in individuals with neuromotor impairments. This technique has evolved to support individuals with central nervous system disorders, enabling participation in physical activities that would otherwise be impossible due to neuromotor impairments. FES applications range from improving muscle activation and endurance to supporting cardiovascular function, offering potential physiological effects in clinical settings (1, 2). Although this thesis is not focused on spinal cord injury, it explores exercise modalities that apply broadly to individuals with severe neuromuscular impairments.

FES cycling enables people with limited or absent voluntary muscle control to engage in pedalling motions on a specialized ergometer through electronically controlled, sequenced muscle contractions of the lower extremities (3-5). FES cycling in SCI subjects reports several changes including improvement in cardiorespiratory function (6, 7) altered muscle tissue characteristics (8), regional circulatory increases (9, 10), and variable shifts in body composition measurements (11). Despite potential applications, several practical barriers limit widespread clinical implementation, including substantial resource requirements and diminishing measurement improvements after initial adaptation periods. Isometric FES offers an alternative approach promoting static muscle contractions without joint movement, potentially providing a technically simpler method with lower equipment requirements joints (12).

This thesis aims to compare the physiological and biomechanical responses elicited by FES cycling and isometric FES, focusing on cardiorespiratory parameters and muscle force production. The central hypothesis is that isometric FES exercise, with its potentially simpler technical implementation, might produce measurable physiological responses that could be compared with those from FES cycling, despite lacking joint movement. This research specifically employs a unique approach to isometric FES by implementing controlled intermittent stimulation protocols rather than continuous stimulation. By systematically investigating these responses, this thesis seeks to contribute to the development and optimize FES exercise protocols that might inform future applications in clinical settings and be beneficial for individuals with muscle paralysis.

Purpose

The primary objective of this thesis was to investigate and evaluate two distinct functional electrical stimulation (FES) exercise modes, FES cycling and isometric FES, —in terms of their acute cardiorespiratory responses and muscle force output in able-bodied individuals. By analysing these acute physiological responses, this thesis aimed to contribute evidence regarding the immediate effects of static versus dynamic FES exercise modes, without making claims about long-term training outcomes. Additionally, the research sought to explore critical stimulation parameters, such as contraction frequency (CPM) and duty cycle, modulate torque production, oxygen uptake (VO_2), heart rate, and perceived exertion. These parameters are important to optimize FES exercise protocols for future use in individuals with significant neuromotor impairments.

To achieve these objectives, the thesis focused on the following key aims:

- To systematically review and synthesize the existing literature on the cardiorespiratory and physiological responses to different functional electrical stimulation exercise protocols and modalities
- To compare the acute cardiorespiratory response elicited by isometric FES exercises with those produced by FES cycling,
- To determine the effect of the contractions per minute (CPM) on the muscle torques and cardiorespiratory response elicited during isometric FES exercise,
- To assess the effect of varying duty cycles on the cardiorespiratory responses and muscle torque produced during isometric FES exercise.

CHAPTER 1

INTRODUCTION

1.1 Background to Muscle Paralysis

Muscle paralysis, defined as the loss of voluntary control over muscle contractions, is a significant medical condition that imposes substantial limitations on motor function, personal autonomy and overall well-being (1, 2). Paralysis may be localized, involving individual muscles or groups of muscles, or generalized, involving whole limbs or areas of the body (3). Conditions that lead to paralysis encompass a wide range of aetiologies, including traumatic brain injuries, neurological diseases, infections, brain tumours, congenital and inherited abnormalities (4). The pathology of muscle paralysis is multifactorial as it typically involves both the central nervous system (CNS) and peripheral nervous system (PNS) as well as the muscles under their control (5, 6). Recognizing the interplay between the nervous system and muscles is key to diagnosing and addressing the diverse forms of paralysis.

Muscle paralysis can be broadly categorized into two types based on the characteristics of muscle tone: flaccid paralysis and spastic paralysis (also referred as non-flaccid paralysis) (7, 8). In the condition of flaccid muscle paralysis, an individual loses the ability to voluntarily regulate their muscle contractions, resulting in weakened muscles and a progressive deterioration of muscle strength (9). Flaccid paralysis typically results from lower motor neuron (LMN) injury, which disrupts the direct neural connection to muscles, impairing voluntary movement and leading to muscle weakness and atrophy (10). In contrast, spastic paralysis results from injury to the CNS, particularly the upper motor neurons (UMN) (11). This type of injury is associated with increased muscle tone, muscle stiffness and involuntary muscle contractions (11).

The global prevalence of paralysis is on the rise, largely due to the increasing number of individuals living with chronic conditions that contribute to its onset. This trend can be

attributable to a several factors, including higher occurrence of stroke and traumatic injuries, and improved awareness of neurological diseases (12-14). Currently, as reported by WHO, neurological disorders make up the biggest group of the worldwide disability, and stroke is one of the key causes of muscle paralysis (15, 16) Paralysis is most particularly prevalent in regions with limited access to quality healthcare, where individuals do not receive timely and quality medical attention (17, 18).

1.1.1 Anatomy and Physiology of the Central Nervous System

The nervous system is the body's central control network, continuously monitoring and responding to both internal and external stimuli. It regulates a wide range of functions, from simple reflexes to higher-order cognitive processes such as memory and decision-making. The system is divided into two primary components: the CNS and the PNS. The CNS consists of the brain and spinal cord, serving as the primary processing centre for sensory information and motor commands (19). It controls voluntary movements and regulates critical involuntary processes such as respiration, circulation, and digestion (19).

The PNS, comprising all neural structures outside the CNS, is responsible for relaying information between the CNS and the rest of the body (19, 20). It is further divided into the somatic nervous system (SNS), which governs voluntary motor control, and the autonomic nervous system (ANS), which regulates involuntary physiological processes, including heart rate, digestion, and respiratory rate (21). While the SNS enables conscious muscle control, the ANS operates subconsciously to maintain homeostasis (22, 23). The CNS and PNS work together to integrate sensory input, coordinate motor responses, and regulate internal stability, ensuring efficient interaction with the environment. Overall, the nervous system ensures the

body's adaptability and efficient functioning across all physiological systems, supporting resilience and homeostasis (24-26).

The brain is a complex organ that controls thought, memory, emotion, touch, motor skills, vision, breathing, temperature, hunger, and every other bodily function (21, 27). The brain is organized into specialized regions to optimize its ability to process information and coordinate specific tasks. For instance, the cerebral cortex plays a key role in processing sensory input and generating motor responses (28, 29). Within the cerebral cortex, the motor cortex specifically governs the control of voluntary muscle movements (30). The brain is further subdivided into structures such as the midbrain, pons, medulla, and cerebellum. The midbrain acts as a conduit between the brain and spinal cord, facilitating communication and regulating essential autonomic functions such as respiration and heart rate (31). These intricate divisions of the brain enable efficient and coordinated control over both voluntary and involuntary physiological processes (32, 33).

The spinal cord is segmented into regions corresponding to different anatomical regions. The severity of paralysis resulting from an injury to the spinal cord is determined by the location of the injury. Quadriplegia, for example, is characterized by paralysis of the upper and lower limbs following a lesion in the cervical region of the spinal cord. By contrast, damage to the thoracic or lumbar spinal segments affects primarily the lower body, leading to paraplegia, which involves paralysis of the trunk and lower extremities. As a result of spinal cord injury (SCI), motor and sensory dysfunction vary based on the severity of the lesion, with higher lesions (like those in the neck region) usually causing more severe impairments (like respiratory problems). In these cases, motor and sensory deficits are directly caused by neural pathways that innervate specific body regions (34-38).

Motor control is mediated by a complex network of neurons, beginning with the upper motor neurons located in the motor cortex. These neurons send their axonal projections to the brainstem and spinal cord, where they synapse with lower motor neurons (39). The lower motor neurons, relay signals to the muscles, thereby facilitating voluntary movement (40, 41). Disruption at any point along this neural pathway can impair communication between the CNS and the muscles, potentially leading to paralysis due to the absence of motor signals required for muscle contraction.

The CNS also has other purposes including processing of sensory information as well as controlling reflexes (42). In situations where the CNS is affected for instance by trauma, stroke or neurodegenerative diseases, paralysis presents motor and sensory losses. This makes the rehabilitation and recovery of neurological injuries even more difficult because apart from losing the ability to perform certain movements, the patient may also end up losing sensation and proprioception as well as the ability to control their autonomic functions (43).

1.1.2 Causes of Muscle Paralysis from the Central Nervous System

Muscle paralysis is often caused by injuries to the CNS, including damage from traumatic brain injury (TBI), stroke, SCI, or neurodegenerative disorders like multiple sclerosis (MS) and amyotrophic lateral sclerosis (ALS) (6). These conditions interfere with the transmission of signals from the brain or spinal cord to the muscles, resulting in varying degrees of paralysis. The extent and specific muscles affected depend on the injury's location and severity within the CNS.

Traumatic brain or spinal cord injuries, often caused by road traffic accidents, falls and sports activities are a leading cause of paralysis (35, 44). The severity of these injuries, as well as the specific location of the trauma, determines the extent of paralysis, which may range from partial to complete loss of motor function. SCI disrupts neural signalling below the site of trauma, while injuries to the motor cortex or brainstem impair movement control pathways, causing paralysis (34, 45).

Strokes, or cerebrovascular accidents (CVAs), result from interrupted blood flow to the brain due to vessel blockages or ruptures, causing ischemic or haemorrhagic damage. This leads to brain cell death in the affected region, often impairing motor control. Strokes commonly cause hemiplegia, a paralysis affecting one side of the body, with the severity determined by the location and extent of brain damage (46-48).

Some infections and inflammatory diseases affect the CNS and cause paralysis as one of the complications. For instance, meningitis, which is an inflammation of the membranes, covering the brain and spinal cord results in neurological complications like paralysis (49, 50). Likely, autoimmune diseases like Guillain-Barré syndrome, despite involving mainly the peripheral nervous system, may sometimes affect the CNS, resulting in paralysis (51).

While the previous discussion demonstrates the diverse aetiologies of muscle paralysis, the remainder of this thesis concentrates on literature and applications related to SCI. This focus reflects the fact that most of the published research on FES cycling, and isometric FES has been conducted in the SCI population, providing the most extensive evidence base for these interventions (52, 53). Individuals with SCI typically retain intact lower motor neurons below the lesion level, allowing for effective muscle activation through electrical stimulation (54, 55).

Although the experimental studies presented in this thesis were conducted on able-bodied participants to optimize and refine FES parameters under controlled conditions, the findings are intended to inform future applications in individuals with SCI who possess intact lower motor neurons below the lesion level.

1.1.3 Physiological Mechanisms of Muscle Paralysis

The patterns of physiological changes in muscles vary depending on the type of nervous system lesion. Several key mechanisms contribute to this disruption: upper motor neuron damage, lower motor neuron damage, and disruption of synaptic transmission. Upper motor neuron (UMN) lesions refer to damage affecting the motor neurons located in the motor cortex of the brain and the descending pathways that transmit neural signals from the motor cortex to the spinal cord, particularly the corticospinal tract (56). These neurons are essential for initiating and coordinating voluntary movements of skeletal muscles, including those of the torso, arms, and legs (56, 57). When UMN lesions occur, individuals typically experience a loss of voluntary motor control; however, some degree of muscle bulk and tone may be preserved. However, the characteristics of muscle tone are altered, with a marked increase in spasticity (58). Additionally, reflex activity is often exaggerated in individuals with UMN lesions, leading to hyperreflexia, where reflexes such as the patellar reflex become more pronounced than usual (8). These changes in muscle tone and reflexes reflect the disruption in the normal communication between the brain's motor centres and the spinal cord, resulting from the damage to the UMNs (8, 55, 59).

Lower motor neurons, located in the spinal cord and brainstem, relay motor commands from upper motor neurons to skeletal muscles, facilitating movement and reflexes. Damage to LMNs disrupts this communication, resulting in flaccid paralysis, muscle weakness, hypotonia, and

muscle atrophy (54, 60). Muscle weakness in LMN lesions is typically more severe than in UMN lesions, as it directly affects the neurons responsible for muscle activation (61). The lack of motor stimulation leads to muscle atrophy, as muscles gradually shrink due to disuse. Reflex responses are also diminished or absent, as the neural circuits involving LMNs are disrupted (59, 61). Conditions like SCI highlight the severity of LMN lesions, as the loss of LMN function leads to profound functional impairment (59, 61-63).

Paralysis can arise under certain conditions due to disruptions in synaptic transmission, either between neurons or between neurons and muscle fibres. For example, in MS, lesions form in the myelin sheath surrounding nerve fibres, impairing the conduction of electrical signals along the affected nerves and particularly disrupting motor signal transmission fibres (64, 65).

1.1.4 Impact of paralysis on peripheral limb health

Immobility often forces individuals to remain in prolonged seated or recumbent postures, leading to sustained pressure on specific skin areas. This pressure impairs blood flow to the underlying tissues, impaired circulation delays tissue healing, elevating infection risks (66) and ultimately resulting in ulcer formation (67). If inadequately managed, these ulcers may lead to secondary infections, further complicating the individual's health status (68, 69). Compromised circulation can also result in deep vein thrombosis (DVT), a condition arising from the formation of blood clots in the deep veins of the legs (70-72). The health risks from DVT formation remain high because clots that break free from their initial location can reach the pulmonary vasculature before leading to a possibly fatal pulmonary embolism (PE) (70).Prolonged immobility also contributes to muscle atrophy and joint contractures, exacerbating disability and pain (73, 74), while also reducing bone density, which heightens the risk of osteoporosis and fractures (75-77).

Functional Electrical Stimulation (FES) exercise stands as a vital tool for combating the negative effects of physical inactivity because it induces muscles to contract during stimulation to preserve muscle mass and function while also enhancing cardiovascular and pulmonary functions (78). Research into the interconnected physiological systems between cardiovascular health and muscle and skin condition levels is necessary to develop effective interventions that combine to enhance physical abilities and improve the quality for people with paralysis (79).

1.1.5 Activity Levels in People with Paralysis

Individuals with paralysis often experience reduced mobility due to impaired muscle function and must rely on aids or physical therapy to maintain joint flexibility, promote circulation, and prevent secondary complications such as cardiovascular disease, obesity, diabetes, and respiratory issues (54, 80-82). Despite the availability of mobility aids like wheelchairs and standing frames, people with paralysis face additional challenges such as restricted mobility, impaired sensation, dexterity issues, and environmental barriers, which limit physical activity (83-86). Psychological factors, including lifestyles changes and stress, also contribute to reduced activity levels and affect quality of life (87, 88).

Engaging in physical activity is crucial for maintaining overall health and functionality in individuals with paralysis, especially those affected by SCI (54). Conventional exercise routines often present significant difficulties due to neuromuscular deficits and the inability to voluntarily control muscle movement. Structured physical activity is vital for enhancing cardiovascular fitness, metabolic health, muscle integrity, and overall well-being (89).

People with SCI typically display lower aerobic capacity because of factors like autonomic dysfunction, reduced venous return, and limited active muscle mass (54). These physiological

limitations heighten the risk of cardiovascular diseases, which are a leading cause of death in this group (90, 91). Studies show that upper-body workouts, including arm cycling and pushing a wheelchair, can improve stroke volume, cardiac output, and oxygen uptake ($\dot{V}O_2$), thereby fostering better cardiovascular health (92, 93).

Regular involvement in aerobic exercises enhances metabolic efficiency and insulin sensitivity, consequently decreasing the risk of metabolic syndrome, a cluster of conditions that increase the risk of heart disease, stroke, and diabetes (94, 95). Metabolic syndrome is more prevalent among individuals with paralysis (96, 97). Additionally, moderate to high-intensity physical activity has been linked to better lipid profiles, reduced systemic inflammation, and improved autonomic function (98, 99). One pressing issue for those with paralysis is the rapid loss of muscle mass and bone mineral density (BMD) resulting from decreased mechanical loading on the lower limbs, leading to a higher risk of osteoporosis (100). Resistance training focusing specifically on paralysed lower limb muscles through electrical stimulation has shown some capacity to counteract atrophy by promoting localized muscle activation and potentially preserving tissue characteristics (101, 102). Upper-body exercise may complement these interventions by improving overall cardiovascular conditioning but does not directly address lower extremity muscle preservation (103). Furthermore, passive weight-bearing activities may also help in maintaining skeletal health and lowering the chances of fractures (104). Consistent physical activity can help alleviate spasticity, improve blood circulation, and enhance neuromuscular coordination, all of which contribute to greater independence in daily functioning (105). Many individuals participating in structured exercise regimens report enhanced endurance and strength, making vital tasks like propulsion in wheelchairs and transfers easier (106).

Despite the numerous advantages of exercise, the participation rates among individuals with paralysis is lower than recommended guidelines, largely due to barriers such as limited access, absence of specialized equipment, and safety concerns (107, 108). Addressing these challenges requires a focus on developing adaptable, cost-effective exercise protocols that cater to varying levels of impairment. Expanding access to tailored physical activity programs has the potential to significantly enhance cardiovascular, metabolic, musculoskeletal, and psychosocial health in this population. Prioritizing inclusivity and innovation in rehabilitation strategies fosters long-term health improvements and a better quality of life for individuals with paralysis.

1.1.6 Aerobic Fitness in Persons with Paralysis

Cardiovascular fitness, or aerobic fitness, refers to the ability of the heart, lungs, and muscles to deliver sufficient oxygen to meet the demands of prolonged physical activity (109). Although closely related, cardiovascular fitness and cardiovascular health are distinct concepts: fitness reflects functional capacity, whereas health encompasses the absence or management of diseases (e.g., hypertension, atherosclerosis, and coronary artery disease.) Improving aerobic fitness in this population is essential for reducing the risk of cardiovascular diseases and enhancing respiratory function and overall physical health (110). This emphasizes the need for targeted interventions to enhance cardiovascular capacity and reduce immobility-related health issues, such as cardiovascular diseases and respiratory complications (111).

A significant distinction exists between interpreting VO_2 as aerobic fitness and muscle activity. In voluntary exercise, VO_2 increase reflects aerobic fitness when accompanied by cardiovascular adaptations: increased stroke volume, cardiac output, and mitochondrial oxidative capacity. However, during FES, muscles are activated through non-physiological recruitment patterns, including synchronous fibre activation, preferential recruitment of fast-

twitch motor units, and a reversed recruitment order (112), which elevate metabolic cost per unit of mechanical work without necessarily indicating greater cardiovascular capacity (113). Following FES cycling, VO_2 increases indicate fitness improvements only when coupled with central cardiovascular adaptations (increased stroke volume, enhanced venous return, improved arterial compliance). Without these adaptations, higher VO_2 may simply reflect greater muscle recruitment or altered stimulation parameters rather than improved fitness. Therefore, interpreting VO_2 changes from FES exercises requires additional cardiovascular measures (heart rate, stroke volume, work output) to confirm true aerobic fitness improvements.

Individuals with SCI typically exhibit substantially reduced aerobic fitness compared to non-paralysed populations. Peak oxygen consumption (VO_{2peak}) values for individuals with tetraplegia range from 0.6 to 1.4 L/min or 10-20 mL/kg/min, while paraplegics may achieve higher values, ranging from 1.8 to 2.4 L/min, depending on the level and completeness of injury (114-116). These figures represent a 50–75% reduction in VO_{2peak} compared to able-bodied individuals, where values typically range from 2.5 to 4.0 L/min for men and 1.6 to 3.0 L/min for women (or 35-50 mL/kg/min for men and 25-40 mL/kg/min for women) (117). This reduction in VO_{2peak} is primarily attributed to the inability to recruit large muscle groups, which are critical for effective cardiovascular training, as paralysis limits voluntary control over these muscles. Long-term FES training programs can address these deficits by improving oxygen delivery, increasing stroke volume, and enhancing arterial compliance, thereby reducing the incidence of cardiovascular complications (118).

Cardiovascular fitness improvements depend on adaptations such as increased stroke volume, cardiac output, and mitochondrial capacity (119). VO_2peak is only a reliable fitness indicator

when it reflects these changes, not just greater muscle recruitment. In FES, acute VO_2 mainly represents the metabolic cost of electrically induced contractions, influenced by muscle mass and stimulation parameters rather than true cardiorespiratory capacity (113). Therefore, higher VO_2 during FES does not necessarily mean improved fitness. Post-training VO_2 increases should only be considered evidence of fitness gains if supported by cardiovascular adaptations (120). In this thesis, acute VO_2 is used to compare exercise intensity between modalities, not as a direct fitness measure. Heart rate, work output, and torque are also assessed to separate metabolic cost from true physiological adaptation, clarifying whether FES protocols reach intensities needed for cardiovascular benefit (52).

Structured aerobic exercise programs can positively influence the physiological consequences of paralysis by improving cardiovascular fitness, enhancing exercise tolerance, and promoting overall health (121-123). The benefits consist of reinforced variability of the heartbeat, optimal blood pressure, and increased maximal volume of the lungs (124). Workloads during FES cycling can range between 20 to 50 watts, increasing by 50–70% of VO_{2peak} (125). These enhancements not only boost aerobic fitness but also contributes to fatigue resistance, enabling individuals with SCI to engage in sustained physical activity.

1.2 Voluntary Exercise in individuals with paralysis

Voluntary exercise is a critical activity for maintaining physical health, enhancing metabolic function, and preventing chronic diseases (126). In able-bodied individuals, voluntary exercise relies on the coordinated interaction of neural and muscular systems, beginning in the motor cortex of the brain. UMNs transmit signals through the corticospinal tract to synapse with LMNs in the spinal cord, which then relay impulses to muscle fibres at the neuromuscular junction. The release of acetylcholine (ACh) at the neuromuscular junction initiates muscle

contraction, enabling voluntary movement (127). This process is marked by an efficient recruitment strategy, where smaller, fatigue-resistant motor units are engaged initially, and additional motor units are progressively activated to meet increasing force demands. Such a mechanism ensures optimal energy utilization and delays the onset of fatigue during sustained physical activity (128).

The energy metabolism underlying voluntary exercise encompasses three primary pathways to regenerate adenosine triphosphate (ATP): the phosphagen system for immediate energy, anaerobic glycolysis for short-term energy, and aerobic metabolism for prolonged exercise. These pathways fuel muscle contractions and drive physiological adaptations (129). For instance, aerobic exercise enhances mitochondrial density, capillary perfusion, and oxidative capacity, while resistance training promotes muscle hypertrophy and neuromuscular efficiency (130). Regular voluntary exercise also induces cardiorespiratory adaptations, including increased stroke volume, cardiac output, and oxygen delivery to active tissues, collectively improving endurance, strength, and overall fitness (131).

1.2.1 Benefits of voluntary exercises

Voluntary exercise provides numerous evidence-based benefits for individuals with paralysis, specifically enhancing cardiovascular capacity, skeletal muscle hypertrophy, joint mobility, and psychological well-being. These physiological adaptations contribute significantly to improved functional independence and quality of life (105, 132).

Structured exercise guidelines from the American College of Sports Medicine (ACSM) in their "ACSM's Guidelines for Exercise Testing and Prescription" specifically for individuals with physical disabilities emphasize both aerobic and resistance training for individuals with

disabilities. Aerobic activities, such as arm cycling and adapted ergometers, should be performed at moderate intensity (40–59% of heart rate reserve) for 20–30 minutes, 3–5 times per week, to enhance cardiovascular health. Resistance training should be conducted 2–3 days per week using weights, resistance bands, or functional resistance machines, targeting major muscle groups to increase strength and prevent musculoskeletal complications (105).

Despite these beneficial outcomes, individuals with neuromotor impairments face significant physiological limitations when applied to individuals with neuromotor impairments. Upper-body exercises such as arm cranking are constrained by the relatively small active muscle mass engaged during movement, which fundamentally limits maximal oxygen consumption. Comparative physiological analyses demonstrate that individuals with complete spinal cord injury (SCI) typically exhibit peak oxygen uptake (VO_{2peak}) values that are substantially reduced compared to non-disabled populations. This cardiorespiratory limitation is primarily attributable to the decreased muscle mass available for voluntary activation during exercise (54). Evidence-based exercise interventions must therefore be specifically designed to accommodate these physiological constraints while still promoting clinically meaningful adaptations in both cardiorespiratory and musculoskeletal system. Functional Electrical Stimulation (FES) exercise stands as a vital tool for combating the negative effects of physical inactivity because it induces muscles contract during stimulation to preserve muscle mass and function while also enhancing cardiovascular and pulmonary functions (78).

1.3 Functional Electrical Stimulation

1.3.1 Overview of Functional Electrical Stimulation

Functional Electrical Stimulation (FES) applies controlled electrical impulses to stimulate paralysed or weakened muscles, enabling movement-based activities such as leg cycling. FES

is also used for therapeutic purposes that do not involve clear movement, such as isometric muscle contractions intended to focus on muscle strength and hypertrophy, cardiovascular health, or metabolic function. The process involves placing electrodes on the skin's surface to deliver electrical currents, which trigger muscle contractions by directly activating motor neurons. Unlike natural voluntary muscle contractions, which rely on finely tuned neuromuscular pathways, FES-induced contractions are less efficient and often lead to faster muscle fatigue due to non-selective recruitment of muscle fibres (55, 125, 133, 134). FES has been shown to improve motor function and prevent muscle atrophy in individuals with neurological impairments, particularly in cases where voluntary muscle activation is severely limited (55, 125, 133, 135, 136). Additionally, FES contributes to metabolic and psychological well-being, offering improvements in insulin sensitivity, lipid metabolism, and quality of life (52, 53).

Several types of FES exercises exist, including FES cycling, FES rowing, FES walking, FES standing, and isometric FES (52). However, this thesis focuses on FES cycling and isometric FES, as they represent two distinct approaches to muscle activation, dynamic and static stimulation. FES cycling is a well-established intervention that facilitates systemic physiological adaptations, while isometric FES is particularly valuable in early rehabilitation stages when movement is limited.

1.3.2 Implementation Approaches for FES

FES is applied through different methods depending on the rehabilitation goal and the patient's condition. The three primary delivery approaches discussed in this section include FES cycling, isometric FES, and FES leg extension exercises. Each method offers distinct advantages and is suited to different phases of rehabilitation.

1.3.2.1 FES Cycling

FES cycling involves using a cycle ergometer's rotation phase to synchronise the sequential electrical stimulation of lower-limb muscles, usually the quadriceps, hamstrings, and gluteal muscles (54). Surface electrodes administer current pulses (often 20-50 Hz frequency, 200-400 μs pulse width) with intensities typically ranging from 30-100 mA, dependent upon individual tolerance and muscle recruitment requirements (137, 138). With position sensors on the ergometer, stimulation time is accurately regulated, causing the right patterns of muscle activation to produce effective pedalling motion. Modern systems utilise a closed-loop control to modify stimulation parameters according to cadence, resistance, or physiological reactions (139, 140).

Muscle activation during FES cycling extends beyond directly stimulated muscle groups. While electrodes target quadriceps and hamstrings, other muscles such as gluteal muscles, gastrocnemius, and soleus contribute to pedalling mechanics (52). Healthy individuals may exhibit voluntary co-contraction concurrently with electrically induced activation affecting force production and metabolic responses (125). Without electromyography, quantifying non-stimulated muscle contributions remains challenging, yet these muscles influence measured VO_2, torque, and fatigue. These non-stimulated muscles perform mechanical work that influences measured physiological responses, such as VO_2, heart rate, and torque output. This activation complexity means identical stimulation parameters may produce variable responses depending on voluntary contribution and ancillary muscle engagement, critical considerations when interpreting FES exercise outcomes and comparing different FES exercise modalities.

FES cycling can be done using either motorized or non-motorized stationary bikes, or even on specially designed tricycles for mobile use (141-143). Modern systems such as the RT300 and iFES-LCE integrate advanced features like motor-assisted pedalling, isokinetic resistance, and

real-time biofeedback (144-147) which are particularly useful to enable individuals with limited voluntary control to engage in exercise (148).

FES cycling triggers immediate cardiovascular responses, including increased heart rate and improved venous return through the "muscle pump" effect, where rhythmic muscle contractions enhance blood flow back to the heart (149, 150). These effects boost cardiac output and help counteract the circulatory stagnation common in individuals with SCI (151, 152). By inducing rhythmic muscle contractions, FES cycling enhances blood flow, oxygen delivery, and nutrient exchange supporting oxygen delivery and utilization (153). While it does not activate muscles as extensively as voluntary exercise, FES cycling can still increase oxygen consumption (VO_2) by engaging large muscle groups, improving cardiac output, stroke volume, and arterial compliance over time (119, 120, 154). Regular FES training has been shown to improve peak oxygen uptake (VO_{2peak}), though values remain lower than in able-bodied individuals (154). Despite this attenuation, FES cycling provides significant cardiovascular benefits, reducing the risk of complications such as venous thromboembolism and inadequate tissue perfusion (155).

One potential effect of FES cycling compared to other FES modalities is its ability to engage muscles through dynamic, repetitive contractions. When contrasting FES cycling with isometric FES and other forms of electrical stimulation, several studies suggest that the dynamic loading pattern may produce distinct tissue responses (156). The sequential activation during cycling involves multiple muscle groups through continual contraction-relaxation cycles that may affect muscle fibre characteristics differently than sustained or random stimulation patterns (157-160). While evidence for maintaining bone density is limited, FES cycling may reduce bone loss by generating mechanical stress on bones through repeated

contractions (102, 161). This loading stimulates osteocytes, which regulate bone remodelling by influencing osteoclast and osteoblast activity (102, 158, 162, 163) (161).

Beyond its physiological effects, FES cycling offers significant metabolic benefits. Regular FES cycling improves insulin sensitivity by promoting glucose uptake in muscles through contraction-driven activation of GLUT-4 transporters (164). FES cycling also enhances lipid metabolism by activating enzymes that regulate fat breakdown and storage, thereby improving cholesterol profiles and lowering triglycerides (165-167). However, these metabolic benefits are generally observed in long-term studies and were not examined in this thesis.

Challenges in FES cycling

While FES cycling investigations have examined various physiological responses, several technical and practical considerations affect its implementation. Neuromuscular fatigue represents a significant challenge, occurring through non-selective motor unit recruitment patterns inherent to electrical stimulation (113, 138). The preferential activation of more excitable, less fatigue-resistant Type II muscle fibres contributes to rapid torque decline during stimulation (138, 159, 168). This characteristic is particularly relevant to experimental design for studies measuring acute responses, as it necessitates careful consideration of stimulation duration and rest intervals. The technological implementation of FES cycling systems involves substantial complexity in both hardware configuration and stimulation control algorithms. Current commercially available systems require significant financial investment, specialized maintenance, and technical expertise for proper configuration and operation (53, 133). These practical constraints inform the rationale for investigating alternative electrical stimulation approaches, including the isometric protocols examined in subsequent chapters of this thesis. Studies comparing different FES modes of exercise must account for these considerations when

designing FES experimental protocols and interpreting physiological responses. In this thesis, FES cycling was examined under acute, laboratory-controlled conditions to assess immediate cardiorespiratory and torque responses in able-bodied individuals, rather than therapeutic or rehabilitative outcomes.

1.3.2.2 Isometric FES Exercise

Isometric FES refers to the use of surface electrical stimulation to elicit muscle contractions without associated joint movement and represents an alternative approach to dynamic FES cycling (169). In this modality, targeted muscle groups such as the quadriceps are stimulated in a fixed position, typically with limbs secured to avoid movement, enabling controlled measurement of force production and muscle activation patterns (170). However, whether isometric FES elicits comparable physiological responses to FES cycling without equipment complexity remains unclear, a critical issue for practical implementation and broader accessibility.

Unlike FES cycling, where stimulation is sequenced and phase-dependent, isometric FES employs synchronized, bilateral stimulation with predefined parameters (e.g., frequency, amplitude, duty cycle) that are applied statically. In the present thesis, isometric FES was implemented using a wheelchair (one experiment) and seated dynamometer setup (two experiments), where participants' legs remained stationary, and muscle torque was measured under different levels? of muscle contractions and duty cycles.

Isometric FES protocols and stimulation parameters differ from FES cycling in several key aspects. Duty cycles typically employ ratios between 1:1 and 1:3 (on: off), with longer rest periods necessary due to rapid fatigue onset during sustained static contractions (171).

Conventional isometric FES is typically employed as a strength training intervention, utilizing a small number of maximal contractions per session, typically 10-15 repetitions (172). Stimulation amplitudes are adjusted based on individual tolerance and desired force output, typically ranging from 20-80 mA (172). Contraction durations typically range from 3-6 seconds per repetition (138, 171). In contrast to this conventional strength training approach, the present investigation employs isometric FES to elicit sustained cardiorespiratory responses.

Isometric FES has been proposed as a lower-cost alternative to FES cycling, particularly where equipment access, patient tolerance, or setup time are limiting factors (169). However, this thesis does not directly evaluate accessibility or cost-related outcomes, and such implications should be interpreted as contextual rather than confirmed.

Prior studies have shown modest increases in quadriceps cross-sectional area (173) with isometric FES over several weeks (172), but such training-induced adaptations were not assessed in this work. Likewise, while static contractions have been hypothesized to promote bone loading via compressive forces (174), the evidence remains inconclusive, and isometric FES is generally considered less effective than dynamic loading for improving bone health. Finally, claims regarding restoration of neuromuscular coordination or motor control should be treated with caution. While FES may influence motor unit recruitment patterns, the extent to which this occurs in static protocols without voluntary involvement remains unclear and was not measured or inferred in this thesis.

1.3.2.3 FES leg Extension

FES leg extension involves the use of electrical stimulation on the quadriceps muscle group to induce knee extension while the individual is seated. The exercise is often performed on a

specialised or commercial leg extension equipment, where the limb is stabilised, and an external load (e.g., weights, resistance bands, or predetermined torque levels) is applied at the ankle or shin to counteract the contraction (175). This configuration allows the measurement of muscle torque production under regulated conditions (172).

In contrast to voluntary resistance training that depends on neural drive, FES leg extension passively elicits muscle contraction via peripheral motor neurone stimulation, circumventing central command (133, 176). The technique often employs fixed stimulation parameters (e.g., 30–50 Hz frequency, 300–400 μs pulse width), while the resistance level is progressively augmented by modifying mechanical load or stimulation intensity (138, 177, 178). The FES leg extension serves to preserve muscle mass and strength in patients with restricted mobility, but it does not seek to reinstate voluntary motor control. The objective is to facilitate neuromuscular engagement in populations with limited physical activity, such as those with spinal cord injury, rather than restore functional motor pathways.

1.3.3 Stimulation Parameters

The results of FES exercise depend on appropriate stimulation settings. The three primary electrical stimulation parameters are amplitude/intensity (pulse height), frequency (pulses produced per second), and pulse width/duration (time duration for a single pulse) (179). Together, these parameters are adjusted to achieve desired outcomes for FES exercise.

Amplitude/Intensity

Amplitude (also termed magnitude or intensity) determines the strength of an electrical impulse in FES. Stimulation intensity, specifically the electrical current used to induce muscle contractions, is typically measured in milliamperes (mA). The amplitude is a critical factor in

achieving effective and comfortable muscle activation (138, 180). In FES applications, amplitudes typically range up to 140 mA in commercial systems, although they vary based on factors such as the dimensions of stimulating electrodes, muscle size, and the extent of neuromuscular impairment (181, 182).

Increasing the stimulation intensity amplifies the depolarizing effect on the nerve structures beneath the electrodes, leading to greater muscle activation (183). High-intensity electrical stimulation combined with isometric contractions is associated with significant improvements in strength, as demonstrated in training programs that incorporate electrical stimulation (184). While elevated stimulation amplitudes recruit more muscle fibres, resulting in stronger peripheral contractions, they can also accelerate fatigue during prolonged stimulation (138, 185, 186).

Higher stimulation amplitudes increase spatial recruitment by activating a larger number of motor units simultaneously, resulting in greater absolute force production (113). However, this does not necessarily cause faster relative fatigue of individual motor units, since fatigue progression is primarily governed by stimulation frequency and the metabolic profile of the recruited fibres. In this thesis, amplitude selection was based on participant tolerance and should not affect fatigue rates.

Frequency

The frequency of a waveform is the number of electrical impulses delivered to a muscle per second, and is expressed in units of Hertz (187), for example, 30 Hz = 30 pulses per second (138, 188). In FES exercises, frequencies between 30 - 50 Hz are the most common (159, 189) and though lower frequencies of 20-25 Hz are reported (159, 190), they are less common.

The selection of frequency depends on the type of desired muscle contraction either a twitch or a sustained (tetanic) contraction (191). Low-frequency stimulation (1-10 Hz) is primarily used for endurance training and muscle recovery, promoting slower but sustained contractions that aid in muscle conditioning (192). In contrast, higher frequencies (20-50 Hz) are necessary to elicit strong muscle contractions, which are crucial for strength training and functional movements (138). However, frequencies exceeding 50 Hz can lead to rapid muscle fatigue because motor units are activated continuously and repetitively (193, 194).

Pulse Duration

Pulse duration, measured in microseconds (μs), refers to the duration of each electrical pulse delivered during stimulation. In biphasic waveforms commonly used in FES (as shown in Figure 1), pulse duration specifically describes the time duration of each individual phase, whereas the complete pulse cycle includes both phases. Shorter pulse duration (20-200 μs) are optimal for motor stimulation without eliciting pain responses, whereas longer pulse duration (400-500 μs) facilitates greater muscle torque production (195). Broader pulse duration facilitate the recruitment of muscle fibres, resulting in stronger contractions; however, this can also elevate discomfort because of the necessity of applying higher electrical impulses (182).

Figure 1. Functional electrical stimulation parameters.

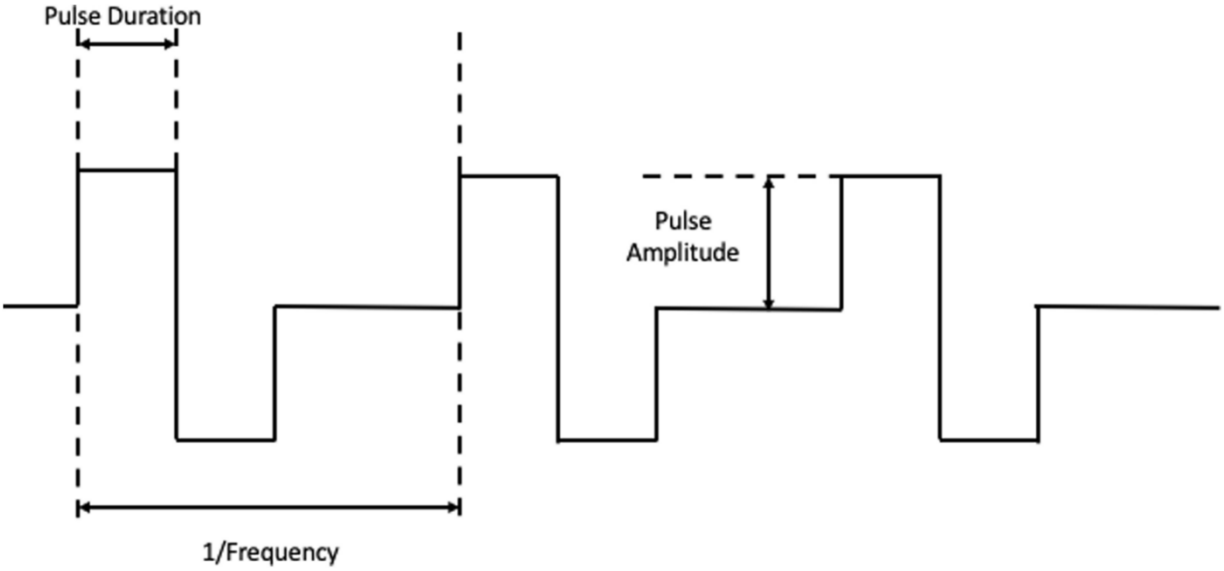

Figure was adapted from (Source: Karamian, B. A., et al. (2022) (196)

Duty Cycle

The term "duty cycle" refers to the ratio of stimulation time (on-time) to the total cycle time, which includes both on-time and off-time during an FES exercise session (Fig 2). It is typically expressed as a ratio (e.g., 1:2, indicating 10s on and 20s off) or a percentage (e.g., 70%, denoting the proportion of on-time relative to the total time) (138, 171, 197). This parameter plays a critical role in modulating the muscle fatigue, torque production, and patient comfort.

Early studies in individuals with SCI showed that intermittent stimulation in which periods of force production are interrupted with rest periods, allowed muscle tissue to recover more efficiently than continuous stimulation patterns, leading to greater torque production and reduced fatigue (138, 197, 198). Different duty cycles can be employed depending on training goals, with variations in the ratio of stimulation time to rest periods (195, 199).

In clinical settings, duty cycles are adjusted based on therapeutic goals. A 1:2 duty cycle is commonly used for endurance training, whereas a 1:1 duty cycle is employed for strength training (171). An appropriate duty cycle minimizes fatigue while sustaining effective contractions, making it essential for achieving consistent training responses. Despite extensive FES research, systematic comparisons of duty cycle and contraction pattern variations which may influence acute physiological responses, have not been investigated.

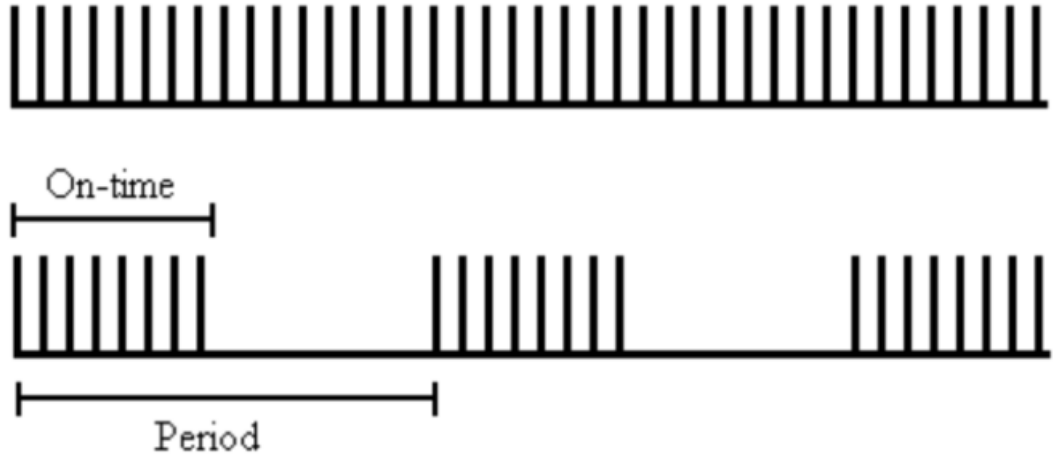

Figure 2. Duty cycle

Effective application of FES for exercise:

The effective application of FES for exercise has been extensively reviewed by many authors who outlined key criteria essential for its success (133, 138, 159). First, FES-induced muscle contractions must be sufficiently forceful, with the ability to control and consistently replicate the strength of these contractions. Second, the stimulation applied should be non-painful to ensure patient comfort. Third, intact LMN are important for transmitting stimulation effectively to produce functional muscle contraction. Finally, the FES delivery system must be acceptable and user-friendly to ensure compliance and therapeutic and functional outcomes, such as muscle strength or facilitating movement.

Additional considerations for designing an FES exercise system have been proposed, focusing on safety, selecting appropriate muscle groups for stimulation, and defining optimal stimulation parameters (55, 159, 200). These criteria also emphasize the importance of performing the required movements, which involves establishing appropriate inclusion criteria based on the level of spinal cord injury and the American Spinal Injury Association classification (133, 201). Ensuring the participant's ability to safely engage in exercise without risk of injury or harm is critical.

Measuring physiological responses during FES exercise presents distinct challenges as follows:

VO_2 Measurement:

VO_2 measurements during FES exercise typically indicate the presence of local muscle metabolic demand and exercise intensity rather than cardiorespiratory exercise. The muscle mass that is activated is determined by stimulation parameters and electrode configuration rather than central cardiovascular drive. Therefore, VO_2 is a marker of exercise intensity for comparing different FES methods and parameter combinations. When combined with heart rate and work output measurements, VO_2 enables assessment of metabolic cost efficiency across different exercise protocols, critical for identifying parameter combinations that maximize cardiovascular stress while minimizing fatigue (140)(202). Torque production indicates effective muscle recruitment and preserved neuromuscular function, an essential factor for optimizing FES parameters to enhance muscle engagement (171). In this thesis, torque measurements enable comparison of how different stimulation parameters (duty cycle, contraction frequency) affect force production and fatigue.

Discomfort and Tolerability:

Participant discomfort during FES, assessed through visual analogue scales, is a practical constraint on stimulation intensity independent of physiological capacity. Discomfort is caused by the current density, electrode placement, and pulse characteristics (138, 202). Excessive discomfort limits the intensity of stimulation, potentially preventing target metabolic or force responses. In this thesis, discomfort assessment enabled identification of parameter combinations that achieve physiological objectives within tolerable limits essential for the implementation of practical FES protocols.

One of the limitations of this study is the absence of direct assessments of muscle activity and metabolic markers, specifically electromyography (EMG) and blood lactate. Although stimulation parameters were standardized, verification of actual motor unit recruitment was not feasible. EMG could have provided objective data on muscle activation and fatigue but was omitted due to electrical artifacts and technical challenges (203). Blood lactate sampling, which would have indicated anaerobic metabolic contribution (204), was precluded by the non-invasive study design. However, the findings indicate that identical stimulation protocols can elicit divergent physiological responses across functional electrical stimulation (FES) modalities, highlighting the need for future research using direct physiological measurements, such as EMG, blood lactate, or near-infrared spectroscopy.

1.4 FES Exercise

FES has become an essential tool in rehabilitation for individuals with paralysis or paresis caused by SCI and other neurological conditions. FES facilitates muscle contractions through electrical impulses, enabling these individuals to engage in exercise despite compromised motor function. By targeting muscle metabolism, cardiovascular conditioning, and functional mobility, FES contributes to improved physical and mental health outcomes. While FES

technology and parameters have been introduced, this section explores the application of FES as a therapeutic exercise intervention, emphasizing how structured FES programs can enhance exercise capacity.

1.4.1 Acute responses to FES Exercise

The immediate physiological impact of FES exercise on individuals with paralysis encompasses a range of crucial areas, leading to various rapid physiological changes known as acute responses (52, 102, 153, 205). These responses, similar to those observed during voluntary exercise, can be influenced by factors such as the level of motor impairment and the specific characteristics of the applied electrical current. To date, most studies have focused on the application of FES to individuals with paralysis, distinguishing their physiological responses from those observed in able-bodied individuals (52, 53, 133, 206). The immediate physiological responses induced by FES exercise are primarily classified into muscular/peripheral and cardiovascular effects, both of which are vital for the therapeutic efficacy of FES (125, 207, 208). Muscular and peripheral responses involve modifications in muscle activation and metabolic function, while cardiovascular responses include changes in heart rate and circulation changes (55, 209). These acute effects play a pivotal role in the overall rehabilitation process, enhancing the potential of FES in improving exercise performance in patients with paralysis.

1.4.1.1 Peripheral/Muscular effects of FES

In the short-term, FES primarily induces acute changes by stimulating the contraction of peripheral skeletal muscles. During FES, muscle fibre recruitment differs from voluntary contractions in that FES activates muscle fibres in a non-selective, synchronous manner, recruiting both small and large motor units simultaneously, whereas voluntary contractions

follow Henneman's size principle with orderly recruitment from smaller to larger motor units. Additionally, FES causes all stimulated fibres to contract at the same time, while voluntary contractions involve asynchronous, coordinated activation patterns, with implications for exercise performance and fatigue during FES exercise sessions.

FES-induced muscle contractions significantly increase blood flow to the active muscles, facilitating oxygen delivery and the removal of metabolic by-products, which are critical for maintaining muscle performance (153, 210). However, fatigue can occur quickly during FES due to the synchronous activation of all stimulated muscle fibres and the non-physiological recruitment patterns, which lead to rapid depletion of energy substrates and accumulation of metabolic by-products (211). This fatigue can occur quickly during sustained contractions, potentially limiting the duration and effectiveness of the FES sessions. To manage fatigue during FES exercises such as isometric contractions or simple movements, parameters can be adjusted. For example, in clinical FES applications for muscle strengthening, incorporating intermittent stimulation patterns with appropriate rest intervals helps maintain muscle performance over extended exercise sessions (193, 211).

Discomfort and Pain during FES exercise:

The discomfort experienced during FES significantly influences adherence and effectiveness of rehabilitation programs (53). Often described as tingling or burning, the sensation varies widely depending on an individual's sensory awareness and the extent of neurological impairment. For individuals with partial SCI or CNS disorders, preserved sensory pathways may amplify discomfort, reduce participation and hindering effective muscle activation (54, 212). Understanding and mitigating this discomfort are essential for improving the practical applicability of FES in clinical and home-based rehabilitation settings.

The mechanisms underlying discomfort in FES are primarily attributed to the activation of cutaneous sensory fibres during electrical stimulation. Higher current amplitudes and extended stimulation sessions intensify nociceptive feedback, resulting in heightened sensations of discomfort or pain (213). Larger pulse widths exacerbate sensory discomfort by allowing deeper electrical current penetration (138). This discomfort can overshadow the therapeutic benefits of FES, leading to disengagement from the treatment. Furthermore, individuals with intact sensory pathways, such as those with partial neural injuries, may experience greater discomfort than those with complete neural disruptions, in which sensory feedback is often diminished (55). Research has consistently shown an inverse relationship between perceived discomfort and patient compliance with FES therapy, underscoring the need for individualized stimulation protocols (133, 214).

Addressing discomfort in FES requires a multi-faceted approach involving optimization of stimulation parameters, advanced electrode designs, and patient-centred strategies. Modifying parameters, such as reducing pulse widths and, current amplitudes, and utilizing frequencies in the range of 30–50 Hz, can reduce discomfort while maintaining muscle activation (202, 215). Enhanced electrode designs, such as spatially distributed or sequentially activated systems, help decrease the density of stimulation over specific cutaneous areas, thereby minimizing sensory irritation without compromising efficacy (133). Familiarization sessions, in which the stimulation intensity is gradually increased, have also been shown to improve tolerance and adherence (141). For populations with preserved sensation, customized stimulation protocols tailored to individual sensory thresholds and real-time adaptive feedback systems can significantly enhance patient outcomes and compliance (208). Addressing psychological barriers, such as fear of pain or prior negative experiences, through counselling and education

regarding the benefits of FES is equally crucial. These comprehensive strategies are essential for optimizing FES applications in individuals with intact or partially intact sensation.

1.5 Rationale of the research project

FES is a widely researched exercise-based intervention, with applications spanning dynamic activities such as FES cycling and simpler modalities such as isometric FES. FES cycling, which involves rhythmic dynamic muscle contractions, is well established for its role in oxygen uptake, lower limb peripheral health, and muscle engagement in people with paralysis and muscle weakness.

In contrast, isometric FES, which induces static muscle contractions without joint movement, is a cost-effective and accessible alternative. It may be particularly suitable during the initial phases of an exercise program when muscle conditioning is a primary focus for example, when individuals have severely deconditioned muscles that cannot tolerate dynamic movements, or when joint stability is compromised, and static strengthening is needed before progressing to dynamic exercises. Despite these advantages, the physiological efficacy of isometric FES in promoting cardiorespiratory and muscular adaptations compared to FES cycling has not been thoroughly explored. Moreover, critical stimulation parameters such as CPM and duty cycle remain understudied, further highlighting the need for further research to enhance other FES exercises protocols.

This thesis addresses these gaps by systematically comparing the physiological outcomes of FES cycling and isometric FES and investigating how specific stimulation parameters influence these responses. The outcomes of this study are expected to expand the application

of isometric FES as a feasible and effective rehabilitation tool, especially in individuals with paralysis.

1.6 General Methodology

This project was conducted in the Susan Wakil Health Sciences Building at the Faculty of Health Sciences, University of Sydney. The research encompassed three interconnected experiments designed to explore the efficacy of FES modalities in able-bodied individuals. The goal was to optimize and refine FES protocols, specifically comparing isometric FES and FES cycling, while investigating the effects of CPM and duty cycle.

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CHAPTER 2

A Systematic Review and Meta-analysis of the Aerobic and Musculoskeletal Benefits of Functional Electrical Stimulation in Individuals with Lower Limb Paralysis

PREFACE

The systematic review and meta-analysis presented in this chapter represents a comprehensive evaluation of the existing evidence regarding the physiological effects of various functional electrical stimulation (FES) exercise modalities in individuals with lower limb paralysis. While previous reviews have primarily focused on specific applications such as FES cycling, this analysis offers a broader perspective by synthesizing findings across multiple FES modalities, with particular attention to isometric FES and their comparative effects. The analysis highlights significant gaps in the current evidence base, particularly regarding the direct comparison of isometric and dynamic FES protocols under controlled conditions.

This review examines both aerobic and peripheral musculoskeletal outcomes across various FES applications, providing a multisystem perspective that better reflects the complex needs of individuals with neuromotor impairments. By establishing what is currently known and what remains to be determined about the comparative efficacy of isometric versus dynamic FES, this chapter creates the essential framework for advancing our understanding of optimal FES implementation in clinical exercise settings.

Author Attribution Statement

The co-authors of the paper *A Systematic Review and Meta-analysis of the Aerobic and Musculoskeletal Benefits of Functional Electrical Stimulation in Individuals with Lower Limb Paralysis* confirm that Prakash Dhopte had made the following contributions:

- Conception and design of the research
- Conducted literature searches, eligibility screening, and quality appraisal of the data
- Extraction of relevant data
- Interpretation of the findings
- Writing the paper and critical analysis of the manuscript

As the primary supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statements above are correct.

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ABSTRACT

Objective

To examine the acute and long-term changes of functional electrical stimulation (FES) exercise modalities on cardiorespiratory responses and peripheral musculoskeletal health in individuals with lower limb paralysis.

Data Source

Eight electronic databases: MEDLINE, EMBASE, Scopus, Cochrane Library, CINAHL, PsycINFO, SPORTDiscus, and Web of Science, encompassing a diverse collection of articles from the earliest available to September 20, 2023.

Study selection

Interventions included FES cycling, isometric FES, and other FES exercise modes. Outcome measures included aerobic and cardiorespiratory responses (e.g., oxygen consumption/VO_2), central cardiovascular function (e.g., cardiac output), and musculoskeletal health (e.g., muscle mass, bone mineral density).

Data extraction

From 4177 articles, 82 met the inclusion criteria and 20 articles were included for meta-analysis. Data were extracted on the specific muscle groups stimulated, most commonly the quadriceps, hamstrings, and gastrocnemius, as well as on the stimulation parameters. The Kmet, Lee & Cook Checklist was used to assess methodological quality.

Data Synthesis

FES cycling elicited greater increases in VO_2 (mean difference: 0.48 L/min; 95% CI: 0.42–0.55, $p < 0.00001$) compared to isometric FES (0.28 L/min; 95% CI: 0.22–0.34, $p <$

0.00001). FES cycling training improved peak VO_2 (0.16 L/min; 95% CI: 0.04–0.27) and cardiac output (3.00 L/min; 95% CI: 1.79–4.21). Individual studies reported muscle hypertrophy with isometric FES. Bone mineral density improvements required sustained, high-volume training (≥6 months, ≥5 sessions/week).

Conclusion

FES cycling demonstrated superior cardiorespiratory benefits, while isometric FES showed potential for localized muscle adaptations. However, limited direct comparisons between FES modalities with standardized parameters highlight the need for further controlled research to optimize clinical applications.

Keywords: Functional Electrical Stimulation, Lower limb paralysis, Cardiovascular outcomes, Musculoskeletal

BACKGROUND

Lower limb paralysis, often resulting from spinal cord injury (SCI) or other central neurological disorders, has a profound impact on an individual's voluntary motor control and muscle function, impacting both health and daily living (1). This condition can affect multiple systems, including bowel and bladder control, respiration, and sensory feedback, leading to muscle atrophy, cardiovascular deconditioning, metabolic dysfunction, and secondary health complications (2-5). These complications collectively reduce cardiorespiratory fitness, muscular endurance, and quality of life, while increasing the risk of chronic diseases. The magnitude of these physiological changes varies depending on the level and completeness of injury, with higher-level injuries typically resulting in more severe cardiovascular and metabolic impairments (6). Traditional exercise approaches are often insufficient for individuals with complete motor paralysis, as they are unable to voluntarily activate the muscles needed for exercise due to loss of supraspinal control (7).

Functional Electrical Stimulation (FES) delivers high-voltage electrical pulses, through surface electrodes placed on the skin, to elicit involuntary skeletal muscle contractions helping to counteract muscle atrophy in individuals with paralysis (8). FES has been demonstrated to be effective in enhancing muscle and bone health, blood circulation, tissue healing, and pain management in individuals with SCI (9, 10).

FES cycling, an active variant of FES that synchronises stimulation to generate rhythmic pedalling on a stationary bicycle, has been extensively documented for its efficacy in enhancing aerobic capacity (11) and aiding neuromuscular reactivation in the absence of voluntary movement (12). While FES cycling appears promising for promoting cardiovascular and muscular adaptations through structured, repetitive limb movements, the optimal parameters

and comparative effectiveness remain subjects of ongoing investigation. However, variations in protocol intensity, cadence, and stimulation parameters across studies make it difficult to establish standardized treatment protocols and limit the ability to draw definitive conclusions about optimal intervention strategies.

In addition to FES cycling, other FES exercise modes have been explored, including, isometric FES, FES knee extension, and neuromuscular electrical stimulation (NMES) resistance training exercise (13-15). Isometric FES generates muscle contractions without inducing joint movement, leading to sustained muscle activation under static conditions (14, 16). FES-induced contractions, including those used in leg cycling, have been shown to improve muscle bulk, metabolic efficiency, and peripheral circulation in individuals with SCI (7, 17). However, the specific exercise responses associated with isometric FES, such as oxygen consumption, and muscular adaptations, are less well-characterized compared to those associated with FES cycling.

Despite these facts, it provides distinct practical advantages for individuals with severe paralysis. The Isometric FES requires only surface electrodes and basic positioning support, eliminating the need for specialized ergometry and enabling implementation in clinical or home settings at a significantly lower cost (4). However, the fundamental question is whether isometric FES protocols can achieve the same physiological effectiveness as dynamic FES and potentially exceed it for specific outcomes. For individuals with a complete SCI, severe spasticity, or restricted joint motion, isometric exercise provides effective mechanical loading and localized circulatory stimulation without the limitations of dynamic protocols. Moreover, preliminary evidence suggests that when stimulation parameters are matched, isometric FES produces acute VO_2 responses comparable to FES cycling (14), challenging the conventional

assumption that rhythmic limb movement is essential for metabolic benefit. However, this finding remains controversial, with recent work by Frazão Murillo et al. (2022) (18) and others questioning whether true metabolic equivalence exists under varied protocols. This systematic review examines these contradictory findings by rigorously evaluating metabolic and cardiovascular responses across isometric FES studies and other FES resistance exercises, excluding protocols with extreme stimulation parameters that lack clinical feasibility.

FES knee extension elicits dynamic quadriceps contractions to produce knee extension torque, and is primarily used for restoring functional movement, modelling muscle activation timing, and supporting tasks such as standing and sitting-to-standing transitions (13, 19). NMES resistance, which is often used interchangeably with FES terminology in resistance training applications, has been shown to increase muscle mass in individuals with SCI (15, 20).

Physiological responses to both FES cycling and other FES isometric exercise modes are strongly associated with stimulation parameters such as pulse width, amplitude, stimulation frequency, and the muscle involved (21). Fornusek, Gwinn et al. (2014) provided a comprehensive comparison of cardiorespiratory responses between FES cycling and isometric FES under matched stimulation parameters, demonstrating important insights into the physiological differences between these exercise modes (14). Therefore, building upon this foundational work, a more systematic investigation of cardiorespiratory responses and peripheral musculoskeletal outcomes across different FES exercise modes continue to be valuable to deepen our understanding of their physiological mechanisms and broader clinical applications.

Objective

This systematic review aimed to examine the acute and long-term effects of functional electrical stimulation (FES) exercise modalities on cardiorespiratory responses and peripheral musculoskeletal health in individuals with lower limb paralysis, predominantly from spinal cord injury. Specifically, we investigated the changes in cardiorespiratory responses and, muscle and bone health during FES cycling and isometric FES. The goal was to identify which FES exercise modes provide more effective aerobic and lower limb peripheral benefits.

METHODS

This systematic review was conducted following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement (22). The study was registered in PROSPERO, the International Prospective Register of Systematic Reviews CRD42022351768.

Information sources

The academic databases searched were MEDLINE (Ovid), EMBASE, Scopus, Cochrane Library, CINAHL, PsycINFO, SPORTDiscus, and Web of Science, using database-specific subject headings and text terms. The initial database search was conducted from the earliest record to September 20, 2022, and a subsequent updated search was conducted on September 20, 2023, to capture recent publications. Despite this, most included studies were published before 2013, as very few recent papers met the predefined eligibility criteria. Searches were limited to the English language and human articles. Reference lists of included studies and any previous systematic reviews were checked for relevant references.

Search strategy

A health sciences librarian developed the search strategy and performed literature searches of eight databases. The MEDLINE strategy was developed with input from the project team and peer-reviewed by another researcher (Appendix 1). After the initial MEDLINE strategy was

finalized, it was adapted for use in other databases. See Appendix 1 for keywords used in the search.

Study eligibility criteria

Participants: People with leg paralysis due to central nervous system disorders, including but not limited to SCI, multiple sclerosis, cerebral palsy, hereditary spastic paraplegia and stroke.

Interventions: FES exercise delivered through the lower limbs, including FES Cycling, isometric FES, FES knee extension, FES knee rowing, and NMES resistance exercise. As VO_2 was the primary outcome of this review (with muscle hypertrophy as a secondary outcome), we specifically excluded hybrid FES cycling protocols (voluntary upper-limb exercise combined with FES-driven lower-limb activity). Voluntary arm exercise contributes to oxygen uptake, making it difficult to determine whether observed VO_2 changes result from lower-limb FES or combined arm-leg activity. Due to our objective to isolate the effects of lower-limb FES on VO_2, including hybrid studies in our protocol would have been compromised the validity of the comparisons.

Outcome measures:

The primary outcomes were measures of long and short-term exercise response and training improvements in oxygen consumption (VO_2), and peripheral benefits indicated by measures of muscle mass such as muscle volume, or thigh girth. Additionally, peripheral benefits of lower limbs such as improvement in bone mineral density were also considered as secondary outcome measures.

Settings: Hospital, multicentre clinics, academic or research institutions, laboratory, out-patient clinics, and home-based clinics.

Study designs: Randomized control trials, non-randomized clinical trials, cross-sectional, cohort intervention, before and after studies, case studies and case series were included. Systematic and narrative reviews, conferences, and abstracts were excluded.

Selection process

The complete search results from the databases were imported into Endnote, and duplicates were removed. The remaining references were imported into the Covidence database, where additional duplicates were eliminated. Two investigators (PD and SM) independently screened the title and abstracts of relevant papers, and any discrepancies were discussed and resolved through consensus by a third investigator (CF). Full-text reviews were independently performed by two reviewers (PD and SM). A final agreement for text screening was obtained by two reviewers (PD and CF).

Data extraction

Data were extracted from each study by one reviewer, and another reviewer (SM) checked and confirmed the accuracy of the data with disagreements discussed with a third investigator (CF).

Data synthesis and statistical analysis

Data were synthesised using qualitative and quantitative analysis. This review aimed to assess the physiological impacts of FES exercise modes, with a particular focus on three outcome domains: (1) acute aerobic exercise responses, (2) improvements in cardiorespiratory fitness, and (3) peripheral health or conditioning improvements in the lower limbs. Meta-analysis was conducted when it was possible to calculate the mean change and standard deviation (SD) in the outcomes of interest from baseline to post-FES exercise.

The primary outcomes included:

- Acute aerobic exercise response, assessed through changes in oxygen uptake (VO_2) from rest to the end of a single FES exercise session.

- Cardiorespiratory fitness, evaluated by changes in cardiovascular parameters following training interventions.

- Cardiac Output (CO) was extracted from studies that reported pre- and post-training measurements during either resting or submaximal exercise. Data were included in the meta-analysis if CO values were clearly reported or derivable, and if assessments were made under similar physiological conditions across timepoints.

- Peripheral conditioning improvements, such as changes in muscle mass, muscle cross-sectional area, or bone density, were measured using imaging techniques (MRI, DXA) or anthropometry.

These variables were extracted and presented as mean (±) and standard deviations (SD) (±). If the measurements were not reported directly as mean or SD, the percentage change was calculated from baseline to post-intervention period. Studies with standard errors (SE) were converted to SD to ensure consistency of the results.

The analysis centred on different types of FES exercise and, cross-sectional measurements taken during or immediately after interventions to capture acute responses. This approach allowed for comparability of the physiological stimuli generated by diverse FES modalities, measured in real-time to differentiate their impact on the body without interference from

external factors occurring after the stimulation. Similarly, training studies were conducted to understand the changes observed over an extended period.

For the acute VO2 analysis, FES modes were classified as FES cycling versus other FES exercise modes (i.e. isometric FES, knee extension, and rowing). While FES rowing shares dynamic characteristics with cycling, it was grouped with 'other' modes due to limited available studies (n=2), insufficient stimulation parameter reporting preventing dose comparison, and distinct biomechanical patterns (simultaneous bilateral versus alternating reciprocal movements). This conservative classification prioritized methodological rigor given the limitations of data.

For BMD outcomes, the distal femur was prioritized for analysis. If data for this region were unavailable or insufficient, the femoral neck was considered, followed by the proximal tibia, and then the entire lower extremity, if applicable.

For statistical analysis using the RevMan software, the random effects model was used to provide a relatively conservative estimate with a 95% confidence interval (CI) of the pooled per cent changes (23). Heterogeneity across studies was tested using I^2 and Cochran's Q test. A P-value <0.1 for chi-squared testing of the Q statistic or an I^2>50% was regarded as the existence of significant heterogeneity (23). Heterogeneity was assessed using Cochran's Q test (considering heterogeneous results with $P < 0.1$) and I^2 index. Fixed-effect models were used in analyses if the P value was greater than 0.1 and I^2 was less than 50%; otherwise, random-effect models were used. P values < 0.05 were considered significant.

A subgroup analysis was performed to gain a deeper understanding of the impact of specific study design characteristics on physiological outcomes associated with different FES exercise modes. Specifically, we focused on two important aspects: study type (acute vs. chronic) and the FES training dosage. Duration was based on whether the condition was acute or chronic/training. Acute meant the short-term response of the participants to different modes or interventions whereas chronic/training involved a number of training sessions. We categorized the studies into two groups: "acute" and "chronic/training."

Acute aerobic response: This category included studies that investigated the immediate physiological responses to different FES modes. Specifically, it examined how individuals responded to FES during or directly after its application, focusing on outcomes such as muscle activation, or other relevant effects observed within a short duration.

Exercise Training: In contrast, the chronic/training category included studies that examined the long-term physiological and functional adaptations resulting from repeated FES interventions. This category was essential for assessing how ongoing exposure to FES over multiple sessions influenced muscle strength, endurance, aerobic capacity, and neuromuscular plasticity. We analysed how FES interventions impacted individuals after several sessions, which could range from days to weeks or even months.

Stimulation Parameter Extraction

Stimulation parameter data was gathered from the Methods section as well as figure captions and supplementary materials for each study included. The extracted data included pulse width (μs), pulse amplitude (mA), stimulation frequency (Hz), number of channels and muscle groups stimulated. Both maximum device capacity data and estimated actual amplitude values

during exercise sessions were gathered when they were available. The final stimulation value or range was documented when adjustments were made dynamically based on participant tolerance or other factors such as fatigue or cadence. The derived metric known as the estimated unit charge (μC) represents the theoretical maximum stimulation dose through the product of the pulse width, amplitude, and number of stimulation channels. This metric was interpreted with caution and annotated to distinguish it from delivered dose where actual use differed from device capacity.

Methodological data quality assessment

Methodological quality was assessed independently by one reviewer (PD) using Kmet et al. (24) known as the "Standard Quality Assessment Criteria for Evaluating Primary Research Papers from a Variety of Fields." This tool was chosen for its comprehensive coverage of methodological quality and the risk of bias in both qualitative and quantitative studies. However, in our study, we used checklist for assessing the quality of quantitative studies. The checklist consisted of 14 items, with a scoring system of “yes” = 2, “partial” = 1, and “no” = 0 for each category. Categories that were not applicable to a specific study design were marked "n/a" and excluded from the summary score calculation (Appendix 2). While no second independent assessor was involved in the scoring, the reviewer cross-referenced any ambiguous ratings with the published checklist descriptors to ensure consistency and minimise bias. The summary score was used to objectively quantify the quality of each study, based on the agreement score between the two independent reviewers, with a maximum score of 1.0 (100%). Studies with stronger design and more accurate data received higher scores. Importantly, no study was excluded from the review based on its quality. In cases of any discrepancies in scoring and rating, the authors resolved them through consensus.

RESULTS

Study Characteristics: A total of 4,177 records were identified through database searching and other sources. After the removal of duplicates, 3893 studies were screened based on the predetermined inclusion and exclusion criteria and 192 studies were retrieved for full-text screening. After thorough examination of these 192 studies, 82 articles were ultimately selected for both qualitative and quantitative analysis (Figure 1. Flowchart of study selection procedure (PRISMA)). The 82 included studies encompassed 1,012 subjects with SCI and other neurological disorders, including stroke and MS. Among these participants, 709 were male and 175 were female. However, gender information was not specified for 128 participants across multiple studies, either due to incomplete reporting or studies presenting aggregate participant data without a gender breakdown. The age of the participants ranged from 18 to 67 years, although three studies did not report age. Patient and FES characteristics are presented in Supplementary Table 1 at the end of the manuscript.

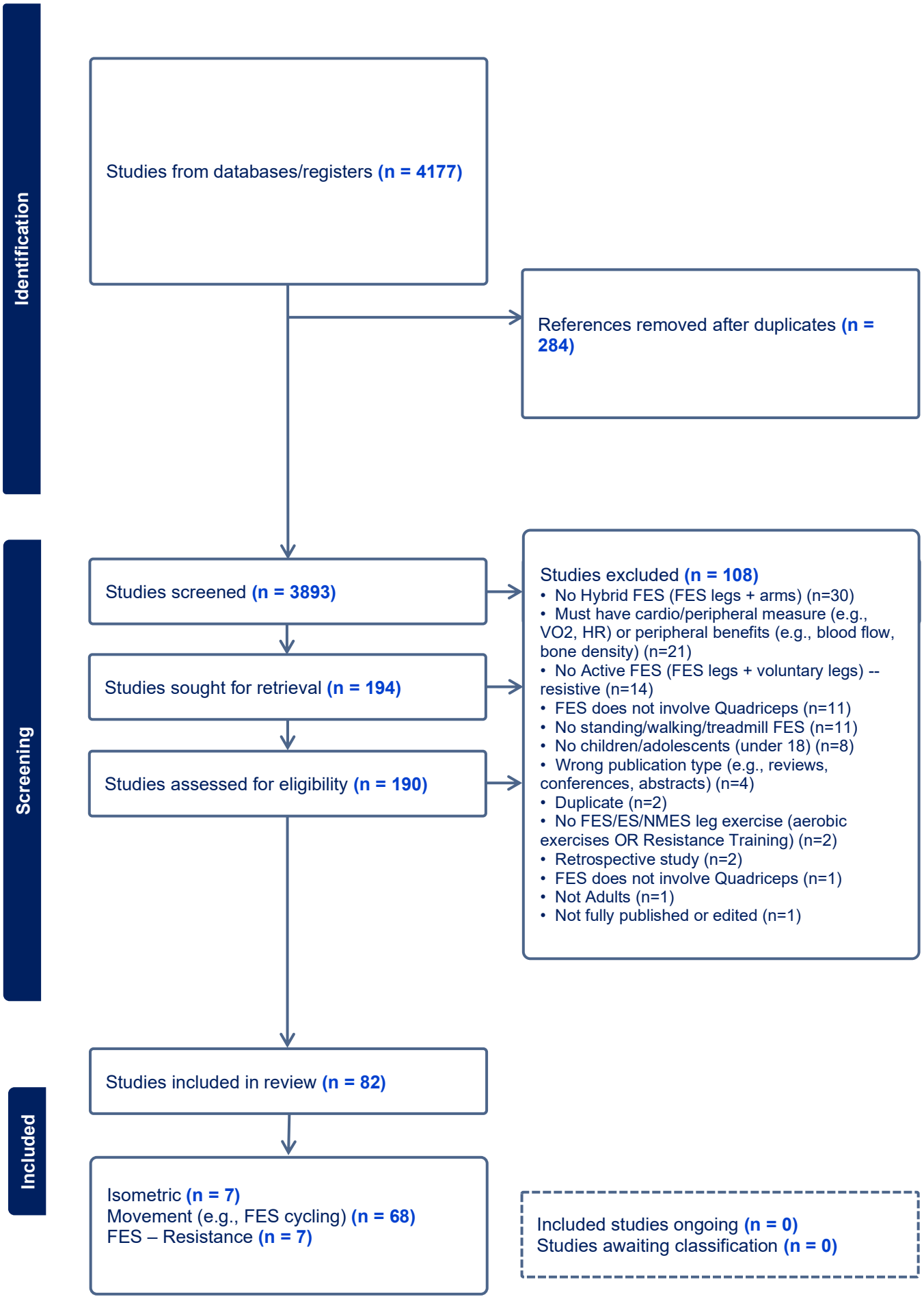
Of the 82 studies included, 80 (97%) involved participants with SCI. Twelve studies (15%) focused exclusively on individuals with paraplegia, whereas two studies included only participants with tetraplegia. Additionally, 15 studies (19%) included a mixed population of individuals with paraplegia, tetraplegia, or quadriplegia. In studies with mixed injury levels, subgroup data (e.g., paraplegia vs. tetraplegia) were extracted where available when clearly reported to ensure accurate stratification in the analysis.

The 82 studies included 1,012 subjects, of whom approximately 862 (85%) had SCI and 150 (15%) had other neurological disorders, such as stroke and MS. Among the participants with reported gender data, 709 were male and 175 were female; gender information was not included for 128 participants across multiple studies. While 80 studies (97%) focused solely

on SCI populations, the participant-level analysis indicates that our findings reflect predominantly but not exclusively SCI-specific responses to FES intervention.

Methodological Quality Assessment The quality of included studies varied widely, with scores ranging from 0.21 to 0.96 (the average score = 0.83). Common methodological limitations included small sample sizes ($n < 15$), lack of participant blinding, and incomplete reporting of stimulation protocols. Studies with lower quality scores often failed to adequately report stimulation parameters, electrode configurations, or FES exercise protocols. Appendix 2 provides an overview of individual study quality scores and detailed assessment criteria.

Figure 1: PRISMA flow diagram of the review


Identification
Screening
Included
Studies from databases/registers (n = 4177)
References removed after duplicates (n = 284)
Studies screened (n = 3893)
Studies sought for retrieval (n = 194)
Studies assessed for eligibility (n = 190)
Studies excluded (n = 108)
• No Hybrid FES (FES legs + arms) (n=30)
• Must have cardio/peripheral measure (e.g., VO2, HR) or peripheral benefits (e.g., blood flow, bone density) (n=21)
• No Active FES (FES legs + voluntary legs) -- resistive (n=14)
• FES does not involve Quadriceps (n=11)
• No standing/walking/treadmill FES (n=11)
• No children/adolescents (under 18) (n=8)
• Wrong publication type (e.g., reviews, conferences, abstracts) (n=4)
• Duplicate (n=2)
• No FES/ES/NMES leg exercise (aerobic exercises OR Resistance Training) (n=2)
• Retrospective study (n=2)
• FES does not involve Quadriceps (n=1)
• Not Adults (n=1)
• Not fully published or edited (n=1)
Studies included in review (n = 82)
Isometric (n = 7)
Movement (e.g., FES cycling) (n = 68)
FES – Resistance (n = 7)
Included studies ongoing (n = 0)
Studies awaiting classification (n = 0)

Primary outcomes

(i) Cardiorespiratory:

There were 47 studies that reported cardiovascular outcomes that included oxygen consumption, and cardiac output (CO).

Oxygen consumption (VO_2)

From the 47 articles identified, 31 studies assessed peak VO_2 and overall VO_2 outcomes. Of these, 20 studies focused on immediate (acute) responses, while 11 studies examined the effects of FES over a training period.

For the acute comparison of aerobic exercise response, 13 studies were included in the meta-analysis. Among these, nine studies (14, 25-32) examined VO_2 during FES cycling. The remaining five studies (13, 14, 33-35) employed isometric FES, FES knee extension, or FES knee rowing (Figure 2). While acute responses to isometric FES were observed across five studies, long-term outcomes were not adequately assessed, with no high-quality longitudinal studies available for inclusion. This likely reflects both the practical limitations of implementing isometric FES as a long-term training modality such as limited movement variety, joint strain, and user discomfort and a general research focus on dynamic modalities like FES cycling for cardiovascular conditioning and VO_2-based outcomes. The current evidence base for chronic isometric FES adaptations remains inadequate.

Acute comparison:

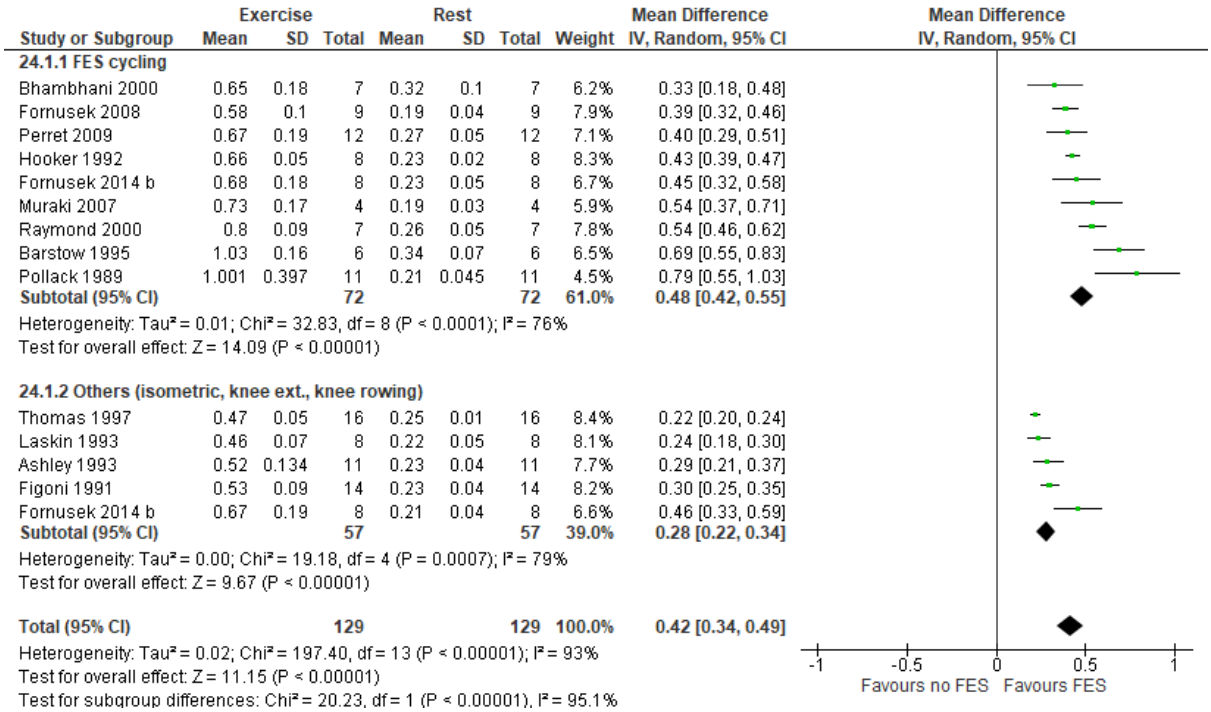


Figure 2: Forest plot of the acute change in VO2 during different types of functional electrical stimulation

The meta-analysis demonstrated a significant increase in VO_2 from resting values during FES exercise (Figure 2). For FES cycling, the pooled mean difference (MD) in VO_2 was 0.48 [95% CI 0.42–0.55] (9 studies, n = 72), with a significant effect size ($Z = 14.09$, $p < 0.00001$). For other FES modalities, the pooled MD was 0.28 [95% CI 0.22–0.34] (5 studies, n = 57), also showing a statistically significant effect ($Z = 9.67$, $p < 0.00001$). The overall effect across all FES modalities yielded a pooled MD of 0.42 [95% CI 0.34–0.49] (13 studies, n = 129), with a statistically significant overall effect ($Z = 11.15$, $p < 0.00001$) and high heterogeneity ($I^2 = 93\%$). Despite differences in study protocols and participant characteristics, the results were pooled to evaluate the general impact of FES modalities on VO_2.

Training comparison:

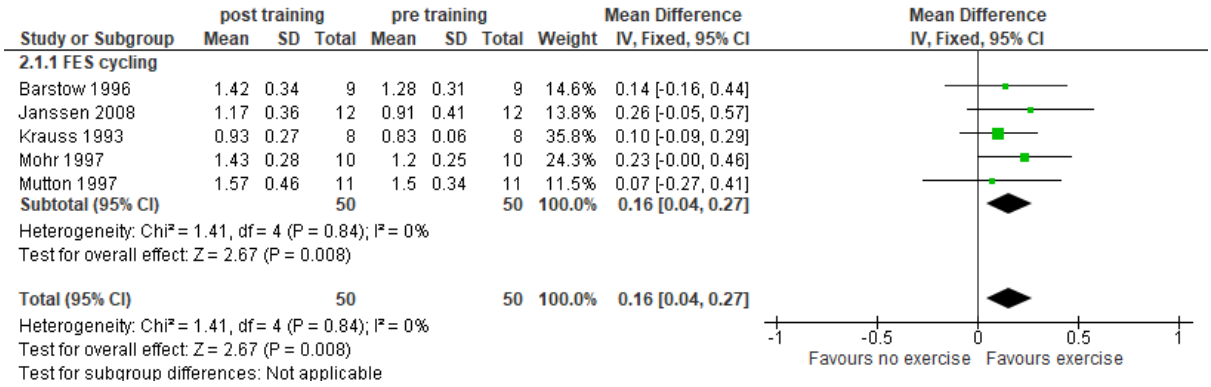


Figure 3: Forest plot of the training change in VO_{2peak} from FES cycling

Figure 3 illustrates the changes in VO_{2peak} resulting from FES cycling training. Five studies evaluated the impact of FES cycling on VO_{2peak}. The meta-analysis revealed a statistically significant improvement, with an MD of 0.16 [95% CI 0.04–0.27] (5 studies, n = 50) compared to baseline (Z = 2.67, p = 0.008). Notably, there was no heterogeneity among the studies (I^2 = 0%, p = 0.84), indicating consistency in the reported findings. To examine variations in physiological responses among FES modes, we retrieved and synthesised data about stimulation parameters and the number of muscles engaged throughout the included studies. Table 3 show a comparison of FES cycling with other FES modalities, specifically isometric contractions, knee extension, and knee rowing activities. FES cycling protocols reliably engaged several bilateral lower limb muscles, including the quadriceps (Q), hamstrings (H), and gastrocnemius (G), with stimulation delivered via approximately six channels. The mean pulse width and amplitude documented for FES cycling were 359 microseconds and 144 mA, respectively. In contrast, other FES exercise modes typically targeted a smaller muscle group set, most commonly the quadriceps, and used fewer channels (average of 4). These modes reported slightly lower average pulse width (288 µs) but comparable amplitude (150 mA).

These data represent maximum stimulator capabilities, though the actual output in practice may vary depending on the study protocol. Table 2 also reflect whether bilateral muscle groups were activated and provide details on stimulation configuration. Across 20 studies evaluating acute

VO_2 responses, FES cycling consistently utilised bilateral stimulation of large lower-limb muscle groups (quadriceps, hamstrings, and gastrocnemius) using 6 channels. Pulse widths ranged from 250–500 μs, and amplitudes typically reached 130–150 mA, though actual intensities were often ramped to participant tolerance. Stimulation doses were highest in FES cycling studies, with values up to 792 μC, reflecting broader muscle coverage and higher session intensities. Other FES exercise modes used fewer channels (2–4), more localized targeting, and lower total stimulation doses (90–360 μC).

Table 2. Stimulation Parameters across FES exercise modes evaluating acute VO_2 responses

Author	Populations	Exercise/Test Type	Max Pulse Width (μs)	Max Amplitude (mA)	Actual Amplitude Used (mA)	Frequency (Hz)	Muscles Involved	Channels	Stimulation (μC)
FES Cycling Studies									
Bhambhani 2000 (26)	SCI (C5 to T12))	Incremental FES cycling test to volitional fatigue with NIRS	NR	132	NR	50	Q, G	4	
Fornusek 2008 (27)	SCI (T4 through T10)	Submaximal, steady-state FES cycling at 3 cadences	250	140	Ramped to max	35	Q, H, G	6	210
Perret 2009 (30)	Complete paraplegic	Incremental exercise test (IET) – gas exchange threshold	500	150	Ramped, not stated	20	Q, H, G	6	450
Hooker 1992 (28)	SCI (quadriplegics, C5-C8/T1)	Subpeak FES cycling + arm exercise	375	130	NR	35	Q, H, G	6	293
Fornusek 2014 (14)	paraplegics (T4–T11)	FES cycling vs. isometric FES (crossover)	300	140	140 (ramped from 40)	35	Q, H, G	6	252
Muraki 2007 (29)	paraplegics (T5–T12)	Prolonged submaximal FES cycling	400	140	Up to 140; adjusted for cadence	30	Q, H, G	6	336

Raymond 2000 (32)	SCI (T5–T11)	Submaximal steady-state FES cycling	375	140	NR	35	Q, H, G	6	315
Raymond 2002 (36)	Paraplegics	Multiple submaximal bouts (12-min)	250	140	NR	35	Q, H, G	6	210
Barstow 1995 (25)	SCI	Submaximal steady-state (gas exchange kinetics)	NR	132	NR	30	Q, H, G	6	
Pollack 1989 (31)	SCI (C4-T6)	Submaximal FES cycling	400	130	NR	30	Q, H, G	6	312
Barstow 2000 (37)	paraplegia (T4 to T12-L1)	Submaximal steady-state FES cycling	NR	132	NR	30	Q, H, G	6	
Figoni 1993 (38)	SCI	Submaximal FES cycling	NR	130	Max 130 stated	—	Q, H, G	6	
Mate 2021 (39)	MS	Submaximal FES cycling	300	126	NR	35	Q, H, G, G	8	302
Fornusek 2014 (40) for MS study	MS	FES cycling for MS – feasibility and strength outcomes	300	140	91 (Q), 86 (H), 69 (G)	35	Q, H, G	6	164
Janssen 2008 (41)	SCI	Progressive intensity FES cycling	500	300	NR	35	Q, H, G, GS, TA	10	260
Other FES Modes									
Thomas 1997 (35)	SCI	FES knee flexion/extension	300	150	NR	50	Q, H, G, TA	8	360
Laskin 1993 (34)	SCI	FES-rowing: stimulation only	—	—	NR	—	Q, H	4	—
Ashley 1993 (33)	SCI	Loaded vs. unloaded FES knee extension	250	160	NR	50	Q	2	80

Figoni 1991 (13)	SCI	Graded FNS knee extension (0–15 kg/load) – VO_2 + hemodynamic	300	150	Max 150 stated	35	Q	2	90

Q = Quadriceps, H = Hamstrings, G = Gastrocnemius, TA = Tibialis Anterior, GS = Gluteus/Soleus.
Stimulation (μC) = Theoretical charge = pulse width × amplitude × channels. This reflects maximum stimulator output capacity.
Actual Amplitude Used (mA) = Reported or inferred current applied during exercise, often ramped from a lower baseline.
NR: Not Reported

Changes (training) in Cardiac Output (CO)

Out of 13 studies examining cardiac output (Q) changes, only two (41, 42) specifically investigated training-induced adaptations with FES cycling and met inclusion criteria for meta-analysis. While meta-analysis is typically conducted with a larger number of studies, these two studies were pooled due to their comparable study designs (pre-post interventions), participants characteristics, similar outcomes (CO in L/min), and consistent duration (6-8 weeks of FES cycling), as recommended by Ryan et al. (2016) (43). Figure 4 illustrates the training-induced changes in CO following FES cycling. The meta-analysis revealed a significant effect with a pooled mean difference of 3.00 [95% CI 1.79–4.21] (2 studies, n = 20; Z = 4.87, p < 0.00001). The absence of heterogeneity among studies (I2 = 0%) contributes to the robustness of these findings, indicating a consistent physiological adaptation to FES cycling training.

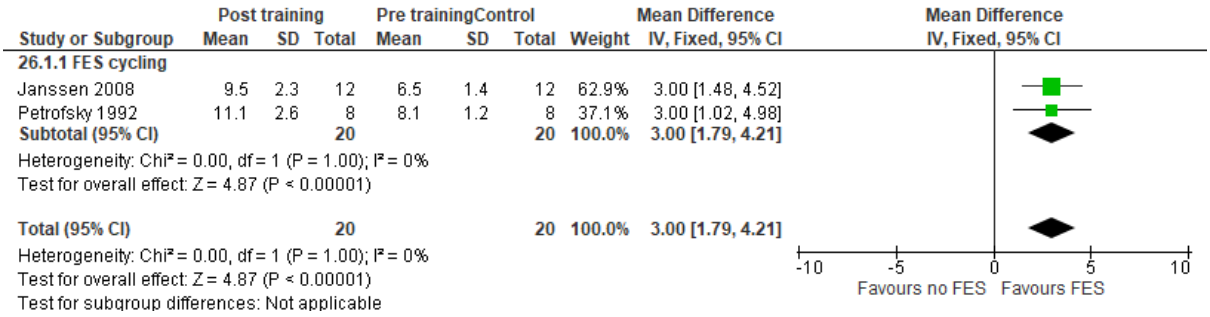


Figure 4 Forest plot for the training changes in CO during FES cycling

(ii) Lower limb physiological health:

A total of 64 studies were analysed to evaluate the peripheral physiological benefits of FES exercise modes, with studies specifically examining lower limb muscle morphology. These studies measured changes in muscle cross-sectional area (CSA), muscle volume and leg composition, details of which along with outcome measurements i.e. MRI, CT, US are reported in Table 3. Among these studies, 6/17 used MRI, 4/17 used DXA, 3/17 used CT, 2/17 used USG, 1/17 used computer software (Bioquant 95, R&B Biometrics, Inc.), and one used whole leg.

Increase in CSA have been consistently reported in studies using both FES cycling and isometric FES. Sloan et al. (1994) (44) and Scremin et al. (1999) (45) reported increases in quadriceps and total thigh CSA using CT, wheras Demchak et al. (2005) (46) showed a 63% increase in muscle fibre CSA using biopsy-derived analysis. Similarly, three studies reported CSA improvements following isometric or resistance-based FES protocols assessed via MRI or ultrasound (47-49). Body composition, specifically leg muscle mass and thickness, was evaluated in four studies using DXA. Dolbow and Credeur (2018) (50) observed an increase in thigh thickness, while two studies reported gains in lean leg mass and lower extremity muscle volume (51, 52). Muscle volume was examined in three studies. Johnston et al. (2016) (53) reported mid-thigh muscle volume increases following both low- and high-cadence FES cycling, with greater volume gains at lower cadences. Ryan et al. (2013) (20) observed substantial quadriceps volume increases following NMES resistance training. Muscle thickness was measured using B-mode ultrasound by Skiba et al. (2021) (54), who reported no significant changes over the intervention period. Where available, absolute values or percentage changes were recorded in Table 3. Based on this comprehensive analysis, FES exercise has demonstrated clinically significant improvements in lower limb muscle morphology, with CSA gains of 10-47% from FES isometric protocols and 9-39% from FES cycling. Lower-cadence FES cycling (20 RPM) increased muscle volume compared to higher cadences (20.4% vs 10.7%), while body composition increased by 3-10% across measures. These morphological enhancements, particularly the up to 63% increase in muscle fibre CSA, are significant adaptations that likely contribute to functional benefits. The evidence suggests that FES isometric or low-cadence cycling protocols (20 RPM) with 15–30 minutes durations for optimal muscle preservation and hypertrophy in individuals with SCI.

Table 3: Muscle morphological changes following different FES exercise modes: comparative analysis of measurement techniques and outcomes

Outcome	**Author/year**	**Populations**	**Measure**	**Mode (FES Cycling / Isometric / NMES RT)**	**Muscles** Targeted	**FES exercise duration (min)**	**Results**
CSA							
	Arija-Blazquez et al. 2014 (47)	SCI (T4–T12)	MRI	FES isometric	quadriceps femoris	47	*↑ 10.08% (Intervention), ↓14.76% (Control)
	Dudley et al. 1999 (10)	SCI	MRI	FES isometric (with/without weight at knee)	quadriceps femoris	15	↓ after SCI, ↑ 20% after intermittent high-force FES
	Gorgey et al. 2017 (49)	SCI	MRI	NMES resistance training	Whole thigh, knee extensors, knee flexors, adductors	30	↑ 13% (whole thigh), ↑18% (knee extensors), ↑ 3% (knee flexors), ↑ 13% (adductors)
	Sloan et al. 1994 (44)	SCI	CT	FES cycling	Quadriceps Hamstrings (total area)	30	↑ 48.1 cm^2 → 52.6 cm^2 (quadriceps), ↑ 90.4 cm^2 → 104.7 cm^2 (total)
	Block et al. 1989 (55)	paraplegia	Quantitative CT	FES cycling	Thigh muscle area	15	↑ 10.6 cm^2
	Scremin et al. 1999 (45)	SCI	CT	FES cycling	Vastus lateralis, vastus medialis-intermedius, rectus femoris, Sartorius, adductor magnus-hamstrings	30	↑ 39% (VL), ↑31% (VM), ↑ 31% (RF), ↑ 22% (S), ↑ 26% (AMH)
	Bochkezanian et al. 2018 (48)	SCI	Ultrasonography	FES isometric	quadriceps femoris	15	↑ 47%
	Everaert et al. 2021 (56)	SCI (C4–T4)	Circumference measurements	FES cycling	Thigh muscle	15–45	↑ up to 16%

	Mahoney et al. 2005 (57)	SCI (C5-T10)	MRI	FES knee extension	quadriceps femoris	30	↑ 37% CSA in both thighs
muscle fibre cross- sectional area (CSAf)	Demchak et al. 2005 (46)	SCI	Computer software – (Bioquant 95, R&B Biometrics, Inc.)	FES cycling	quadriceps femoris	30	↑ 63% in CSAf
Body composition (Leg Only)							
	Dolbow et al. 2018 (50)	SCI	DXA	FES cycling	Thigh thickness (VL)	20–63 (gradual increase)	↑ 1.3 cm (1.3 cm → 2.1 cm
	Griffin et al. 2009 (51)	paraplegia and tetraplegia	DXA	FES cycling	Leg lean muscle mass	30	↑ 3.3% (from 96.8 ± 5.61 lb to 100.0 ± 5.47 lb)
	Skold et al. 2002 (52)	SCI-Tetraplegic	DXA	FES cycling	Lower extremity muscle volume	30	↑ 10% (mean increase of 1300 cm^3)
Muscle volume							
	Johnston et al. 2016 (53)	SCI (C4-T6)	MRI	FES cycling (Low and high cadence)	Midthigh muscle volume	56	↑ 20.4% (20 RPM) and 10.7% (50 RPM)
	Ryan et al. 2013 (20)	SCI	MRI	NMES-induced resistance training	Quadriceps	---	↑ 39% ± 27% (pre vs post, 618 ± 343 vs 815± 399cm^3)
Muscle thickness							
	Skiba et al. 2021 (54)	SCI	B-mode ultrasound	FES cycling	Quadriceps	5 - 15	↔ 7.6% in the FES group and 19.7% in FES + BFR group

*↑ - Increased, ↓ - Decreased, ↔ - No significant change
** weight in pounds (lb)

Bone Mineral Density:

Table 4 summarizes 16 studies that investigated the effects of FES on the BMD of the lower limbs. Eleven studies used DXA, while the remaining studies utilized CT or dual-photon absorptiometry. Interventions lasted 3 to 12 months, with BMD assessed at sites including the distal femur, proximal tibia, femoral neck, lumbar vertebrae, and the whole body. Training frequency ranged from 2.9 to 5 sessions per week.

FES cycling was generally found to maintain or modestly improve BMD, particularly at higher intensities and over extended periods (five sessions per week over 12 months) (58, 59). Improvements were noted at sites such as the distal femur, proximal tibia, and whole body. For example, Mohr et al. (1997) (60) observed a 10.2% increase in proximal tibia BMD, whereas Deley et al. (2017) (58) reported a 19.4% increase at the femoral neck with FES knee extension training. However, some studies have reported no significant BMD changes (44, 53, 61), suggesting that longer durations and higher loading may be needed to elicit bone adaptations. Interestingly, Arija-Blazquez et al. (2014) reported a 7.6% decrease in whole hip BMD following EMS with isometric muscle contractions over 14 weeks (47). Similarly, results for FES knee extension protocols were mixed, with Rodgers et al. (1991) (62) reporting no change in trabecular bone density, while Deley et al. (2017) (58) observed significant BMD improvements.

Table 4: Bone Mineral Density changes following FES exercise modes: comparative analysis across different skeletal sites and FES exercise modes

Author and Year	Populations	Duration	Intervention	Outcome	Measurement Sites	BMD changes
Arija-Blazquez et al (63)	SCI (T4–T12)	14 weeks	EMS with isometric muscle contraction	DXA	Whole hip	↓ 7.6% (0.92 → 0.85 g/cm²)
Ashe, 2010 (64)	SCI	18 weeks, thrice weekly	FES cycling	DXA leg scans	both legs	*↑ by– 1 -16%
BeDell, 1996 (61)	SCI	3 months, 3 times per week	FES cycling	DXA	Bilateral trochanters (T), Wards triangles (WT), and femoral necks (FN)	↔ T (0.61 ± 0.08 → 0.61 ± 0.10), ↔ WT (0.71 ± 0.18 → 0.70 ± 0.16), ↔ FN (0.78 ± 0.14 → 0.82 ± 0.18)
Bloomfield, 1996 (65)	SCI (C5-T7)	3 months, (average 5.9 +/- 1.0 weeks)	FES cycling	DXA.	distal femur	↑ 18%
Chen, 2005 (66)	SCI	6 months, 5 days/week	FES cycling	DXA	distal femur, proximal tibia	↑ 11.1% ± 0.80%, ↑ 12.9% ± 2.24% (but ↓ after discontinuation)
Dolbow, 2014 (67)	SCI (T6)	12 months, 2.9 sessions/week	FES cycling	DXA	Whole-body BMD	↑ 9.5% (0.934 → 1.023 g/cm²)
Eser, 2003 (68)	para- and tetraplegic	6 months	FES cycling	CT	Tibial cortical bone	↓ 0.3% ± 0.6% (intervention), ↓ 0.7% ± 0.8% (control)
Frotzler, 2008 (59)	Complete SCI	12 months, 5/week	FES cycling	pQCT	Trabecular and total BMD, (femoral shaft, Tibia)	↑ 14.4+21.1%, ↑ 7.0+10.8%, ↓ 1.8+3.0%
Johnston, 2016 (53)	SCI (C4-T6)	6 months, 3/week	FES cycling (low: 20 rpm, high: 50 rpm)	DXA	Distal femur	↔ Low cadence: −4% (0.67 ± 0.37 → 0.63 ± 0.32, p = 0.20), ↔ High cadence: −3% (0.80 ± 0.20 → 0.70 ± 0.20, p = 0.12)
Lai, 2010 (69)	SCI	3 months, 3/week	FES cycling	DXA	Distal femur	↓ (Significant (0.913 ± 0.058 → 0.845 ± 0.090 g/cm²)
Leeds, 1990 (70)	Quadriplegia	7 months, 3/week	FES cycling	Dual photon absorptiometry	Ward triangle femoral neck, and greater trochanteric	↔ (WT: 57.43 ± 8.34 → 57.07 ± 11.51, FN: 66.65 ± 5.39 → 66.15 ± 8.68, GT: 57.67 ± 8.90 → 55.13 ± 10.50)
Mohr, 1997 (60)	SCI	12 months	FES cycling	DXA	Proximal tibia	↑ 10.2% (0.49 ± 0.04 → 0.54 ± 0.04 g/cm²)
Pacy, 1988 (71)	paraplegia	32 weeks. 5/week	FES cycling	Dual photon absorptiometry	Lumbar vertebra, right femoral shaft	↑ 4.57% (3.45–5.61), ↓ 4.23% (3.88–4.94)
Sloan, 1994 (44)	SCI	12 months	FES cycling	DXA	Ward's triangle, femoral neck	↔

Deley, 2017 (58)	SCI (T4-T5	12 months	FES Knee extension (KE)	DEXA	BMD - Femoral neck	↑ 19.4% (0.534 → 0.638 g/cm²)
Rodgers, 1991 (62)	SCI	3 months, 3/week	FES Knee extension (KE)	CT	Trabecular bone density ↔	↔

*↑ - Increased, ↓ - Decreased, ↔ - No significant change

DISCUSSION

This systematic review and meta-analysis evaluated cardiorespiratory and musculoskeletal outcomes of FES exercise in individuals with lower limb paralysis, focusing on acute VO_2, cardiac output, muscle morphology, and bone mineral density. FES-induced VO_2 should not be considered as aerobic capacity, as it reflects the metabolic cost of electrical stimulation and is constrained by peripheral muscle fatigue rather than central cardiovascular factors. VO_2 responses during FES depend on protocol parameters such as muscle selection and stimulation settings, rather than individual fitness, with typical values ranging from 0.5–1.0 L/min. Training adaptations are mostly peripheral, not central. According to this review, VO_2 measurements indicate acute metabolic demand for stimulation protocols, not cardiorespiratory fitness. Increased VO_2 during cycling reflects increased muscle recruitment, while matched protocols yield similar VO_2 responses across modalities. To the best of our knowledge, this is the first meta-analysis to provide quantitative comparisons between different FES modalities specifically in spinal cord injury, as 85% of included studies involved SCI participants, with the remainder including other causes of lower limb paralysis.

Key Findings

While the cardiorespiratory benefits of FES exercise are well-established, this review provides the first quantified comparison of effect sizes between FES modalities. FES cycling demonstrated a

larger magnitude of VO_2 response (MD = 0.48) compared to other FES approaches (MD = 0.28) in acute interventions across 13 studies. This quantitative difference between modalities had not been previously established through meta-analysis.

FES interventions produced favourable cardiac output adaptations over time. FES cycling training enhanced cardiac output, with studies reporting increases of +37% (42) and +32% (41). While Petrofsky and Stacy (1992) (42) found no significant cardiac output difference between 3-month and 6-month training periods at matched workloads, Mohr et al. (1997) (72) observed that cardiopulmonary capacity became the limiting factor after 6 months, with cardiac output plateauing despite continued VO_{2max} improvement (+23% at 12 months), suggesting shifting physiological limitations over extended training periods.

Owing to insufficient comparable data, we were unable to perform a meta-analysis of musculoskeletal outcomes in the lower limbs. However, our systematic narrative review of 64 studies examining muscle morphology revealed consistent increases in muscle CSA (10-47% with FES isometric protocols, 9-39% with FES cycling) and muscle volume (10-39%), with individual studies reporting specific improvements in vastus lateralis (39%), vastus medialis (31%), and rectus femoris (31%). Regarding BMD, FES cycling demonstrated variable effects across studies, with more pronounced improvements typically associated with higher-intensity and longer-duration protocols.

While Van der Scheer et al. (2021) demonstrated that FES cycling elicited significant cardiorespiratory responses, our systematic analysis advances this knowledge by providing the

first quantitative comparison showing FES cycling produces 71% greater acute VO2 responses than other FES exercises (MD = 0.48 vs 0.28). However, our review was unable to determine whether these differences result from FES exercise characteristics versus variations in stimulation parameters across studies, as insufficient data was available for subgroup analysis comparing stimulation parameters, representing a knowledge gap requiring further investigation.

Acute cardiorespiratory responses to FES exercises

Our meta-analysis showed that acute FES cycling elicited a mean VO_2 increase of 0.48 L/min [95% *CI*: 0.42-0.55], which was higher than the 0.28 L/min [95% *CI*: 0.22-0.34], observed with isometric FES and other FES exercise modes. FES cycling demonstrated superior acute cardiorespiratory responses, but this appears attributable to differences in implementation rather than inherent exercise superiority. FES cycling protocols generally recruited a greater muscle mass (e.g., bilateral quadriceps, hamstrings, and gastrocnemius) compared to other FES exercise modes. This finding from our systematic analysis indicates that the magnitude of cardiorespiratory response depends primarily on total stimulation dose and muscle recruitment area, regardless of whether movement occurs, a pattern that emerged from comparing effect sizes across the included studies rather than from individual study conclusions.

Although VO_2 responses were used for comparisons, this outcome may not fully capture the intended benefits of isometric or knee extension FES, which are primarily designed to promote local muscle hypertrophy, torque production, or joint stability rather than cardiorespiratory responses. However, VO_2 remains a valid comparative measure since oxygen consumption directly reflects the total muscles recruited, and metabolic work performed. Greater muscle mass

engagement generates significantly higher VO_2, making it an objective indicator of exercise intensity across different FES exercise regardless of their primary therapeutic objective.

This challenges the traditional view, derived largely from voluntary exercise literature, that rhythmic limb movement is essential for achieving aerobic benefit (11, 14). While voluntary dynamic exercise enhances perfusion through activation of the muscle pump (73), this mechanism may be limited during FES exercise, in which contractions are externally imposed and preload is not significantly augmented (37, 74). Moreover, FES-induced exercise, whether dynamic or isometric, is generally limited by the rapid onset of muscular fatigue (45, 75).

While our meta-analysis demonstrated superior acute VO_2 responses with FES cycling (0.48 vs 0.28 L/min), the single study by Fornusek et al. (2014) that matched stimulation parameters found no significant differences between modalities. However, this limited evidence is inadequate to conclude that FES exercise mode is irrelevant to physiological outcomes. Our review reveals a critical understanding gap: we were unable to perform subgroup analyses comparing stimulation parameters due to heterogeneous reporting across studies. Therefore, if the observed differences between FES modalities result from inherent exercise characteristics or variations in stimulation protocols remains uncertain and requires future investigation with standardized parameters. Our findings highlight the need for future studies directly comparing FES modalities under matched stimulation conditions to determine the relative contributions of movement versus stimulation intensity to physiological adaptations.

Long-Term cardiorespiratory responses to FES training exercises

Our meta-analysis demonstrated a statistically significant improvement in VO_2 of 0.16 L/min [95% CI: 0.04–0.27] following long-term FES training, with no heterogeneity across included studies (I^2 = 0%). This suggests a consistent, although modest, training-induced aerobic benefit in individuals with lower limb paralysis (75, 76).

The physiological mechanisms underlying these VO_2 improvements appear to be predominantly peripheral. Barstow et al. (1996) and Hooker et al. (1992) found that increased arteriovenous oxygen difference (A-VO_2 diff), rather than enhanced cardiac output, accounted for improved oxygen kinetics following FES training (28, 77). This indicates that the observed VO_2 gains are more reflective of enhanced peripheral oxygen utilization, rather than central cardiovascular remodelling.

The predominance of peripheral adaptations over central ones highlights a key difference between FES training and voluntary exercise, where central cardiovascular changes are more significant. The limited central adaptations with FES training may explain the modest magnitude of VO_2 improvements observed across studies, as central cardiovascular adaptations (increased stroke volume and enhanced cardiac contractility) are largely absent due to the lack of autonomic cardiovascular control in many individuals with SCI (76).

While isometric FES produces primarily peripheral adaptations, these changes are critically important for health in SCI. Enhanced peripheral insulin sensitivity directly addresses metabolic dysfunction including insulin resistance and type 2 diabetes (78), while peripheral vascular adaptations reduce cardiovascular disease risk, the leading cause of mortality in chronic SCI (79).

Localized muscle hypertrophy reduces pressure ulcer risk and provides mechanical loading that attenuates bone loss (80). These peripheral adaptations address the primary health issues in the SCI population, demonstrating that substantial health benefits can be achieved without significant central cardiovascular changes. The predominant peripheral nature of isometric FES does not diminish its clinical value for improving health outcomes in individuals with SCI.

Long-term FES cycling training produced significant increases in cardiac output (MD = 3.00 L/min), suggesting some degree of central cardiovascular adaptation. These CO improvements likely reflect enhanced ventricular filling via increased plasma volume and potentially improved myocardial contractility with sustained training (41). However, the plateau in CO improvements after six months of training noted by Mohr et al. (1997) (72) suggests that these central adaptations may have physiological limits in the absence of intact autonomic control.

In FES cycling, VO_2peak is determined by the electrically stimulated muscle mass and stimulation parameters, not by cardiorespiratory fitness. Thus, post-training VO_2peak increases reflect protocol-specific effects, not true aerobic gains. Voluntary exercise improves aerobic fitness through central cardiovascular adaptations, while FES training induces primarily peripheral changes mainly increased arteriovenous oxygen difference and muscle oxidative capacity. Therefore, VO_2peak improvements after FES training indicate enhanced peripheral oxygen extraction, not central cardiovascular adaptation, underscoring a fundamental distinction from traditional aerobic training.

Longitudinal adaptations to isometric FES training remain less thoroughly characterized than those to FES cycling. The absence of studies directly comparing long-term cardiorespiratory responses

between these FES modes of exercises represents a significant gap in the literature. Based on acute physiological responses and established principles of exercise physiology, it is reasonable that isometric FES training may elicit peripheral muscular adaptations such as increased capillarization, mitochondrial density, and muscle fibre recruitment, similar to those observed with FES cycling, provided sufficient intensity and volume are achieved. Central cardiovascular adaptations are primarily based on the overall metabolic demand and the increase in cardiac output, rather than the movement pattern alone. Although rhythmic contractions can enhance venous return via the muscle pump, isometric contractions involving large muscle groups and high stimulation intensities may still require substantial circulation demands. The magnitude of cardiovascular adaptation is more closely correlated to the level of muscle activation and metabolic stress than to whether the contractions are rhythmic or static.

Peripheral Benefits: Muscle and Bone Health

Van der Scheer et al. highlighted significant effects of FES cycling on muscle health, including increased muscle CSA (75). Our review supports improvements in muscle CSA with FES cycling, although fibre-type transitions and endurance effects were not consistently reported.

Our review highlighted substantial variability in the effects of FES interventions on muscle size and composition. While both isometric FES and FES cycling were associated with increases in muscle CSA and mass, the magnitude of these changes varied based on factors such as mode of FES application (cycling vs. isometric), stimulation parameters (e.g., amplitude, frequency, pulse width, contraction duration), training duration, and measurement techniques used to assess outcomes. For example, Arija-Blazquez et al. (2014 (47)) reported a 10.08% increase in quadriceps

CSA following isometric FES, while Sloan et al. (1994) (44) reported a 9.3% increase in quadriceps CSA following a 3-month FES cycling intervention, with sessions gradually increasing to 30 minutes per session over time. These findings suggest that both FES exercise modes can counteract muscle atrophy, however the degree of muscle adaptation depends heavily on the load intensity, cadence, and torque produced.

Isometric FES appeared to be particularly effective in promoting muscle hypertrophy. Bochkezanian et al. (2018) (48) reported a 47% increase in quadriceps CSA following a 12-week high-intensity isometric NMES training protocol. This indicates that muscle hypertrophy is dependent on sustained, high-load protocols. Consistent with other reports (44, 53, 81), the extent to which FES can counteract atrophy is strongly influenced by training load, torque production, and cadence, with higher torque or low cadence cycling protocols producing the greatest hypertrophic responses.

The effects of FES exercises on BMD were less consistent, with some studies reporting significant improvements and others showing no change. FES cycling has been associated with increases in BMD at the distal femur and proximal tibia, with gains ranging from 1% to 16% (64, 66). Alternative FES exercise modes, such as FES knee extension, also showed promise in improving BMD. Deley et al. (2017) (58) reported a 19.4% increase in femoral neck BMD following 12 months of FES rowing, suggesting that dynamic resistance movements may offer greater benefits than cycling alone. However, the variability in BMD outcomes across studies highlights the influence of skeletal site, training intensity, and mechanical loading pattern. For instance, Eser et

al. (2003) (68) found no significant changes in tibial cortical BMD following FES cycling, indicating that certain skeletal sites may be less responsive to FES.

Collectively, these findings suggest that future protocols aiming to improve BMD in SCI populations should emphasize high-load, site-targeted approaches, such as FES knee extension, rather than relying solely on cycling. Optimizing stimulation intensity and mechanical strain appears to be more important than exercise modality.

Critical Analysis of Conflicting Evidence

The review highlights several conflicting findings that warrant critical analysis. The most in the literature was about acute VO_2 responses. Our pooled analysis demonstrated significantly greater mean VO_2 acute increases during FES cycling compared with isometric FES exercise and other FES exercise modes. These findings are consistent with several FES cycling studies demonstrating significant VO_2 responses (26, 28, 31). In contrast, isometric and knee-extensor studies generally demonstrated smaller increases (33, 35). Our stimulation parameter analysis (Table 2) shows that FES cycling protocols consistently utilized greater muscle recruitment and higher total stimulation doses compared to isometric methods. However, Fornusek et al. (2014) reported equivalent VO_2 responses when stimulation parameters were carefully matched between FES cycling and isometric FES conditions (14). The high heterogeneity (I^2 = 93%) further supports the interpretation that variability in stimulation parameters, participant characteristics and protocol design, not FES exercise modes, explains much of the conflict.

A major challenge in interpreting the evidence was the lack of consistent reporting of stimulation protocols across studies. In particular, the actual amplitudes delivered during exercise (as opposed to maximum device capacity), duty cycles, contraction durations, and muscle targeting strategies were often missing or only qualitatively described (e.g., “ramped to tolerance”). Although pulse width and maximum amplitudes were reported in most studies, without precise information on delivered intensities, comparisons of dose response responses across modalities remain unreliable. Such inconsistency limited the ability to conduct subgroup analyses to determine optimal stimulation configurations for hypertrophy, cardiovascular adaptation, or functional recovery. Future FES trials should adopt standardized reporting frameworks that specify the delivered stimulation parameters, the total session duration, and the targeted muscle groups to enhance reproducibility and facilitate meaningful comparisons.

Clinical Implications

The findings of this review offer several practical implications for clinicians prescribing FES interventions for individuals with lower limb paralysis. Our meta-analysis demonstrated that FES cycling consistently produced the highest increases in oxygen uptake (VO_2 = 0.48 L/min), supporting its utility as a cardiorespiratory conditioning strategy. For muscle hypertrophy goals, both FES cycling and isometric FES demonstrated substantial effectiveness, with CSA increases ranging from 9-63% for FES cycling protocols and 10-47% for isometric FES exercise protocols. Rather than FES exercise mode, the magnitude of muscle adaptations appears more dependent on stimulation intensity and muscle recruitment area.

These results suggest that FES mode alone is not the critical determinant of physiological outcomes. Rather, stimulation parameters, specifically pulse width, amplitude, duty cycle, and muscle mass recruited, are more influential in driving adaptations.

Study limitations and future directions

While this review provides valuable insights into the effectiveness of FES exercise modes, several limitations must be acknowledged. A major limitation was the large heterogeneity among studies, particularly in acute VO_2 outcomes (I2 = 93%). This heterogeneity was due to many reasons such as participant diversity (injury levels C4-T12, ASIA A-D classifications, age range 18-67 years, and baseline muscle mass variations), extensive stimulation parameter differences (pulse width 150-500 μs, amplitude 10-300 mA, frequency 20-60 Hz, channels 2-10), and varying exercise protocols. Baseline muscle mass differences were particularly significant, as participants with recent versus chronic injuries and varying FES experience demonstrated substantial differences in muscle volume, directly influencing VO_2 responses since greater muscle mass recruitment generates higher oxygen consumption.

Despite employing random-effects modelling, the high heterogeneity substantially limits the strength of pooled conclusions and indicates that standardized protocols are needed. The heterogeneity paradoxically supports our hypothesis that stimulation parameters and total muscle mass recruited, rather than exercise modality, are the primary determinants of physiological response. Therefore, findings should be interpreted with considerable caution, particularly claims regarding superiority of specific FES modalities.

Second, the majority of included studies focused on individuals with SCI, limiting the generalizability of the findings to other populations with lower limb paralysis, such as those with stroke or MS. Future studies should explore the effects of FES interventions in a more diverse population to establish their broader applicability. Third, the long-term effects of FES interventions remain poorly understood. Finally, the role of exercise intensity, stimulation parameters, and intervention protocols in achieving optimal outcomes requires further investigation. Specifically, factors such as pedalling cadence, pulse width, and amplitude may significantly influence aerobic and peripheral adaptations.

CONCLUSION

This systematic review and meta-analysis provide the first quantitative comparison of acute cardiorespiratory responses between FES exercise modalities in individuals with lower limb paralysis. Our meta-analysis revealed that FES cycling elicited greater acute increases in oxygen consumption than other FES exercise modes, reflecting the higher total stimulation dose and greater muscle mass recruitment typically employed in FES cycling protocols. For lower limb peripheral health, protocols emphasizing high mechanical loading, whether through isometric contractions or low cadence cycling, produced the most substantial hypertrophic responses. For BMD, significant improvements were observed only with high-volume protocols (≥6 months with multiple weekly sessions), regardless of the FES exercise modes. These findings support focusing on optimizing stimulation parameters rather than selecting specific FES exercise modes to achieve desired physiological outcomes in clinical setting for individuals with lower limb paralysis.

Supplementary Table 1 Characteristics of the Patients and FES

Author, Year	Sample size	Population	Demographics Age/Gender/Neurological/Experience with FES				Maximum Stim available	Frequency	Pulse width (μs)/pulse duration (ms)
Arija-Blazquez 2014 (47)	8	SCI: complete motor post-traumatic SCI between T4–T12	18 to 55	Male	Yes	No	140 mA	30 Hz	200 μs
Arnold 1992 (82)	12 (M=12, F=2)	SCI (C5-T4) Paraplegia=7, Quadriplegia=5	SCI = 29 ± 5.2 AB=27 ± 4.2	(M=12, F=2)	NR	No	130 mA	NR	NR
Ashe 2010 (64)	3	SCI	16 to 46	Female	Yes	No		60 Hz	500 μs
Ashley 1993 (33)	11 -SCI, 5- Able bodied	SCI (7=Quadriplegia, 4-=paraplegia)	35 (±11)	SCI (M=9, F=1), AB (M=3, F-2)	NR	Yes	0-160 mA	50 Hz	square monophasic waves, 250 ms
Baldi 1998 (17)	26	SCI	20-50	FES-CE: (M=7,F=2), FES-IC: (M=6,F=3) , Control(M=7,F=2)	NR	No	0 and 140 mAmp	60 Hz	500 msec
Barr 1989 (83)	19	paraplegia	19 to 51	Female-3, Male-16	Yes	Yes		20 Hz	200 μs

Barstow 1995(25)	6	SCI (ASIA- Class A)	SCI= 25-41, AB=18-22	Male	Yes	Yes	current varied (10-132 mA)	30 Hz	NR
Barstow 1996 (77)	9	SCI (ASIA- Class A)	Control (0-3): 27.7+6.8 (0-6): 26.6+5.5 FES-IC (0-3): 25.8+4.7 (0-6): 25.0+4.2 FES-CE (0-3): 28.2+6.6 (0-6): 27.8+7.3	Male	NR	No	current varied (10-132 mA)	30 Hz	NR

Barstow 2000 (37)	8	paraplegia (ASIA Class A). level of injury ranged from T4 to T12-L1	27.3±6.4	M	NR	NR	10 – 132 mA	NR	NR
BeDell 1996 (61)	12	SCI (ASIA-modified level A, Ashworth Spasticity 2-4)	20-35	M		No	10 to 132 mA	30 Hz	pulse duration = 400 [mu]sec
Bhambhani 2000 (26)	14 (7 in each group)	(SCI, injury levels from C5 to T12)	18-60	Male =10 and Female =4	NR	At the time of testing, four of these subjects were training on the FES cycle ergometer, two had some experience on this instrument and one had never used it.	10 and 132 mA	50 Hz	NR
Block 1989 (55)	3	paraplegia	≥18	M=2, F=1	NR	NR	frequency-30-40Hz, pulse width-300us (biphasic)	30-40Hz	300us (biphasic)

Bloomfield 1996 (65)	9	SCI - C5-T7	35.8 ± 5.0	Male-4 Female-5		No	130 mA	30 Hz	350 msec
Bochkezanian 2018 (48)	5	SCI	34.4±5.6	(M=4, F-1)	NR	Yes	30 to 99 mA	30-Hz	biphasic pulses (0.033-s interpulse interval; 1000 Ks)
Bremner 1992 (84)	6	SCI (Incomplete =4, complete =2)	SD: 34 (6.9)	Mixed	NR	NR			
							NR	35	298
Brurok 2011 (85)	6	SCI (ASIA Impairment Scale grade A)	41.7± 9.1	M	NR	No	140 mA	NR	NR
Chen 2005 (66)	15	SCI	34.3+6.7	M	NR	No	maximal intensity, 120mA	20 Hz	300 msec
Deley 2017 (58)	1	SCI between T4-T5 (ASIA -A)	range: 19 and 26	F	NR	NR	110 mA	40 Hz	450 µs
Demchak 2005 (46)	10	SCI	average age of all subjects was 24.9	SCI: M=8, F=2, AB:M=4, F=1	NR	NR	140mA	NR	NR
Dolbow 2014 (67)	1	SCI (T6, ASIA A)	17-40	F	NR	NR	140 mA	33.3–50 Hz	250–300 ms
Dolbow 2018 (50)	1	SCI (AIS) B	28-65	F		No	55 mA for quadriceps, 45 mA for hamstrings, 20 mA for gluteals	40 Hz	300 ms
Dudley 1999 (10)	3	SCI (ASIA- A)	27, 45 and 51	M	NR	Yes	NR	30 Hz	450 µs biphasic

Duffell 2008 (86)	11	Complete SCI	21-39 (mean +/- SE: 28.2 +/- 1.8 years)	M=9 F=2	NR	No	80 Nm	50 Hz	200 us
Duffell 2010 (87)	10 (5 -SCI and 5 - AB)	Complete SCI	NA	SCI --M=4 F=1; AB-- M=3 F=2	NR	Yes	80 Nm	20 and 50 Hz	200 msec
Eser 2003 (68)	38 (19 in each group)	para- and tetraplegic	40 years of age or less	M=30 F=8	NR	No	140mA	30, 50, and 60 Hz	300 ms
Everaert 2021 (56)	3	SCI (C4–T4, AIS A–C)	18-54	M=2, F=1	NR	Yes	140mA	35 Hz	300 µs
Faghri 1989 (88)	13	SCI (6-paraplegics and 7-quadriplegics)	22-53	M=12, F=1	NR	No	**FNS knee extension**: 150mA, **ES cycle ergometery:** 130mA	**FNS knee extension=**35Hz, **FES cycle ergometery=**30Hz	**FNS knee extension**: 0.3msec.**FES cycle ergometery:** 0.375msec
Faghri 1992 (89)	7	SCI (4 quadriplegics and 3 paraplegics)	22 to 32	M	NR	No	Intensity-130mA.	30Hz	375 msec
Figoni 1991 (13)	14	quads =7 and para =7	Range 21–48	SCI	NR	Yes	150 mA	35 Hz	biphasic square-wave pulses of 0.3 msec
Figoni 1993 (38)	1	SCI	between 15–54	Male	NR	NR	130 mA	NR	NR

Fornusek 2008 (27)	9	T4 through T10 spinal cord injury (SCI) (American Spinal Injury Association Grade A)	23 –37	M=7. F=2	NR	Yes	Intensity- 70 mA to 140mA.	35Hz	250μs
Fornusek 2013 (90)	8	Chronic SCI ASIA]-A, ASIA-C	18–55		NR	No	40mA to 140mA.	35Hz	250ms
Fornusek 2014 (14)	8	paraplegics (T4–T11)	36	M	NR	Yes	40 to 140 mA	35Hz	300 ms
Fornusek 2014 (40)	8	Multiple Sclerosis	17-50	F	NR	No	30mA and then slowly increased.	35 Hz	300 μs
Frotzler 2008 (59)	11	Complete SCI	60	M=9 F=2	NR	No	between 80 and 150 mA	50 Hz	300–400 μs
Gerrits 2001 (91)	9	SCI -- (ASIA- A,B,C,D)	31	M	NR	No	140mA	30 Hz	450s
Gorgey 2017 (49)	5	chronic (>1-year postinjury) motor-complete spinal cord injury (SCI)	NA	M	NR	Yes	0–100 mA	30 Hz	400-μs
Griffin 2009 (51)	18	paraplegia or tetraplegia	41.8 +/- 2.3	M=13 F=5	NR	No	140 mA	50 Hz	NR
Groah 2010 (92)	26	SCI	SCI 45.0 (±3.2); AB 42.2 (±6.3)		NR		0 to 125 mA,	25 Hz	300 microseconds,
Hamzaid 2012 (93)	5	SCI	Interverntion:21 -58. Control: 20-60		NR	Yes	between 110 mA and 140 mA	35 Hz	monophasic 400 μs

Hooker 1990 (94)	14	7 quadriplegia and 7 paraplegia	38 ± 7	M=12, F=2	NR	Yes	130mA.	35 Hz	0.375 mses
Hooker 1992 (28)	8	SCI (quadriplegics, lesion levels C5-C8/T1)	37 ± 6	M=7, F=1	NR	Yes	130mA.	35 Hz	0.375 msec
Janssen 2008 (95)	12	Stroke	24-38	M=6, F-6	NR	No	The stimulation used was a 60-Hz symmetrical, biphasic sine pulse and a pulse duration of 450s	60-Hz	450ms
Janssen 2008 (41)	12	SCI. 6 tetraplegia [TP] and 6 with paraplegia [PP]	27-41	M	NR	Both (trained=4, novice=8)	Maximal current amplitude was set to 300 mA for the G and thigh muscles and 110 mA for the shank muscles	35 Hz	500 µs
Johnston 2016 (53)	17	C4-T6 motor complete chronic SCI. ASIA Impairment Scale grade A or B	Mean=26	M=14 F=3	NR	No	140mA	33Hz	250ms
Kjaer 2001 (96)	10	Spinal cord injured individuals (six tetraplegic and four paraplegic)	32 ± 8 yr	M=8 F=2	NR	No	maximum of 130 mA	30 Hz	monophasic rectangular pulses lasting 350 ms
Krauss 1993 (97)	8	SCI para=7, quadri=1	35.6±4.9	M=7, F=1	NR	No	132 mA	NR	NR

Kuhn 2014 (98)	30	SCI - (10 with AIS grade A, 3 with B, 15 with C, 2 with D). (13 tetraplegics and 17 paraplegics)	27	NR	NR	Yes	10 and 130 mA	30 Hz	250 ms
Lai 2010 (69)	24	SCI	37.4 ± 10.9y	FES group- M=10 F=2 Control M=10 F=2	NR	No	NR	20 Hz	300 µsec
Laskin 1993 (34)	8	SCI quadr =6 (C6-Tl) and para =2 (T3-6)	NA	M=7, F=2	NR	NR	NR	NR	NR
Leeds 1990 (70)	6	Quadriplegia	39 ±14y	M	NR	No	0 to 132 mA	30 Hz	350 ms
Liu 2007 (99)	18	incomplete SCI	21-62	M=16, F=2	NR	No	10–132mA	30 Hz	300 µs
Mahoney 2005 (57)	5	chronic, complete SCI (C5-T10)	28-63	M	NR	NR	NR	NR	NR
Mate 2021 (39)	9	advanced multiple sclerosis (MS)	30–57	M=2, F=7	NR	Both	30 mA or as tolerated	35 Hz	300 ms
Mohr 1997 (72)	10	SCI ((six with tetraplegia and four with paraplegia)	41.9±7.5 years	M=8 F=2	NR	No	130mA.	NR	NR
Mohr 1997 (60)	10	SCI	28-61	M=8 F=2	NR	No	NR	NR	NR

Muraki 2007 (29)	4	paraplegia (PARA; ASIA-A, T5–T12). Six able-bodied males (AB; 30 ± 10 y) were also recruited for comparison	18-50	M	NR	NR	140 mA	30 Hz	400 ms monophasic rectangular pulses
Mutton 1997 (100)	11	SCI (ASIA - A)	27-56	M	NR	No	varied (10 to 132mA)	30Hz	NR
Pacy 1987 (101)	4	paraplegia	Mean for ES 26.2 and mean for control 31.1	M	NR	No	The electric stimulation used during anaerobic exercise ranged from 65-90 volts and for aerobic exercise 80-125 volts.	40Hz	300 us
Pacy 1988 (71)	4	paraplegia	41-61	M	NR	No	Range during the first exercise was 65-90 V, and for the second regimen was 80-125 V.	40 Hz	300us
Panisset 2020 (102)	24	motor complete or incomplete spinal cord injury (SCI)	29.0+/-1.3	M=23 F=1	NR	No	140 mA	35 Hz	0.3 and 0.5 ms
Perrett 2009 (30)	12	complete paraplegic	32.6 +/- 0.6	M=10 F=2	NR	No	150 mA; 500 usec)	20 Hz	stimulation intensity (150 mA; 500 ms), requency (20 Hz)
Petrofsky 1992 (42)	8	paraplegia	46.6		NR	No	varied in current from 0 to 180 mA	35Hz	350-µs biphasic square wave stimulation

Petrofsky 2000 (103)	90 (divided into nine groups of ten subjects each)	complete spinal cord injury between T4 and T11	19-39	Male	NR	NR			
Pollack 1989 (31)	11	SCI (C4-T6) . Cervical = 7 Thoracic= 4	18–70	M=9 F=4	NR	No	80 and 120 mA 0 to 130mA	30 Hz 30 Hz	300 µs rectangular monophasic pulses 400us
Ralston 2013 (104)	14	spinal cord injury (UMN)	Mean ± SD = 36 ± 16	M=11 F=3	NR	No	140mA	33Hz,	NR
Raymond 2000 (32)	12 (6 PARA and 6 AB)	paraplegics	22-67	M	NR	Yes	140 mA	35 Hz	0.375 ms
Raymond 2002 (36)	7 Six AB men of similar age (38 6 5 yr) and physical activity levels participated in this study as a cohort group	SCI (T5–T11)	27–41	M	NR	NR	140 mA	35 Hz	0.25 ms

Robinson 1988 (105)	12	SCI. Divided into three groups based on time since injury: one year or less (n=4), two to five years (n=3), and ten to 16.5 years (n-5). quadriplegia=5, paraplegia at T12 or above=5, incomplete paraplegia at T6/7=1, complete quadriplegia at C-7=1	38.3± 12.9	NR	NR	NR	100mA	20Hz	NR
Rodger 1991 (62)	12	SCI (8-quadriplegia and 4-paraplegics)	23-41	M=9 F=3	NR	Out of 12, only one had previous experience of FES	NR	NR	NR
Ryan 2013 (20)	14	SCI	between 20 and 67	M = 11 F = 3	NR	NR	70-200mA	35Hz	250/50ms
Sabatier 2006 (15)	5	SCI	FES -range 22–37. Control - range 20–38	M	NR	No	NR	30 Hz	450 ms biphasic pulses

Scremin 1998 (106)	5	SCI	between 23-38		NR	NR	10 to 100mA	30Hz	300psec
Scremin 1999 (45)	13	complete motor sensory SCI. ASIA Impairment Scale A.	18 to 65	M	NR	NR	NR	30Hz	300
Skiba 2021 (54)	32	complete spinal cord injury (ASIA A)	35.6±4.9	M	NR	No	10 mA	5 Hz	rectangular pulses of 150 µs
Skold 2002 (52)	15	SCI-Tetraplegic	18-27	M	NR	No	130 mA	60 Hz (30 Hz/electrode)	Mono-phasic rectangular pulses lasting 350 ms
Sloan 1994 (44)	12	SCI	26-61	M=7 F=5	NR	No	90 mA	25 Hz	300 uS
Stoner 2007 (107)	5	chronic, complete SCI	35.6 ± 4.9	M	NR	No	NR	30 Hz	450 ms biphasic pulses.
Thomas 1997 (35)	16 (8 SCI and 8 AB)	SCI	18-65		NR	NR	150mA	50 Hz	monophaisc pulses 0.30 ms
Verellen 2007 (108)	5	four paraplegic men with ASIA class A (T5 – T12), and one man with an incomplete injury (C7 – T4) classified as ASIA class C	RANGE 27-59	M	NR	Yes	NR	NR	NR
Vodovnik 1984 (109)	7	SCI	27 – 45	M	NR	NR	100mA		monophasic square 300us
Yoshida 2013 (110)	10	chronic SCI	27–45	M=6 F=4	NR	NR		40 Hz.	bipolar and biphasic

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CHAPTER 3

Cardiorespiratory Responses of Functional Electrical Stimulation Cycling compared to Isometric Functional Electrical Stimulation in Able-Bodied Adults: A Randomized Crossover Trial

PREFACE

This chapter presents an experimental comparison of acute cardiorespiratory responses to isometric FES and FES cycling in able-bodied adults. Using a randomized crossover design with matched stimulation parameters, this study addresses the critical gap regarding direct comparison of static versus dynamic FES exercise modes. The findings provide foundational evidence for optimizing FES selection in clinical practice

Author Attribution Statement

The co-authors of the manuscript *Acute Cardiorespiratory Responses to Functional Electrical Stimulation Cycling Versus Isometric Exercise in Able-Bodied Adults: A Randomized Crossover Trial* confirm that Prakash Dhopte had made the following contributions:

- Assisted in conception and design of the research
- Collected the data
- Analysed the data
- Interpretation of the findings
- Writing the paper and critical analysis of the manuscript

As the primary supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statements above are correct.

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ABSTRACT

Objective: To compare acute cardiorespiratory responses between functional electrical stimulation (FES) cycling and isometric FES in healthy individuals using identical stimulation parameters.

Design: A randomised crossover experimental trial.

Participants: Twenty healthy adults (13 males, 7 females; mean age 25.5±7.2 years).

Interventions: Each participant completed 4 familiarisation and 2 test sessions (FES cycling at 50 RPM and isometric FES). The stimulation applied during the test sessions was identical. Stimulation was applied to the quadriceps and hamstrings bilaterally.

Primary Outcomes: Peak oxygen uptake (VO_2), carbon dioxide output (VCO_2), and minute ventilation ($\dot{V}E$) assessed using breath-by-breath analysis.

Results: FES cycling generated approximately 10% higher oxygen consumption than isometric FES (peak VO_2: 789±200 vs 716±186 mL/min, $p=0.015$; $d=0.63$), despite identical stimulation parameters. VCO_2 showed similar differences (926±235 vs 827±225 mL/min, $p<0.001$), while ventilatory requirements were proportionally elevated during cycling (27.1±8.5 vs 24.8±8.0 L/min, $p=0.027$). Heart rate responses were comparable between modalities (116±16.9 vs 114±19.9 bpm, $p=0.41$). Power output during cycling averaged 12.9±6.1W, while both interventions produced similar discomfort levels (5.1±2.0 vs 5.3±1.8, $p>0.05$).

Conclusion: FES cycling elicited a small but significantly greater cardiorespiratory responses compared to isometric FES under identical stimulation conditions. These findings build on our prior systematic review and highlight that FES exercise modes independently affect physiological outcomes, even under matched stimulation settings. Future research should refine stimulation parameters (e.g., contraction frequency, duty cycle) and tailor FES modes selection to specific exercise goals.

INTRODUCTION

Cardiorespiratory fitness (CRF) is a key determinant of health, that reflects cardiovascular function, metabolic efficiency, and mortality risk (1, 2). A meta-analysis by Ezzatvar et al. (2021) found that 1-metabolic equivalent (MET) increase in CRF reduces cardiovascular disease-related and all-cause mortality by 12–13% (3). Furthermore, CRF has been identified as a stronger predictor of health outcomes than obesity in a meta-analysis of 20.9 million observations (2). Given its clinical significance, CRF should be recognized as a critical clinical parameter, particularly for individuals with neuromotor impairments who are at high risk of cardiovascular complications due to inactivity (4).

Individuals with spinal cord injury (SCI) often exhibit lower peak oxygen uptake (VO_2 peak), diminished cardiac output, and impaired pulmonary function (5, 6). Chronic paralysis is associated with physical deconditioning (7) and increased susceptibility to metabolic disorders (8). Current guidelines recommend at least 150 minutes of moderate-intensity aerobic exercise per week (9, 10), these recommendations are often impractical for individuals with SCI due to paralysis and mobility limitations (11, 12). For some individuals with neuro-motor impairment, stationary recumbent leg cycling is a safe and effective mode of exercise because it requires less balance and reduces the risk of falls (13). However, those with severe leg paralysis lack the coordination and muscle strength needed to perform the rhythmic contractions required for cycling or other lower-body aerobic exercises (14). Additionally, for SCI populations, upper-body exercise capacity can become compromised due to reduced cardiac output, lower autonomic control, and decreased venous return, leading to diminished cardiorespiratory response compared to leg exercise (15, 16).

Functional Electrical Stimulation (FES) exercise offers a potential solution by using electrical pulses delivered through gel electrodes to induce muscle contractions, assisting or replacing voluntary leg movement (17-19). FES cycling, in particular, has been shown to reverse atrophy, develop muscle strength and endurance, and improve circulation through increased vasodilation (11, 17, 20, 21). However, FES cycling requires specialized equipment and remains inaccessible to many individuals due to cost and complexity (22, 23).

An alternative approach is isometric FES exercise, which involves static muscle contractions without joint movement (24, 25). This method may offer similar physiological benefits, such as improvements in strength and aerobic functions, and may be more accessible due to the simpler equipment requirements. However, it has been less extensively studied in comparison to FES cycling. Several studies have explored the potential of isometric FES to elicit comparable cardiovascular responses to FES cycling. Fornusek et al. (2014) directly compared FES cycling with isometric FES, using similar stimulation parameters such as 140 mA, matched frequency, and matched channels (26). They found no significant differences in oxygen consumption, heart rate, or ventilation. Importantly, their protocol utilized consistent current intensity and muscle recruitment, which strengthens the validity of the comparison. However, their study was performed in individuals with SCI who may have altered physiological responses due to neurological impairment, making it difficult to isolate the specific effects of movement versus muscle activation.

Elder et al. (2006) conducted a study on able-bodied individuals and found that the higher metabolic response in dynamic FES was due to greater recruited muscle mass, as oxygen

consumption normalized to muscle mass showed no significant difference from isometric FES (25). Similarly, Frazão et al. (2022) studied able-bodied participants and reported that FES cycling resulted in higher metabolic and ventilatory demands compared to neuromuscular electrical stimulation (NMES); however, their findings should be interpreted with caution, as the trial duration was limited to only 2 minutes with low stimulation intensities (20–35 mA) (27). These studies in able-bodied populations provide significant preliminary evidence but highlight methodological shortcomings that justify the need for a more rigorous comparison. These conflicting findings and methodological limitations highlight the need for a controlled comparison using identical stimulation parameters to determine whether movement is affecting cardiorespiratory responses during FES exercise.

Despite this growing evidence, the comparative benefits of FES cycling versus isometric FES in eliciting aerobic responses remains less explored, particularly under matched stimulation parameters in able-bodied individuals. Chapter 2's systematic review and meta-analysis revealed that while FES cycling elicited significantly greater acute increases in oxygen consumption (mean difference: 0.48 L/min) compared to isometric FES (0.28 L/min), these differences may be attributable to variations in stimulation parameters rather than the FES exercise modes itself. The review highlighted that FES cycling protocols typically employed higher stimulation doses and activated more muscle groups than isometric protocols, suggesting that when parameters are matched, physiological responses might be comparable While the long-term goal is to optimize and refine intervention parameters for individuals with SCI, the first step in this series of research trial involves testing in able-bodied individuals to establish baseline cardiovascular and muscular responses under controlled conditions. This foundational step is critical to isolate the

effects of stimulation parameters without the confounding influence of injury-specific physiological alterations (25).

It appears that no previous studies have matched both current intensity and channel configuration during FES cycling and isometric FES exercise modes in able-bodied individuals. Thus, this study offered a novel comparison under standardized stimulation conditions, to determine the isolated effect of FES exercise modality on aerobic response. This study aimed to compare the aerobic response elicited from FES cycling and isometric FES exercise in healthy, able-bodied individuals. The primary research question was whether the mode of leg electrical stimulation (FES cycling vs. isometric FES) affected the cardiorespiratory response when stimulation parameters were held constant. The hypothesis was that when identical stimulation parameters were applied, there would be no significant difference in oxygen consumption between the two modes.

MATERIALS AND METHODS

This study adopted a randomized crossover model to compare two types of FES exercise: FES cycling and isometric FES.

Participants

Twenty healthy, able-bodied adults were recruited were recruited through flyers posted on university bulletin boards, the Ossicle newsletter, social media platforms, and other locations frequented by potential volunteers. Permission was obtained from the appropriate organizations to post the flyers on their websites or poster boards. All procedures were approved by the Human

Ethics Committee at The University of Sydney, (Project no. 2023/548) and all participants provided written informed consent.

No formal a priori power analysis was conducted given the exploratory, randomized, cross-over study trial design. The sample size of twenty participants was based on similar crossover studies in FES research and practical constraints of the study design. A sensitivity check indicates that, with n=19 paired observations (α=0.05, two-tailed), the design has ~80% power to detect a within-subject standardized mean difference of approximately Cohen's dz ~ 0.64–0.68 (28).

Screening

Each participant underwent a comprehensive health and fitness assessment using the Exercise and Sports Science Australia (ESSA) pre-exercise screening system stages 1 and 2. Individuals identified as high risk or unfit based on the screening were excluded from the study. Given that electrical stimulation typically elicits a low-intensity aerobic response, participants categorized as low or moderate risk without contraindications to electrical stimulation exercise were deemed suitable for inclusion.

Inclusion Criteria

Participants recruited for this study were required to be between 18- 50 years of age to ensure musculoskeletal maturity and to reduce the likelihood of age-related changes in cardiovascular or neuromuscular functions. Eligibility criteria included the absence of neurological or neuromuscular disorders, as well as an adequate range of motion in the knee and hip joints to facilitate passive leg cycling using a motorized ergometer. Participants were also required to have normal vision and cognitive function to follow instructions and comply with the study

protocol. Additionally, individuals needed to be able to effectively communicate pain or discomfort to the researchers. Participants with a history of seizure disorders were included only if their condition was well-controlled.

Exclusion Criteria

Participants with hypersensitivity to electrical stimulation, or unresponsiveness to stimulation were not recruited, as these factors could affect the safety and consistency of the intervention. To ensure participant safety, participants with cardiovascular instability, arrhythmias, or severe blood pressure abnormalities were excluded. Participants with unhealed wounds, pressure sores, joint laxity, fractures, lower limb trauma, or advanced osteoporosis were also not considered to minimize the risk of complications. Additionally, pregnant individuals were excluded to prevent potential adverse effects associated with muscle stimulation and exercise.

Study Design

This study employed a randomized crossover design, in which each participant completed two distinct sessions: FES cycling and isometric FES exercise. The order of these sessions was randomized using a computer-generated random sequence to minimize potential order effects.

FES Familiarization Sessions

Participants underwent four familiarization sessions (2 FES cycling and 2 isometric FES), to familiarize themselves with the sensations induced by FES. Each session lasted 45 minutes and was undertaken on separate days at least one day apart. These sessions helped to determine each participant's stimulation tolerance level. During each session, both quadriceps and hamstrings

were stimulated for 20 minutes, with participants completing separate sessions for FES cycling and isometric FES. The stimulation pulse amplitude was gradually increased over the initial 10 minutes of each trial. Participants reported their discomfort levels using a numeric rating scale from 0 to 10, with 0 indicating no discomfort and 10 representing extreme discomfort. If discomfort exceeded 7, the stimulation intensity was reduced to maintain the participant's comfort, but the FES was not completely stopped. The peak stimulation value achieved for each participant during these sessions was used to establish appropriate intensities for subsequent experimental trials.

The threshold of 7 on the 0-10 numerical rating scale was selected as a practical limit that balanced achieving sufficient stimulation intensity to elicit meaningful quadriceps and hamstring contractions while ensuring participant comfort and study completion. Values above 7 are typically associated with severe discomfort that may contribute to exercise tolerance and increase withdrawal risk in able-bodied individuals with intact sensation.

Experimental Trials

The experimental trials involved two 1-hour sessions: FES cycling and isometric FES exercises, conducted on separate days with a minimum of 48 hours between sessions (Figure 1). Participants were randomized into two groups: Group A started with FES cycling followed by isometric FES, while Group B began with isometric FES followed by FES cycling. The stimulation intensity was gradually increased, depending on the participant's tolerance, to achieve maximum muscle contraction without causing discomfort. Both trial conditions were designed to be comparable, differing only in the presence or absence of leg pedalling movement.

While stimulation parameters were matched, muscle activation was not verified through EMG. Measuring EMG during high-intensity electrical stimulation requires specialized equipment and technical expertise (29). The biphasic pulses at 35 Hz generate significant electrical interference, requiring specialized high-common-mode-rejection amplifiers and artifact suppression algorithms. Due to these technical and equipment limitations, our study focused on comparing FES exercise modes with standardized stimulation parameters.

Figure 1 illustrates the study protocol, outlining the sequential steps followed in the experimental trial.

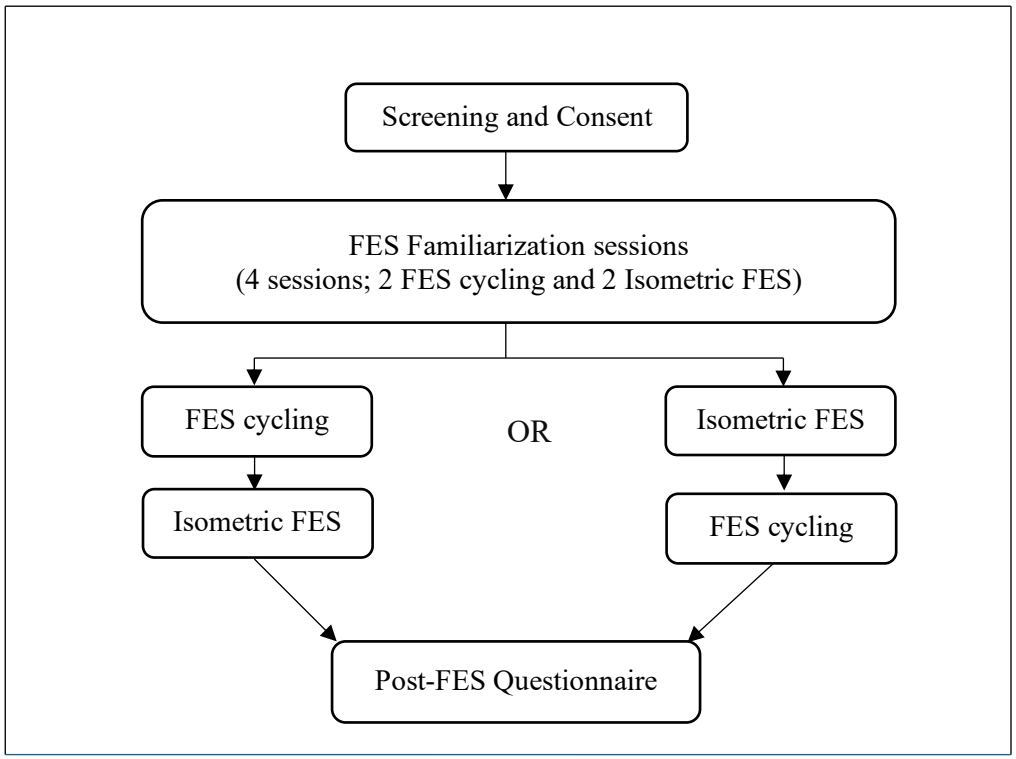


Figure 1 Flow diagram of the study protocol.

Apparatus Setup

The FES-exercise system consisted of the motorized cycle ergometer (MOTOmed Viva; RECK-Technik GmbH & Co, Germany), adjustable seat, a wheelchair, and a muscle stimulator.

Setup of FES machine

A PC laptop was used to control the stimulator hardware and record muscle stimulation parameters. The stimulator's software allowed control over stimulation parameters, including amplitude, timing, pulse width, frequency, and ramp time. The 8-channel muscle stimulator delivered symmetrical biphasic rectangular pulses at a frequency of 35 Hz, pulse width of 250 μsec, and maximum tolerable stimulation amplitude, (ranging from 60 to 110 mA), depending on participant's tolerance. The symmetrical biphasic waveform ensured equal amplitude and duration for each phase, providing net zero charge delivery to minimize electrochemical reactions and skin irritation during prolonged stimulation (30).

Electrode Placement

Reusable, gel-backed, self-adhesive rectangular electrodes (7.5 cm × 13 cm) were used for surface stimulation. Electrode placement was standardized using anatomical landmarks and measured with a flexible measuring tape to ensure consistent positioning across sessions. Electrodes were placed bilaterally on the quadriceps (rectus femoris & vastus lateralis) with the proximal electrode positioned 15–20 cm above the patella along the midline of the rectus femoris and the distal electrode 5–7 cm above the patella on the same muscle belly. For the hamstrings (biceps femoris & semitendinosus), the proximal electrode was placed 15–20 cm below the gluteal muscles along the midline of the hamstring muscle and the distal electrode 5–7 cm above the popliteal fossa. The leads of the electrodes were positioned laterally to minimize interference

and ensure secure placement. The placement of electrodes was consistent across all familiarization and experimental sessions.

FES Cycling Setup

Participants were seated on a cycle ergometer with their feet placed in the pedal boots. Their calves were strapped to the padded leg guides of the ergometer to ensure secure positioning. Muscle stimulation was applied in a specific sequence to elicit contractions in the quadriceps and hamstrings, driving the pedals of the cycle ergometer. The participants were instructed to avoid making any voluntary effort to move the pedals. The stimulation was triggered by pedal rotation at 50 revolutions per minute (RPM).

FES Isometric Exercise

While seated in the wheelchair, participants' feet were placed on the footplates, and their calves were padded and strapped to the front rigging of the wheelchair to minimize leg movement. Muscle stimulation was applied in the same sequence and intensity as in the FES cycling trial to create the same muscle contractions without pedalling motion. During the FES isometric exercise, the stimulation was triggered from the pedal position of MOTOmed cycle ergometer. For both the FES cycling and FES isometric, stimulation was triggered initiated by pedal rotation at 50 RPM.

For FES cycling, muscle stimulation was triggered by current pedal rotation at 50 RPM. For isometric FES, although participants' legs remained stationary, the same stimulation timing was triggered by the MOTOmed ergometer rotating near the participant, which was a position

reference. This ensured that both conditions utilized identical stimulation timing and on/off patterns.

Measurements

Primary Outcome Measure

The primary outcome was the oxygen uptake (VO_2; ml/min) recorded during each FES exercise sessions. Cardiorespiratory responses were continuously monitored using a calibrated Medgraphics metabolic gas analysis system, which recorded breath-by-breath data through open-circuit spirometry. The gas analysis system was calibrated before each session using known gas concentrations to ensure accuracy. Measurements were taken during a 5-minute baseline rest period, the 20-minute FES exercise session, and during a subsequent 5-minute recovery period. Cardiorespiratory responses were measured to compare the relative exercise intensities of both FES exercise modes.

Secondary Outcome Measures

Several secondary measures were included to evaluate the participants' responses to electrical stimulation and the overall exercise performance:

Stimulation Tolerance and Intensity: The participants' tolerance to electrical stimulation was assessed using a Numeric Rating Scale (NRS) ranging from 0 to 10, where 0 indicated no discomfort, and 10 represented extreme discomfort. Participants were prompted to report their discomfort level at two-minute intervals during FES exercise.

Heart Rate (HR) Monitoring: Heart rate was continuously measured using a Polar heart rate monitor arm strap (OH1), at rest, during the entire 20-minute exercise, and post FES exercise recovery phase.

Blood Pressure Monitoring: Blood pressure (BP) was measured using sphygmomanometer before, midway, and after exercise.

Rate of Perceived Exertion (RPE): RPE was monitored throughout each session using the Borg Scale (31), which ranges from 6 to 20, where 6 represents "no exertion at all," and 20 represents "maximum exertion."

Pedalling Power Output and Performance: Pedalling power output, which reflects the mechanical performance of the cycling exercise, was recorded continuously to characterize the mechanical work performed during each session by the FES computer software
Respiratory rate was monitored as part of cardiorespiratory assessment but was not considered a primary comparative measure.

Post-Experimental Questionnaire: At the end of both FES exercise sessions, participants were asked to complete a brief post-experimental questionnaire to capture their subjective perceptions of each modality. The questionnaire included an open-ended item asking whether the two sessions felt similar, which mode they preferred, and their reasons for that preference. These data were used to supplement physiological outcomes and inform future clinical applications.

Cardiorespiratory Response Analysis

The metabolic gas analysis system measured various parameters, including oxygen consumption (VO_2), carbon dioxide production (VCO_2), minute ventilation ($\dot{V}_E$). VO_2 and HR responses were used to compare the two FES exercise conditions.

Statistical analysis:

All statistical analyses were conducted using IBM SPSS Statistics (Version 29, IBM Corp., Armonk, NY, USA). The data from experimental trials were analysed by a blinded researcher to eliminate potential bias regarding the FES exercise mode performed in each session. Descriptive statistics (mean ± standard deviation [SD]) were computed for key outcome variables, VO_2, VCO_2, HR) respiratory rate (RR), ventilation (V_E), stimulation intensity, power output, subjective discomfort and pain (VAS scores).

Given the randomized crossover design, paired samples t-tests were employed to compare the mean values between FES cycling and isometric FES across all physiological and perceptual variables. A two-way repeated-measures ANOVA was used to analyse interactions across different phases of the trials (rest, FES exercise) with post-hoc paired comparisons where appropriate. The primary research questions were addressed through paired t-tests comparing mean values between FES cycling and isometric FES across all physiological and perceptual variables.

For cardiovascular measures, paired samples t-tests were used to compare mean values between FES cycling and isometric FES. In all cases, statistical significance was set at $p < 0.05$, and 95% confidence intervals (CIs) were reported to provide an estimate of the precision of the observed

differences. In order to compare the sources of discomfort, no statistical analysis was performed; therefore, these percentages are provided for descriptive purposes only. Responses from the post-experimental questionnaire were analysed descriptively. No inferential statistical tests were applied due to the qualitative nature and sample size of this data.

Paired t-tests and repeated measures ANOVA were appropriate for this within-subject crossover design because each participant was assigned to their own control, eliminating between-subject variation. The baseline VO_2 differences were derived from the different exercise modes being compared rather than confounding variables requiring adjustment. ANCOVA is typically used to adjust for unrelated baseline covariates, while the pre-exercise VO_2 differences observed here may reflect anticipatory physiological responses specific to each condition.

RESULTS

A total of 20 participants (13 males, 7 females) with a mean age of 25.5 ± 7.2 years completed the study. Their mean height was 171.548 ± 9.7, cm, weight 77.0 ± 22.0 kg, and BMI 25.7 ± 5.2. The data analysis from the experimental trials included 19 participants for FES cycling and 18 for isometric FES. Data from one participant in FES cycling and two participants in the isometric FES was excluded due to technical errors encountered during data acquisition. The stimulation intensities were comparable between conditions, with no significant differences observed. As expected, power output was only generated during FES cycling, while isometric FES did not produce measurable power output due to the absence of crank movement (Table 1). Figure 2 displays the time-course changes in cardiorespiratory responses (VO_2, VCO_2, V_E, RQ, and HR) and perceived exertion measured using VAS over the 20-minutes of both FES exercise modes.

The average maximum stimulation intensity was 85.4 ± 14.6 mA for FES cycling and 84.1 ± 13.6 mA for isometric FES, lower than intensities reported in Chapter 2 for individuals with complete SCI (often >100 mA), likely due to intact sensation in able-bodied participants.

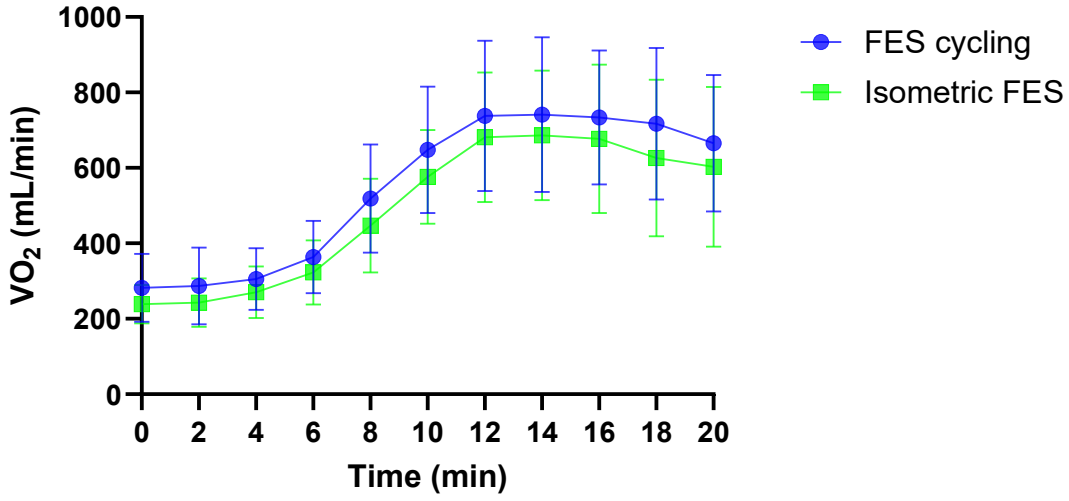
Table 1 Stimulation parameters and power output in FES cycling vs isometric FES

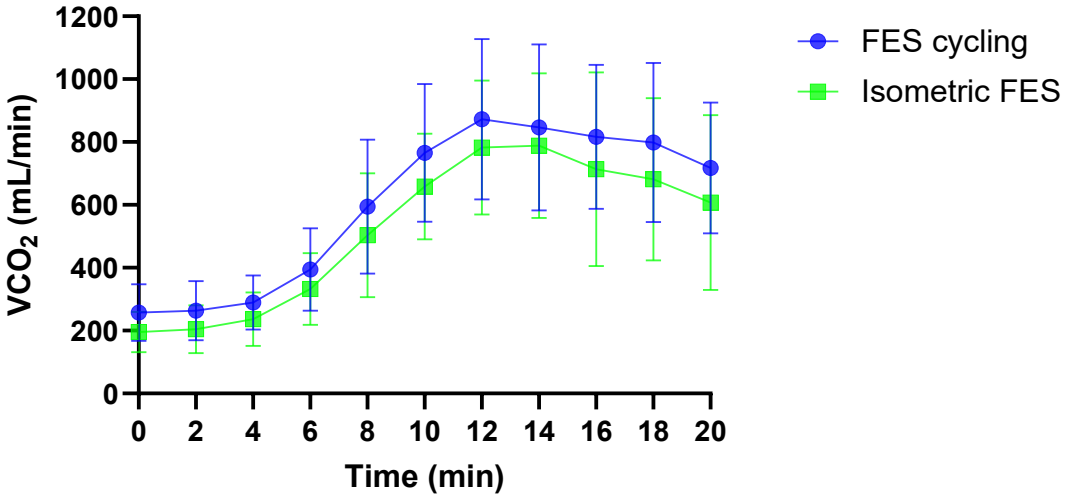
Parameters	FES Cycling (Mean ± SD)	Isometric FES (Mean ± SD)
Duration (min)	20.4 ± 0.5	20.0 ± 0.6
Max Stimulation (mA)	85.4 ± 14.6	84.1 ± 13.6
Avg Stimulation (mA)	66.5 ± 10.4	65.2 ± 9.9
Max Power Output (W)	26.7 ± 11.2	-
Avg Power Output (W)	12.9 ± 6.1	-

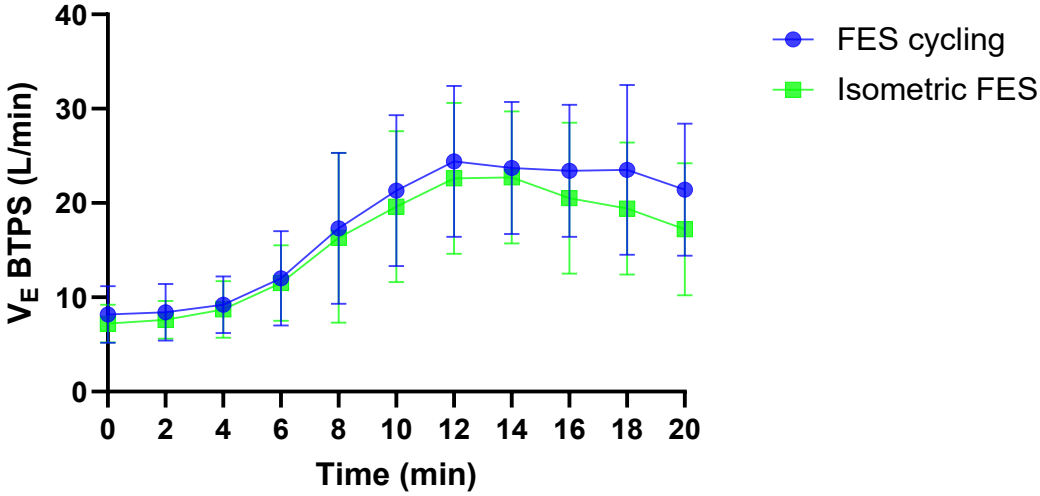
The results revealed that respiratory measure (VO_2, VCO_2) and ventilation (V_E) showed significant differences between exercise modes, while cardiovascular responses (HR) were similar.

Importantly, resting VO_2 was already 29 mL/min higher before FES cycling compared to isometric FES (262 ± 88 mL/min vs. 233 ± 46 mL/min, $p = 0.057$), accounting for approximately 40% of the total observed difference between FES exercise conditions. Similarly, resting HR was comparable between modes (FES cycling: 67 ± 11 bpm vs. Isometric FES: 68 ± 10 bpm, $p = 0.690$). This baseline imbalance suggests that the actual exercise-induced difference between FES exercise modes is considerably smaller than raw peak value indicate.

Peak VO_2 was significantly higher during FES cycling compared to isometric FES ($p = 0.015$). Similarly, average VO_2 was greater with cycling ($p = 0.008$). VCO_2 followed a similar pattern, with significantly greater values in FES cycling ($p < 0.001$). $\dot{V}_E$ was also greater during FES cycling, with both peak and average values showing statistically significant differences ($p = 0.027$ and $p = 0.032$, respectively). Effect size analysis showed moderate-to-large effects for VO_2 peak ($d = 0.63$) and V_E peak ($d = 0.57$). In contrast, differences in subjective exertion were minimal ($d = 0.07$). Table 2 summarizes the physiological responses to FES cycling and isometric FES.




1200
1000
800
600
400
200
0
VCO2 (mL/min)
0 2 4 6 8 10 12 14 16 18 20
Time (min)
FES cycling
Isometric FES


40
30
20
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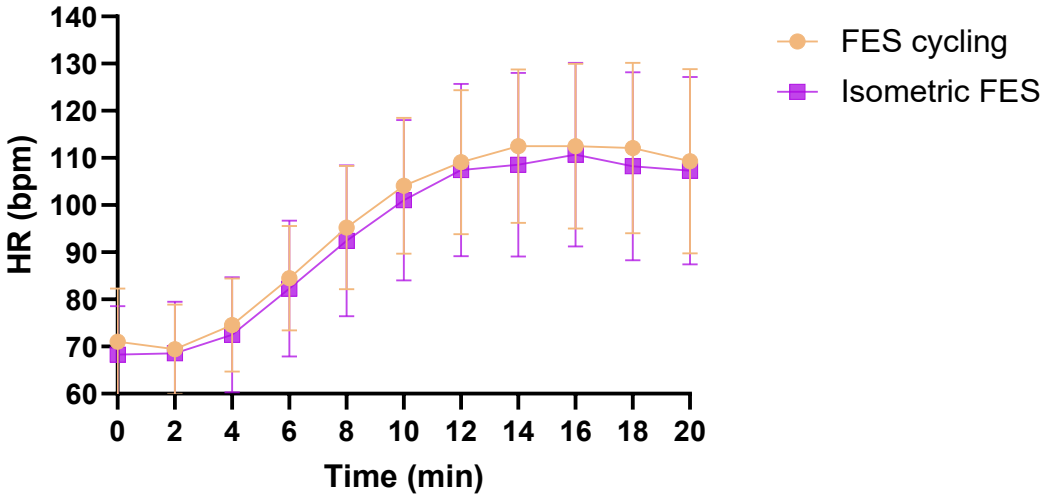
0
VE BTPS (L/min)
0 2 4 6 8 10 12 14 16 18 20
Time (min)
FES cycling
Isometric FES


140
130
120
110
100
90
80
70
60
HR (bpm)
0 2 4 6 8 10 12 14 16 18 20
Time (min)
FES cycling
Isometric FES

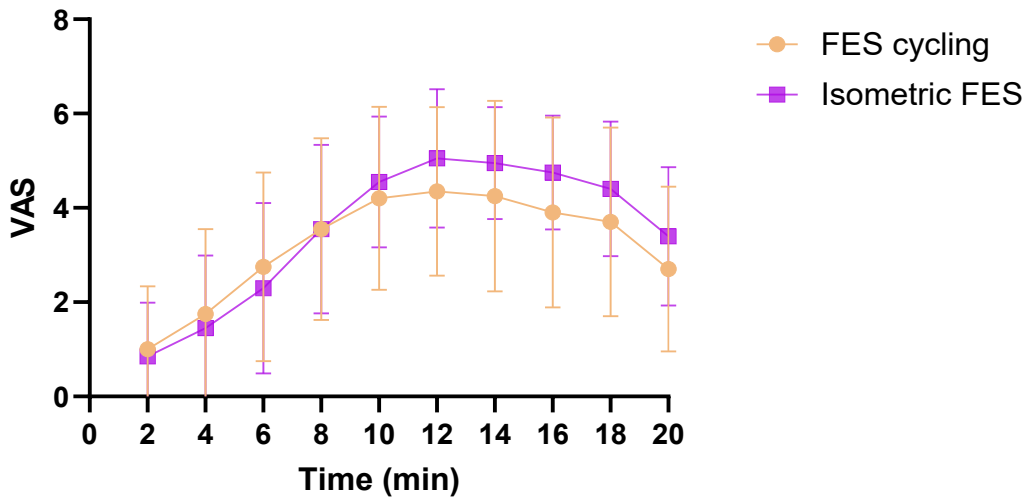


Figure 2 illustrates the time-course changes in $\dot{V}O_2$, $\dot{V}CO_2$, $\dot{V}_E$, HR, and discomfort during FES cycling and isometric FES over a 20-minute session.

Table 2 Cardiorespiratory responses (Mean ± SD; N = 19 for FES cycling –18 for isometric FES). Statistically significant values ($p < 0.05$) are marked with an asterisk (*).

Outcome	FES Cycling	Isometric FES	p value
Peak HR (bpm)	116 ± 16.9	114 ± 19.9	0.41
Peak VO_2 (ml/min)	789 ± 200	716 ± 186	0.015*
Average VO_2 (ml/min)	542 ± 137	483 ± 120	0.008*
Peak VCO_2 (ml/min)	926 ± 235	827 ± 225	<0.001*
Peak Ve (L/min)	27.1 ± 8.5	24.8 ± 8.0	0.027*
Average Ve (L/min)	17.9 ± 5.4	16.2 ± 4.6	0.032*

Discomfort levels were comparable between the two FES exercise modalities with mean ratings of 5.1 ± 2.0 for FES cycling and 5.3 ± 1.8 ($p = 0.41$) for isometric FES. However, the sources of discomfort varied. Isometric FES was more frequently associated with electrical stimulation sensation (45%) and cramping (10%), whereas FES cycling induced more fatigue (10%) and muscle tightness (32%). Joint pain was slightly more common in FES cycling (13%) than isometric FES (10%).

In terms of exercise preference, FES cycling was slightly favoured (48%) over isometric FES (42%), with 10% of participants reporting no preference. Participants who preferred FES cycling noted that movement helped distract from discomfort, while those favouring isometric FES mentioned better control over breathing and reduced fatigue.

DISCUSSION

The present study identified significant differences in specific cardiorespiratory parameters between exercise modes. Notably, VO_2, VCO_2, and V_E were significantly greater during FES cycling compared to isometric FES. In contrast, no significant differences were observed in HR, or perceived discomfort. However, resting VO_2 was already 29 mL/min higher before FES which may account for part of the observed FES exercise difference. These findings do not support the initial hypothesis. While it was anticipated that VO_2 would not differ between FES cycling and isometric FES, the results indicate that FES cycling elicited a more pronounced aerobic response.

Although FES preferentially recruits fast-twitch (type II) muscle fibres due to the reversed motor unit recruitment order (32), the elevated oxygen consumption observed during FES cycling

suggests that aerobic metabolism is also significantly engaged. This is likely due to the continuous nature of FES-evoked contractions and the mechanical requirements of cycling, which require sustained ATP turnover. These energetic demands activate both anaerobic glycolysis and oxidative phosphorylation pathways (33). In the acute setting, the higher oxygen uptake observed in FES cycling is primarily attributed to the metabolic cost of electrically induced muscle work. While FES cycling may improve venous return and enhance oxygen delivery (34), these circulatory mechanisms serve to meet the elevated metabolic demand rather than independently driving VO_2 increases. These findings support the purpose of this thesis to identify the effects of FES modality on acute cardiorespiratory responses under matched stimulation parameters.

The higher VO_2 during FES cycling, despite similar heart rate responses, reflects the distinct characteristics of electrically stimulated muscle activation. Unlike voluntary exercise where anticipatory motor cortex signals and physiological feedback drive proportional cardiovascular responses, FES bypasses these regulations (38). FES reverses normal motor unit recruitment, preferring to activate Type II motor units that rely heavily on anaerobic glycolysis and fatigue rapidly. While VO_2 decreased during FES cycling, this reflects the cost of ATP resynthesis following anaerobic glycolysis, lactate clearance, and oxygen debt repayment. Kjaer et al. (1996) demonstrated that blood and muscle lactate concentrations increased substantially more during FES compared to voluntary exercise at identical oxygen uptake, confirming disproportionate anaerobic contributions (39).

FES-induced exercise produces attenuated cardiovascular responses compared to voluntary exercise at equivalent oxygen consumption levels. Raymond et al. (2000) demonstrated that during FES leg cycling in individuals with paraplegia, cardiovascular responses are mediated primarily through arterial baroreflex rather than physiological feedback, with heart rate showing weak correlation to VO_2 (40). This disparity between VO_2 and cardiovascular responses persists even in individuals with able-bodied bodies during FES. Additionally, only quadriceps and hamstrings were stimulated, indicating relatively small muscle mass compared to whole-body voluntary exercises. The 10% VO_2 difference between FES exercise modes was inadequate to trigger differential HR responses, indicating both conditions were below the threshold for substantial cardiovascular responses.

While passive movement during cycling may contribute to venous return, the degree of electrically activated muscle mass is likely the more crucial factor of oxygen uptake. Elder et al. (2006) demonstrated that when VO_2 was normalised to recruited muscle mass, differences between dynamic and isometric contractions disappeared, suggesting that muscle recruitment rather than movement mechanics primarily governs metabolic demand (25).

Fornusek et al. (2014) demonstrated superior methodological validity through their crossover design using identical current intensity (140mA) and channel configurations in well-characterized SCI participants, with longer exercise duration (35 minutes) allowing steady-state responses, thereby enhancing the internal validity of their findings. (26). They found no significant differences in VO_2, HR, or ventilation between FES cycling and isometric FES in individuals with chronic SCI (T4-T11). Our study included a larger sample of able-bodied

individuals (n=20 vs n=8) under identical stimulation settings. While this limits direct clinical generalizability, it allowed clearer isolation of stimulation effects without the confounding influence of autonomic or vascular impairment. Similar studies using able-bodied participants (25, 27) support this approach.

In contrast, Elder et al. observed greater oxygen consumption during dynamic contractions in able-bodied individuals, though this difference was no longer significant after adjusting for recruited muscle mass (25). They concluded that mechanical characteristics of muscle action rather than muscle mass alone played a key role in determining metabolic cost. However, direct comparison between these studies warrants caution, as the duration of stimulation differed substantially. Fornusek et al. (26) applied 35 minutes of intermittent stimulation per mode, while Elder et al. (25) used only 3 minutes using intermittent contractions at 1:2 duty cycle. This discrepancy in stimulation time could influence metabolic outcomes and suggests that longer stimulation durations, as used in Fornusek's study, may be necessary to fully capture the physiological impact of FES modalities.

Elder et al. also demonstrated that muscle recruitment, rather than movement mechanics, primarily governs metabolic demand. Our findings support this principle, suggesting that FES cycling and isometric FES may result in different muscle activation patterns. This difference likely occurs because dynamic muscle architecture changes during FES cycling bring more nerve fibre branches into the field of electrical stimulation during shortening than during isometric actions, as Elder et al. suggested. The observed metabolic differences between FES exercise

modes in our study may reflect this differential muscle recruitment despite matched stimulation parameters.

Heart rate responses were similar between FES exercise modes despite higher VO_2 during cycling. This suggests that rhythmic muscle contractions during FES cycling enhance venous return through muscle pumping. The improved venous return may increase stroke volume and cardiac output while maintaining comparable heart rate. In contrast, isometric FES lacks this muscle pump mechanism, potentially resulting in lower stroke volume and cardiac output that is comparable to the reduced metabolic demand. This cardiovascular efficiency during FES cycling may be clinically significant for individuals with limited cardiac reserve, though direct stroke volume measurement would be necessary to confirm this mechanism.

VO_2 during FES exercise is primarily driven by the amount of muscle stimulated, rather than by cardiovascular responses. This is due to the nature of electrically induced muscle contractions, which bypass normal motor unit recruitment patterns and can synchronously activate large numbers of motor units (32). However, the cardiovascular system is often only modestly engaged, particularly in low-load FES protocols using able-bodied participants, as reflected by relatively stable heart rate and blood pressure responses (41). Unlike voluntary exercise, FES rarely produces a significant increase in cardiac output, and central adaptations are limited unless stimulation intensity, duration, and muscle mass are significantly elevated. This response pattern aligns with previous studies. Fornusek et al. (2014) (26) found no significant heart rate differences between FES cycling and isometric FES in SCI individuals despite other physiological differences. Raymond et al. (2000) (40) suggested that during FES exercise, heart

rate responses may be mediated more by central command than metabolic demand. Faghri et al. (1992) (42) similarly noted that heart rate changes during FES exercise often didn't correlate with oxygen consumption levels, especially in high-level SCI individuals. However, cardiac output comprises both heart rate and stroke volume, and the latter was not measured in this study.

The stimulation amplitude was individualized based on participant tolerance, with identical parameters applied across both FES exercise and modes for each individual. While the observed difference in VO_2 was statistically significant with a moderate effect size (Cohen's d = 0.63), the absolute difference of approximately 70 mL/min represents less than 0.25 METs, which may have limited clinical significance. These findings contradict our original hypothesis that identical stimulation parameters would produce similar cardiorespiratory responses regardless of FES exercise modes.

The post-exercise questionnaire responses suggested differences between physiological responses and participant preferences. While FES cycling resulted in greater increases in cardiorespiratory responses, many individuals indicated that isometric FES was more comfortable. Common reasons included less perceived fatigue, easier breathing, and a more controlled sensation during stimulation. Conversely, those who favoured FES cycling noted that the movement helped distract from discomfort. These insights emphasize the importance of considering user experience when making clinical decisions. For people with neuromotor impairments, continuous participation in interventions may rely not just on the physiological advantages they offer, but also on how tolerable and manageable they are during FES exercises.

The results of our study have significant clinical implications for FES exercise prescription in individuals with neuromotor impairments. Given that SCI populations exhibit lower aerobic capacity, reduced cardiac output, and an increased risk of metabolic syndrome, selecting appropriate FES exercise modalities is crucial for mitigating secondary health complications (6). Our findings do not suggest that FES cycling is the preferred exercise mode; however, when directly compared to isomeric FES under matched stimulation conditions, FES cycling elicited greater oxygen uptake and ventilation, indicating it may be more effective for enhancing CRF in individuals with lower limb paralysis. However, isometric FES remains a viable alternative for certain clinical populations. Individuals with severe joint instability, or muscle contracture may be unable to tolerate prolonged dynamic exercise such as FES cycling, making isometric FES a more practical option for initial neuromuscular activation.

Study Strengths and Limitations

Several methodological strengths enhance the validity of our findings. The randomized crossover design eliminates inter-individual variability by ensuring that each participant serves as their own control, thereby increasing statistical power. Additionally, the use of a rigorous familiarization protocol minimizes variability in neuromuscular adaptation, ensuring that observed differences are due to the exercise modality rather than disparities in stimulation tolerance. The comprehensive metabolic assessments, including VO_2, VCO_2, V_E, heart rate, and participants exertion, provide an integrated evaluation of cardiorespiratory responses, surpassing prior studies that focused primarily on heart rate or power output. The use of blinded data analysis further strengthens the objectivity of the results.

The limitation of the study was that it was conducted in able-bodied individuals, limiting the generalizability of findings to clinical populations with paralysis or neuromuscular disorders. This study was conducted in able-bodied individuals due to practical constraints including limited time, resources, and technical expertise required for recruiting and working with clinical populations. Although this limits direct generalization to individuals with SCI, the findings remain informative. Able-bodied studies provide preliminary evidence that can guide hypothesis generation for clinical trials. However, individuals with SCI exhibit fundamentally different physiological responses including altered autonomic function, impaired venous return, reduced cardiac output, and chronic muscle atrophy. These SCI-specific adaptations mean that the cardiovascular responses observed in our able-bodied sample cannot be directly inferred to the clinical populations. Stroke volume was not measured, preventing the assessment of cardiac output and limiting our understanding of the cardiovascular mechanisms responsible for the observed VO_2 differences. Additionally, the baseline imbalance in resting VO_2 between conditions confounds interpretation of the exercise differences.

This study limited electrical stimulation to the quadriceps and hamstrings to simplify electrode placement and ensure consistent stimulation parameters between sessions and exercise. While appropriate for our controlled experimental comparison, this approach restricts the applicability of findings to clinical FES applications, where gluteal muscle stimulation is typically utilized. The exclusion of the gluteus maximus, the largest lower limb muscle, likely lowered the absolute magnitude of physiological responses in both situations. Although both FES modes were equally

affected by this limitation, the primary finding of similar cardiovascular responses between modes remains valid for the muscles tested.

Future Directions

Future research should focus on several key areas to expand upon the findings of this study. Longitudinal studies should examine the long-term impact of FES cycling and isometric FES on cardiovascular health, muscle function, and metabolic efficiency. Understanding the long-term impact of these modalities is essential for optimizing rehabilitation strategies and promoting lasting physiological benefits. Additionally, future studies should investigate the applicability of these findings in individuals with SCI and other neuromuscular impairments. Furthermore, refining stimulation protocols remains a key area of interest. While our study employed standardized stimulation parameters, individualized approaches that tailor duty cycle to neuromuscular characteristics may enhance the efficacy of FES-based training.

CONCLUSION

FES cycling increased ventilatory and oxygen uptake responses than isometric FES, but heart rate remained unchanged, indicating limited cardiovascular involvement. These findings indicate that differences are primarily due to the amount of muscle activation rather than the exercise mode itself. Despite previous research, both modes produced low-intensity physiological responses, and should not be assumed to provide substantial cardiovascular benefits. The choice between them should be based on clinical context and practical considerations rather than a presumed physiological superiority.

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CHAPTER 4

Optimizing Functional Electrical Stimulation Parameters to Enhance Aerobic Fitness and Muscle Health

PREFACE

As the previous chapter demonstrated that isometric FES could give similar outcomes to FES cycling, this chapter examines the optimization of contractions per minute (CPM) in isometric functional electrical stimulation (FES). By systematically varying contraction timing while maintaining consistent duty cycles, this investigation isolates the specific effects of CPM on muscle force production and cardiorespiratory outcomes in electrically evoked exercise.

Author Attribution Statement

The co-authors of the manuscript *Optimizing Functional Electrical Stimulation Parameters to Enhance Aerobic Fitness and Muscle Health* confirm that Prakash Dhopte had made the following contributions:

- Assisted in conception and design of the study
- Collected the data
- Analysed collected data
- Interpretation of the findings
- Writing the paper and critical analysis of the manuscript

As the primary supervisor for the candidature upon which this thesis is based, I can confirm that the authorship attribution statements above are correct.

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ABSTRACT

Background: Isometric functional electrical stimulation (FES) shows promise for enhancing muscle health, but optimal contraction parameters remain unclear. This study investigated how different contractions per minute (CPM) settings affected muscle torque production, aerobic responses, and subjective comfort during isometric FES.

Methods: Twelve able-bodied males (26.9±7.4 years) completed four randomized sessions with different CPM conditions (5, 10, 20, and 40 CPM) using a 30% duty cycle across all conditions (e.g., 10 CPM: 1.8s contraction / 4.2s rest; 40 CPM: 0.45s contraction / 1.05s rest), maintaining equivalent total contraction time per minute. Each session involved 20 minutes of bilateral quadriceps and hamstring stimulation (35Hz, 250μs pulse width). Muscle performance was assessed via dynamometry, while cardiorespiratory responses (VO_2, HR) were measured with data analysed from 11 participants. Subjective responses were quantified using visual analogue scale (VAS) and rating of perceived exertion (RPE).

Results: Peak torque decreased significantly with increasing CPM, from 28.24±15.61 Nm at 5 CPM to 19.01±7.04 Nm at 40 CPM ($p=0.026$, $\eta^2=0.316$). Cumulative torque showed even larger differences, declining from 10,566±6,109 Nm·s at 5 CPM to 921±377 Nm·s at 40 CPM ($p<0.001$, $\eta^2=0.739$). While average cardiorespiratory responses did not differ significantly between CPM settings ($p>0.05$), all trials significantly increased maximum VO_2 from rest (252.9±50.7 mL/min) to exercise (569.4-608.8 mL/min, $p<0.001$, $\eta^2=0.834$). Discomfort increased significantly with higher CPM, with VAS scores at 20 minutes ranging from 3.08±1.51 (5 CPM) to 4.33±1.76 (40 CPM) ($p<0.01$).

Conclusions: Lower CPM settings (5-10 CPM) optimized isometric FES by maximizing force production and minimizing discomfort while maintaining equivalent cardiorespiratory stimulation to higher frequencies. These findings suggest that FES exercise protocols should prioritize lower CPM for force outcomes without compromising aerobic benefits.

Keywords: Functional electrical stimulation, isometric exercise, contractions per minute, muscle fatigue, cardiorespiratory response, muscle torque

INTRODUCTION

Functional Electrical Stimulation (FES) is a therapeutic technique that delivers controlled electrical pulses to evoke muscle contractions in individuals with impaired voluntary motor control (1-3). By artificially activating paralysed muscles, FES helps counteract muscle disuse and supports cardiovascular and metabolic health in diverse neurological conditions (4-7). Various FES modalities have been developed to address different clinical needs, with FES cycling, FES knee extension and isometric FES, and FES rowing being among the most extensively studied approaches (8-10).

FES cycling synchronizes electrical stimulation with a motorized ergometer to generate rhythmic pedalling movements (11). This dynamic approach has been widely documented for its ability to enhance cardiopulmonary function, increase leg muscle mass, improve leg blood flow, and positively impact bone mass and glucose metabolism (6, 12-14). Despite these benefits, FES cycling requires specialized equipment and may not be suitable for all individuals, particularly those with joint instability, contractures, or severe spasticity (11, 15).

Isometric FES exercise offers an alternative approach, inducing muscle contractions without joint movement (16-18). Our recent experimental trial demonstrated that while FES cycling produced approximately 10% higher oxygen consumption compared to isometric FES under matched stimulation parameters, isometric FES still elicited substantial cardiorespiratory responses (Chapter 3). This finding challenges the traditional assumption that movement is essential for significant metabolic stimulation. Isometric FES provides practical advantages, including reduced equipment requirements and setup complexity compared to FES cycling.

The physiological responses to both isometric FES and FES cycling are primarily determined by stimulation parameters, though the specific adaptations may differ between modalities. (19).

Despite the established benefits of FES-based exercise, significant limitations persist, including rapid muscle fatigue and relatively low aerobic exercise intensity (3, 20-23). To improve exercise efficiency and clinical outcomes, optimizing stimulation parameters is essential. A key parameter influencing isometric FES exercise performance is contractions per minute (CPM), which defines the number of muscle contractions occurring within a given minute by electrical stimulation (2, 24). CPM is inversely related to the "period" of the stimulation pattern (CPM = 60/period in seconds), meaning that higher CPM settings shorten the inter-contraction interval.

While various FES parameters have been extensively studied, the effects of CPM remain underexplored, particularly in isometric applications. In contrast, studies have typically investigated stimulation frequency (Hz) within individual's contractions rather than CPM over time (25). The few studies examining CPM have generally fixed protocols without systematic comparison across CPM ranges (26). Additionally, most FES parameter studies has focused on either mechanical outcomes or metabolic responses in isolation, with limited investigation of their simultaneous effects (27). Previous research has primarily focused on FES cycling, where Fornusek and Davis (2008) examined cadence variations but found limited effects on cardiorespiratory responses (28).

Recent work by Ma et al. (2023) demonstrated that NMES protocols activating larger muscle groups (gluteals, hamstrings, quadriceps, calves) with higher duty cycles (1:4s contraction:

rest ratio) produced significantly greater energy expenditure increases (+51%) compared to protocols stimulating fewer muscles or using longer rest periods in individuals with SCI (29). Their study utilized high-frequency tetanic stimulation (70 Hz), which resulted in sustained contraction. Our protocol utilized sub-tetanic stimulation (35 Hz) with visible relaxation between pulses, allowing us to isolate the effects of contraction frequency (CPM) on physiological and mechanical responses. These differences in stimulation strategy may be attributed to the distinct response patterns observed between studies.

Despite various parameters of FES having been studied, the effects of CPM remain underexplored, especially in isometric FES exercises. Limited research exists on how CPM affects both muscle force production and metabolic cost. Therefore, this study aimed to address this research gap by examining how different CPM settings influenced acute aerobic responses and torque production in able-bodied individuals. We hypothesized that lower CPM settings would result in greater torque production due to longer recovery intervals between contractions, while oxygen consumption would remain unchanged across CPM conditions given the localized and submaximal nature of isometric contractions.

METHODS

Participants

Twelve able-bodied male participants (mean age ± SD: 26.9 ± 7.4 years, range: 18–41 years) were recruited for this study. Recruitment was conducted via convenience sampling through university advertisements, social media platforms, and departmental newsletters. Inclusion criteria required participants to be physically active, free from neurological or cardiovascular conditions, and either seizure-free or with well-controlled seizures. Exclusion criteria included musculoskeletal impairments, cardiovascular instability (resting blood pressure

>140/90 mmHg), uncontrolled medical conditions, recent lower-limb injuries (within the past six months), sensory impairments affecting response to electrical stimulation, or any contraindication to exercise testing. Participants were screened using the Exercise and Sports Science Australia (ESSA) pre-exercise screening system to ensure they met all eligibility criteria. All participants were provided with a detailed explanation of the study's purpose, procedures, potential risks, and benefits before providing written informed consent. The study was approved by the Institutional Review Board of the University of Sydney (Project no. 2024/HE000199).

Study Design

This study employed a randomized, repeated-measures crossover design to assess the effects of different CPM settings on muscle force production, aerobic responses, and discomfort levels during isometric FES. Participants completed six laboratory visits, two familiarization sessions and four experimental trials. The four experimental sessions involved different CPM conditions (5, 10, 20, and 40 CPM), assigned randomly using a computer-generated concealed randomization schedule to minimize order effects. All sessions were separated by at least 48 hours to ensure adequate recovery and reduce carryover fatigue. Individual stimulation thresholds were established, and electrode placements were precisely marked to maintain consistency across all trials.

Experimental Setup

During familiarization, participants were introduced to the testing procedures, equipment, and the sensation of electrical stimulation. To enhance stimulation tolerance and ensure consistent muscle activation during the experimental trials, stimulation intensities were progressively increased until participants reached a tolerable yet effective contraction level. Individual

stimulation thresholds were determined, and electrode placements were standardized for consistency across trials. These sessions also allowed participants to adapt to the testing environment and minimize discomfort-related variability. In the experimental phase, participants underwent isometric FES testing while seated on a machine, where muscle force, cardiorespiratory responses, and discomfort levels were recorded under different CPM settings. The following sections detail the physical setup, FES implementation, and measurement procedures.

Physical Setup

A Cybex HUMAC Norm dynamometer (CSMi, Massachusetts, USA) was used to measure instantaneous isometric torque produced by the electrically stimulated quadriceps and hamstrings. The dynamometer was calibrated per the manufacturer's instructions before each session. Participants were seated on the dynamometer with the hip joint at approximately 90° of flexion and the right knee joint at approximately 70° of flexion (0° = full extension). This configuration was chosen as it was comfortable for participants and is close to the 90° knee flexion angle commonly used for assessing isometric quadriceps strength and was consistently replicated throughout all sessions. The anatomical axis of rotation of the knee was carefully aligned with the dynamometer's axis. To ensure stability, the upper body, pelvis, and femoral region were secured using a three-point safety belt and a thigh strap. The foot of the tested limb was attached to the dynamometer arm just above the medial malleolus using a Velcro strap, while the non-tested limb was stabilized with a limb support bar. The dynamometer was positioned at the 90° knee flexion position to maintain accurate isometric conditions throughout all stimulation protocols (available ROM: 0° to 90°). The range of motion (ROM) was restricted to 0° extension to 90° flexion. Seating positions and joint angles were recorded during the first session and replicated in all subsequent visits.

Before testing, the procedure was thoroughly explained to each participant. They were instructed not to voluntarily move their leg, maintain contact with the backrest, and hold the machine handles throughout the test. Participants completed two familiarization trials before the actual experiment to ensure familiarity with the procedure. Participants were asked to rate their discomfort every 2 minutes on a VAS scale, where 0 = [no discomfort/pain at all] and 10 = [maximum tolerable discomfort/worst imaginable pain].

FES Implementation

Surface electrodes (7.5 × 13 cm, ValuTrode) were placed bilaterally following standardized anatomical landmarks (30). For quadriceps stimulation, electrodes were positioned over the motor points of the vastus medialis (distal electrode) and vastus lateralis (proximal electrode). Hamstring electrodes were placed over the biceps femoris and semitendinosus muscles.

Electrical stimulation was delivered using a programmable stimulator (MOTOmed Viva 1; RECK-Technik GmbH) generating symmetrical biphasic rectangular pulses at 35 Hz with a pulse width of 250 μs. At the beginning of each session, stimulation amplitude was progressively increased from 0 mA until participants reached their maximum tolerable level, with peak amplitude generally achieved between 9-12 minutes. Once maximum tolerance was reached, the amplitude was maintained constant for the remainder of the 20-minute protocol. Stimulation amplitude was individually determined during familiarization sessions and was set to achieve substantial muscle contraction while maintaining participant comfort (<7/10 on a Visual Analogue Scale [VAS], where 0 = no discomfort and 10 = extreme unbearable discomfort). This threshold was selected based on validated pain severity classification systems (31), where scores ≥8 represent "severe pain" and scores of 6-7 represent "moderate pain. While our participants were able-bodied, we applied these

established cut-off points to ensure that electrical stimulation-induced discomfort remained within the mild-to-moderate range without progressing to what would be considered severe discomfort. A progressive 10-min ramp was employed at the start of each session to achieve a stable, tolerable amplitude; amplitude was then maintained constant.

Experimental trial

Following familiarisation, participants underwent four randomized trials of different CPM protocols (5, 10, 15, and 20 CPM) with a fixed 30% duty cycle. Each trial consisted of a 20-minute stimulation time. Quadriceps and hamstrings were stimulated simultaneously throughout all protocols, producing co-contraction of these anatomically antagonistic muscle groups. This approach maximized participant comfort and recruited greater muscle mass, aligning with our primary metabolic focus. Torque values therefore reflect net knee joint torque (extensor minus flexor contribution), which underestimates total mechanical work by both groups. However, simultaneous activation ensured that both quadriceps and hamstrings contributed to oxygen consumption despite their opposing mechanical actions. Rest periods between contractions were adjusted according to the CPM setting to maintain the same total contraction time per minute. In this experimental trial, a fixed 30% duty cycle means that lower CPM increases each contraction's duration and the inter-contraction interval (Table 1), parameters that influence electromechanical delay, force rise/relaxation, and metabolite clearance. Lower CPM settings provide longer contraction durations, allowing complete force to rise and relaxation cycles, while longer inter-contraction intervals permit more complete metabolite clearance, phosphocreatine resynthesis, and reduced accumulation of fatigue-inducing metabolites. Conversely, higher CPM settings with brief contractions may terminate before peak force is achieved, and shorter recovery intervals limit metabolic restoration between contractions. We hypothesized that these physiological advantages at

lower CPM would result in superior force maintenance, which was confirmed by our results showing significantly higher peak and cumulative torque at lower CPM settings. The stimulation parameters are presented in Table 1.

Table 1: Stimulation parameters for CPM experiment

Protocol	CPM	Duty Cycle	Period (s)	*Contraction Time (s)
1	40	30%	1.5	0.45
2	20	30%	3.0	0.90
3	10	30%	6.0	1.80
4	5	30%	12.0	3.60

* Calculated from Duty Cycle × Period

The protocol began with a 5-minute resting baseline measurement of heart rate (HR), oxygen consumption (VO_2), and blood pressure, followed by a 20-minute stimulation period and a 5-minute recovery phase. During each of the four experimental sessions, participants remained in the same position as the stimulator delivered contractions at the predetermined interval.

Metabolic exercise testing

Cardiorespiratory responses (including VO_2) were measured using a Medgraphics metabolic gas analysis system, which was calibrated before each session using certified calibration gases and a 3-liter syringe to ensure accurate cardiorespiratory measurements. Breath-by-breath data were collected through a mouthpiece during rest, during exercise, and throughout recovery. HR was continuously monitored using a Polar OH1 arm strap, which was secured via an adjustable arm strap, capturing data at rest, during the 20-minute exercise session, and during the rest period. HR and cardiorespiratory variables were averaged over 2-minute intervals, with resting and peak values extracted for analysis. Blood pressure measurements were taken at rest, mid of the FES exercise session, immediately post-exercise, and at 5-

minute intervals during recovery using a manual sphygmomanometer and stethoscope to ensure accuracy and consistency.

Participant reported outcomes

Participant's comfort and exertion were systematically monitored using standardized scales. Discomfort was assessed using a 10-cm visual analogue scale (0-10), with 0 being "no discomfort at all" and 10 representing "extreme, unbearable discomfort", at 2-minute intervals. Perceived exertion was recorded using the Borg rate of perceived exertion (RPE) (32) scale (6-20) at the midpoint (10 minutes) and end (20 minutes) of the stimulation session.

Data Collection and Analysis

Data from all 12 participants were included in the analysis. The sample size of 12, while modest, was deemed sufficient based on an a priori power analysis for repeated measures: detecting a medium effect size ($f \approx 0.25$) in VO_2 or torque across 4 conditions with 80% power at $\alpha = 0.05$ required at least 10 participants. To account for potential dropouts or missing data, we recruited 12 participants.

All physiological and cardiorespiratory data (HR, oxygen consumption/VO2), as well as quadriceps muscle torque data were processed using MATLAB R2024a (The MathWorks, Natick, MA, USA). For each CPM protocol, average and maximum values of HR and VO_2 were extracted for analysis. Resting baseline values were compared to active exercise conditions using repeated-measures ANOVA, with statistical significance set at $p < 0.05$. Post-hoc pairwise comparisons were performed with Bonferroni correction to account for multiple testing. Effect sizes were calculated using Cohen's d for pairwise contrasts and

partial eta-squared (η^2) to assess the magnitude of effects in the ANOVA models. Data normality was tested using the Shapiro–Wilk test, and Mauchly's test evaluated sphericity. When sphericity was violated, the Greenhouse–Geisser correction was applied to adjust the degrees of freedom appropriately.

Torque data were collected and processed throughout each trial using the Cybex HUMAC Norm dynamometer, which continuously recorded instantaneous torque at a sampling rate of 100Hz. The sampling rate was calculated by analysing the time intervals between consecutive samples, where the time step of 0.01 seconds resulted in a sampling rate of 100Hz. Custom MATLAB scripts were used to calculate average torque, maximum torque values for each CPM protocol. For each individual muscle contraction, the maximum torque and torque sum was determined during analysis. Three primary torque values were then calculated: (1) Average Peak Torque = the mean of all individual contraction peak torques; (2) Maximum Peak Torque = the highest single peak torque value; and (3) Cumulative Torque = the integral of torque over time (total work). All torque values were extracted from the entire 20-minute stimulation period for analysis. All results are expressed as mean ± SD, unless otherwise stated. All statistical analyses were performed using SPSS (v29, IBM Corp) and GraphPad Prism (for graphical visualization).

RESULTS

Cardiorespiratory response

The average cardiorespiratory data across all four CPM conditions (5, 10, 20, and 40 CPM) and time points are presented in figures 1A and 1B.

i. Average and Maximum cardiorespiratory response

No significant differences were found in VO_2 or HR across CPM conditions. Average VO_2 did not differ between contraction rates ($p = 0.086$), and maximum VO_2 remained unchanged ($p > 0.05$). Similarly, average HR ($p = 0.342$) and maximum HR ($p > 0.05$) were not affected by CPM settings. Effect sizes were small to moderate (partial $\eta^2 = 0.107–0.404$). Mauchly's test indicated a violation of sphericity for HR ($p = 0.029$), requiring Greenhouse-Geisser correction. However, overall, CPM did not significantly influence cardiorespiratory responses. The effects of different CPM conditions on average values of VO_2 and HR responses are summarized in Table 2.

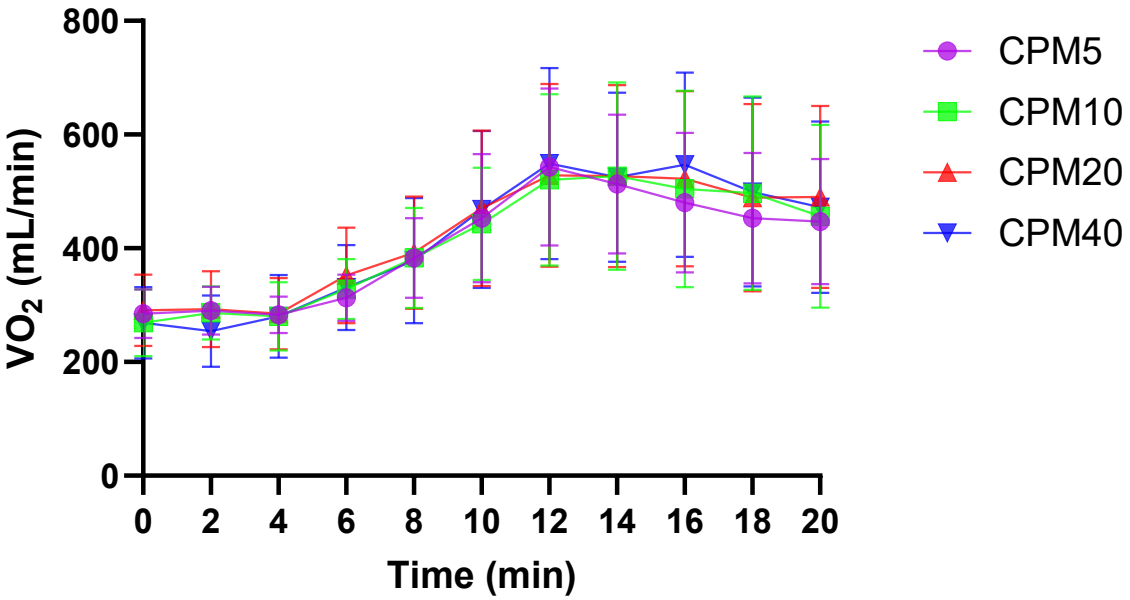

Figure 1A Oxygen consumption rate (VO_2) over time for different CPM conditions (5, 10, 20, and 40). Data points represent mean VO_2 (mL/min) at each time interval, with different symbols corresponding to distinct CPM conditions

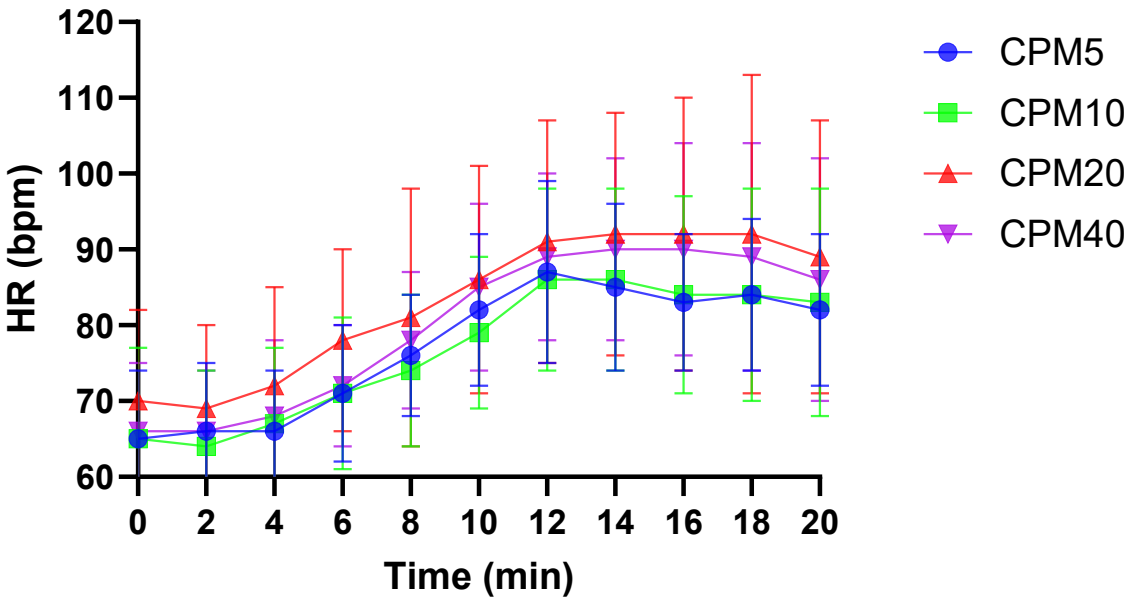

Figure 1B Heart rate (HR) over time for different CPM conditions (5, 10, 20, and 40). Data points represent mean HR (bpm) at each time interval, with different symbols corresponding to distinct CPM conditions.

Table 2. Cardiorespiratory responses during CPM (5, 10, 20, and 40 CPM) protocols (Mean and standard deviation (SD)).

	Rest (Average)	CPM5	CPM10	CPM20	CPM40
VO_2 (mL/min)					
Average - Mean	–	406.2	428.1[a]	444.2[a]	449.1
Average - SD	–	58.9	98.0	128.2	92.1
Maximum - Mean	252.9	569.4	568.0[a]	579.8[a]	608.8
Maximum - SD	50.7	126.3	149.8	148.8	127.8
p-value	Average: 0.086		Maximum: <0.001		
HR (bpm)					
Average - Mean	–	77.3	77.9[b]	83.7[b]	73.3
Average - SD	–	8.5	10.3	14.3	22.9
Maximum - Mean	66.6	89.9	90.8[b]	98.4[b]	95.1
Maximum - SD	7.3	10.9	11.6	20.3	14.0
p-value	Average: 0.342		Maximum: 0.003		

[a]Values from 11 participants for VO_2 measurements. [b]Values from 9 participants for HR measurements. Abbreviations: CPM, contractions per minute; HR, heart rate. No significant differences were found between CPM conditions. Note: cardiorespiratory data were analysed from 11 participants for VO_2 measurements and 9 participants for HR measurements due to technical errors encountered during data acquisition.

Rest versus Maximum cardiorespiratory response

All CPM conditions significantly increased maximum VO_2 and HR from rest ($p<0.001$), but no differences were found between contraction rates (all $p > 0.05$) (Table 2). Maximum VO_2 increased from 2 52.9±50.7 mL/min at rest to 569.4-608.8 mL/min during exercise, while maximum HR increased from 66.6±7.3 bpm to 89.9-98.4 bpm.

Due to the amplitude ramp-up, peak VO_2 and the rest-to-peak VO_2 are highlighted, average VO_2 across the entire 20 min should be interpreted with consideration of this ramp-up phase, as it includes both the progressive amplitude increase period and the stable amplitude period.

Torque Peak and Cumulative (Average and Maximum)

Peak torque decreased significantly with increasing CPM ($p = 0.026$). Average peak torque declined from 28.24±15.61 Nm at 5 CPM to 19.01±7.04 Nm at 40 CPM, showing a significant linear trend ($p = 0.036$). Maximum peak torque showed an even greater decline ($p < 0.001$), from 59.94±30.31 Nm at 5 CPM to 25.75±9.97 Nm at 40 CPM, with significant differences between low CPM (5, 10) and 40 CPM conditions ($p < 0.05$) (Figure 2).

Cumulative torque showed an even more pronounced decline ($p < 0.001$), dropping from 10,566±6,109 Nm·s at 5 CPM to 921±377 Nm·s at 40 CPM. Significant differences were found between 5 CPM and all other conditions ($p < 0.01$), and between both 10 CPM and 20 CPM versus 40 CPM ($p < 0.05$). The effects of different CPM conditions on peak torque measures are summarized in Table 3

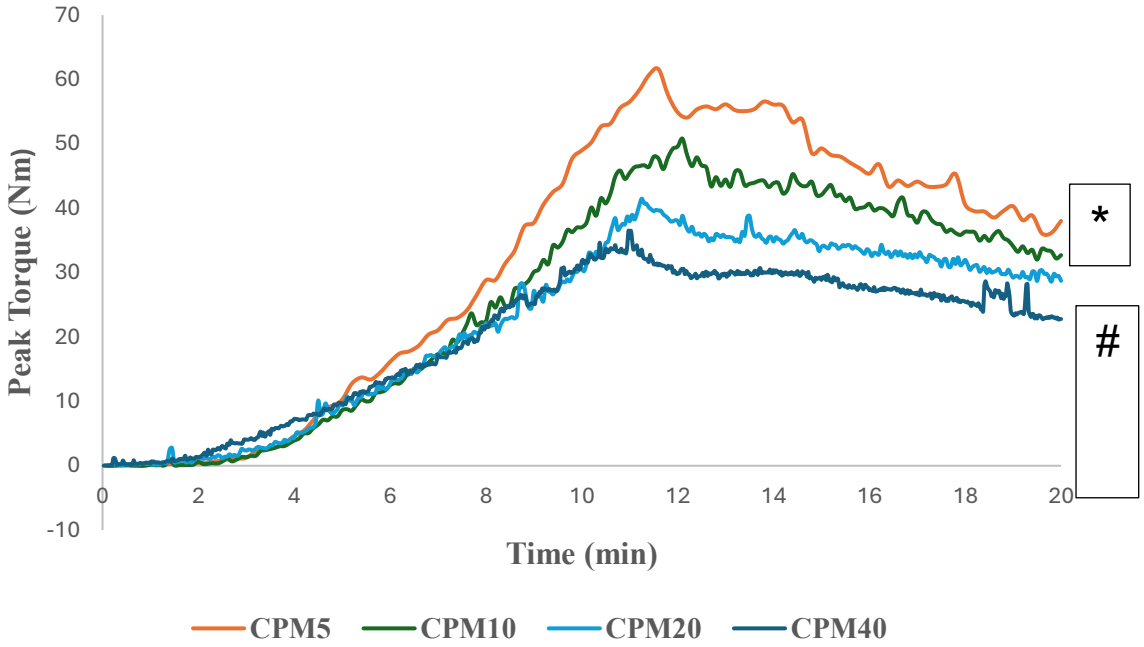

Figure 2. Average peak torque (Nm) over time during isometric FES at different contraction frequencies (CPM: 5, 10, 20, and 40), across participants (n = 11)

*Significant difference between CPM 5 and all conditions

#Significant difference between CPM40 and CPM 10 and 20

The abrupt change in the CPM40 curve near the end of the trial may reflect stimulation dropout or signal noise in one participant's dataset; this was retained following standard preprocessing but should be interpreted cautiously.

Table 3 Comparison of torque-related parameters (Peak Torque, Peak Torque Max, and Cumulative Torque) across different CPM conditions.

	CPM5	CPM10	CPM20	CPM40
Peak Torque (Nm)				
Mean (Nm)	28.2	26.7	21.8	19.0
SD	15.6	16.7	8.55	7.04
p-value	-	0.563	0.127	0.026*
Peak Torque Max (Nm)				
Mean (Nm)	59.9	50.8	34.5	25.8
SD	30.3	31.1	13.4	9.97
p-value	-	0.488	0.024*	<0.001**
Cumulative Torque (Nm·s)				
Mean (Nm·s)	10,566	5167	1980.97	921
SD	6109	3353	822	377
p-value	-	0.004**	0.009**	<0.001**

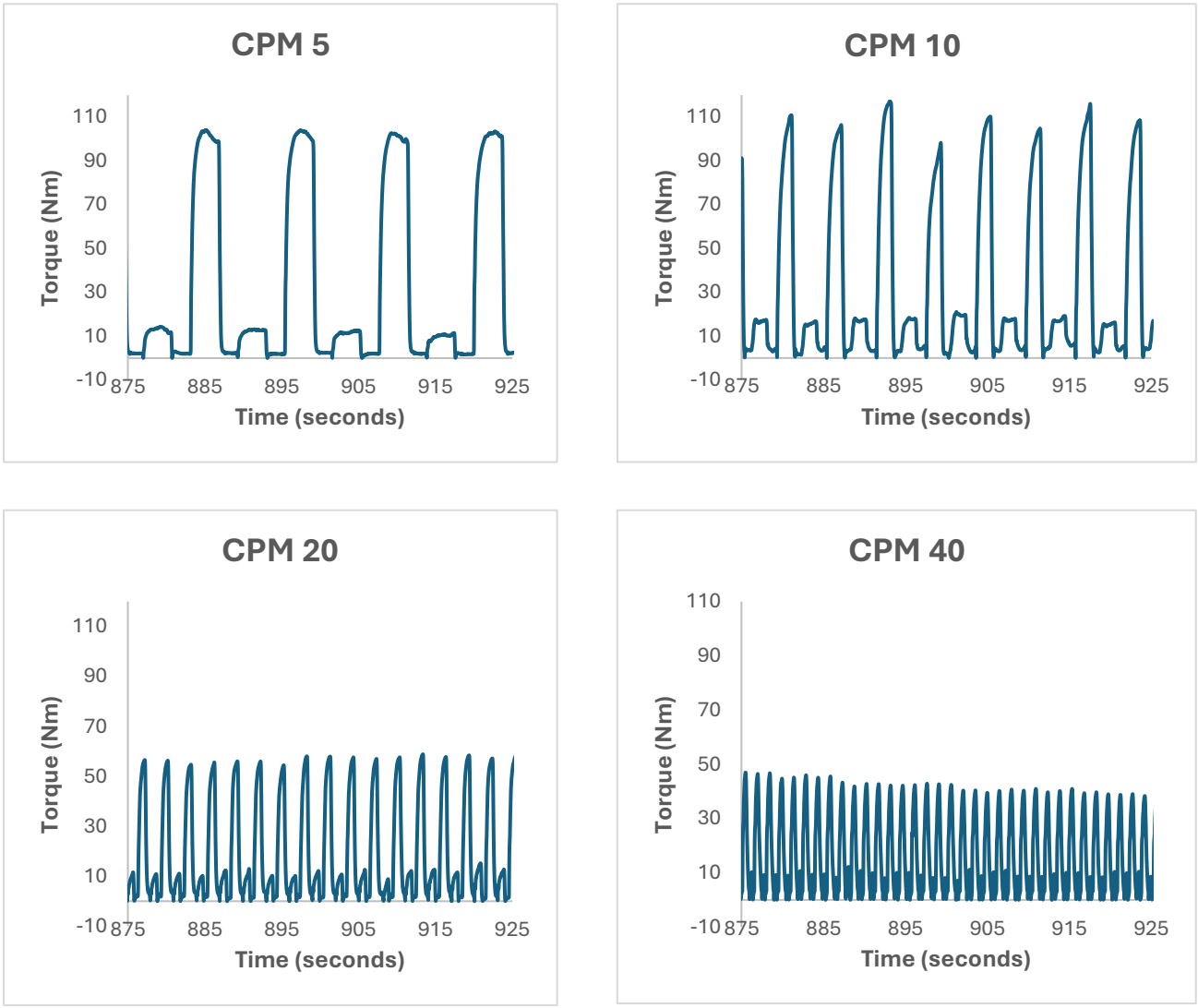

Figure 3. Representative torque traces from a single participant during 50 seconds of isometric FES at different CPM settings. (A) 5 CPM condition showing four complete contraction cycles with consistent peak torque (~103 Nm) and longer contraction durations (3.6 s). (B) 10 CPM condition displaying eight contraction cycles with peak torque of ~110-117 Nm and shorter contraction durations (1.8 s). (C) 20 CPM condition showing approximately 16-17 contraction cycles with reduced peak torque (~55-58 Nm) and shorter contraction durations (0.9 s). (D) 40 CPM condition displaying approximately 33-34

contraction cycles with further reduced peak torque (~47 Nm initially decreasing to ~38 Nm) and the shortest contraction durations (0.45 s).

Participant reported outcomes

Discomfort (VAS scores): A two-factor ANOVA revealed significant effects of CPM condition ($F(3,33) = 7.85$, $p < 0.001$) and time ($F(2,66) = 12.43$, $p < 0.001$), indicating that both higher contraction rates and longer durations significantly elevated perceived discomfort. VAS scores increased progressively over time across all CPM protocols, with higher CPMs leading to greater discomfort. CPM5 showed the lowest discomfort levels, with scores rising gradually from 0.33±0.49 at 2 minutes to 3.08±1.51 at 20 minutes. CPM10 induced similar moderate discomfort, increasing from 0.42±0.51 to 3.33±1.61. CPM20 showed a steeper rise from 0.58±0.67 to 3.42±1.68. CPM40 resulted in the highest discomfort, with VAS scores reaching 4.33±1.76 by session end, showing noticeable increases after the 10-minute mark. Post-hoc analyses confirmed that CPM40 caused significantly higher discomfort than both CPM5 ($p < 0.01$) and CPM10 ($p < 0.05$) by the end of the session. All participant-reported outcomes are presented in Table 4, demonstrating the clear relationship between higher CPM settings and increased discomfort over time.

Table 4. Visual Analogue Scale (VAS) scores across different CPM conditions (Mean ± SD)

	Initial VAS (2 min)	**Mid VAS (10 min)**	**Final VAS (20 min)**
CPM5	0.33 ± 0.49	1.75 ± 0.97	3.08 ± 1.51
CPM10	0.42 ± 0.51	1.83 ± 1.03	3.33 ± 1.61
CPM20	0.58 ± 0.67	2.08 ± 1.08	3.42 ± 1.68
CPM40	0.67 ± 0.65	2.75 ± 1.22*	4.33 ± 1.76*

*Significantly different from CPM5 ($p < 0.05$)

DISCUSSION

This study examined how isometric FES under similar duty cycles with varying stimulation period could influence cardiovascular responses, muscle force production, and subjective experiences in able-bodied individuals. Our findings revealed that while cardiorespiratory responses remained relatively consistent across CPM settings, muscle force production and participant comfort were significantly impacted by contraction frequency.

Muscle torque & recovery

Peak torque was significantly greater at lower CPM (highest at 5 CPM, lowest at 40 CPM). This striking inverse relationship between CPM and force production can be attributed to the distribution pattern of recovery intervals rather than total recovery time, which remained constant across all conditions due to the identical 30% duty cycle. In addition, the temporal constraint imposed by contraction duration on force development is a crucial factor. Every electrically evoked contraction requires a period of time for electromechanical delay; force rise and relaxation. At higher CPM settings, these phases generate a greater amount of the

total contraction time. For example, at 40 CPM with 0.45s contractions, if electromechanical delay and force rise require approximately 0.2-0.3s, the muscle may reach peak force only briefly or not at all before relaxation begins. In contrast, at 5 CPM with 3.6s contractions, the same force rise time allows the muscle to reach and sustain peak force for a significantly longer period. This means that higher CPM conditions not only provide less recovery time between contractions but also reduce the effective force-producing time within each contraction, compounding the reduction in both peak and cumulative torque output.

The physiological concept that during electrically evoked contractions, multiple factors contribute to force reduction when inter-contraction intervals are reduced. The observed decline in force production at higher CPM may be due to incomplete restoration of neuromuscular transmission efficiency and metabolic recovery between contractions (33-35). This is supported by research from Fornusek and Davis (2004), who demonstrated that inadequate recovery time between FES-induced contractions significantly reduced force output due to multiple peripheral and central fatigue mechanisms (36).

Allen et al. (2008) provided further evidence that these mechanisms include impaired calcium handling, reduced membrane excitability, and incomplete metabolite clearance, all of which require sufficient time between contractions to recover (37). This aligns with finding with Fornusek et al.'s (2008) finding that the most important factor in developing muscle hypertrophy is sustained muscle force production rather than stimulation patterns or metabolic demand (28).

Our findings extend this research by analysing the cumulative torque produced across different CPMs. Specifically, torque output decreased from 10,566 Nms at 5 CPM to 922

Nms at 40 CPM, indicating that 5-10 CPM may be ideal for force-focused interventions. Furthermore, the superior force maintenance at lower CPMs likely reflects more effective metabolic recovery between contractions, though the specific mechanisms require further investigation. Although all conditions provided the same total recovery time, the longer individual recovery intervals at lower CPMs may allow more complete restoration of muscle excitability and energy substrates between contractions.

Cardiorespiratory responses

No significant differences in maximum oxygen consumption or heart rate were observed across the CPM conditions tested. While comprehensive metabolic assessment techniques such as metabolic cart measurements or blood lactate analysis were not employed in this study, the consistent VO_2 response across varying CPM conditions merits consideration. The absence of significant differences in oxygen consumption despite increasing contraction frequencies could be attributed to the recruitment characteristics during electrical stimulation, specifically the preferential activation of fast-twitch glycolytic fibres and the non-physiological recruitment order during FES (38). Additionally, the gradual decline in peak torque and cumulative work observed at higher CPMs suggests that performance was more limited by local muscular fatigue than by systemic (i.e., central) oxygen delivery capacity. These observations align with Mizrahi (1997)'s findings that electrically induced contractions demonstrate reduced metabolic efficiency than voluntary exercise (39). This reduced efficiency is attributed to the synchronous recruitment of motor units and altered fibre type activation patterns during electrical stimulation, which differs significantly from the size principle-based recruitment in voluntary contractions.

A noteworthy finding requiring careful interpretation was the dissimilarity between torque production and oxygen consumption in CPM conditions. Several methodological and physiological factors may explain this observation. First, oxygen consumption measurements have inherent variability, and differences between CPM conditions may have been insufficient in measurement error. Secondly, electrical current may have activated non-target muscles (hip flexors, adductors, trunk stabilizers) that remained relatively constant across CPM conditions while target muscle force varied, causing the torque-VO_2 dissociation (38). Third, stimulation intensities (individually adjusted to tolerance) may not have recruited the full motor unit pool, potentially limiting both force and metabolic demand. Additionally, the dynamometer measured net joint moment during simultaneous quadriceps-hamstring co-contraction, indicating both muscle groups utilized oxygen while their mechanical contributions partially cancelled in the net measurement.

Our protocol included a significant number of contraction events (100 at 5 CPM versus 800 at 40 CPM, an 8-fold difference). If each contraction gains relatively low metabolic costs for calcium handling, regardless of the peak force achieved, this could partially explain similar VO_2 despite varying torque production. Recent work on FES metabolic responses has demonstrated that energy expenditure during electrical stimulation relates to both the number of contraction events and the repeated activation-relaxation cycling rather than sustained force alone (29). However, this interpretation requires validation through near-infrared spectroscopy for muscle oxygenation monitoring or metabolic substrate analysis to determine the relative contributions of activation costs versus force maintenance costs in our specific FES protocol.

The disparity between the significant differences observed in muscle torque production across CPM conditions and the absence of corresponding differences in cardiorespiratory responses presents an intriguing physiological phenomenon. This may be attributed to the relatively small muscle mass engaged during quadriceps and hamstring stimulation, which may be insufficient to drive differential central cardiovascular responses despite the varying mechanical outputs. The stimulation parameters employed in this study may have recruited only a portion of the available muscle mass, resulting in submaximal cardiorespiratory difficulty regardless of the CPM setting. Additionally, higher CPM conditions may have maintained similar energy expenditure through ineffective muscle activation, expending energy without proportional force production. Davis et al. (2008) emphasized that even modest increases in cardiorespiratory activity can help mitigate cardiovascular deconditioning in chronically immobilized patients (4). Our findings extend the current understanding by demonstrating that these cardiorespiratory benefits appear to be independent of CPM settings when duty cycle is held constant.

Heart rate increased significantly from rest (66.6 ± 7.3 bpm) to exercise (89.9–98.4 bpm, $p < 0.001$) but showed no differences between CPM conditions ($p = 0.342$). Similarly, oxygen consumption rose from 252.9 ± 50.7 $mL \cdot min^{-1}$ at rest to 569.4–608.8 $mL \cdot min^{-1}$ during stimulation ($p < 0.001$) yet remained stable across CPM settings. This pattern mirrors that reported by Fornusek et al. (2008), where VO_2 and HR remain unchanged across different FES cycling cadences despite large differences in mechanical work output (40). The absence of a proportional HR or VO_2 increase in the present study suggests that the cardiovascular system was not significantly challenged, and that the metabolic demand was met through local oxygen extraction and microvascular adaptations rather than increased central cardiac output. The dissociation between torque and systemic responses therefore

indicates that FES-induced contractions generate sufficient peripheral metabolic demand to elevate VO_2 modestly, but not enough to activate central cardiovascular regulation to the extent seen during voluntary or hybrid exercise. These findings reinforce that under the current stimulation parameters, FES primarily acts as a localized muscular activation stimulus, producing limited cardiovascular responses.

Patient reported outcomes

Participant discomfort ratings showed a complex relationship with CPM settings. While statistical analysis identified higher discomfort at CPM20/40 compared to CPM5/10 ($p<0.05$), it is important to note that stimulation amplitude often required adjustment at the lower CPM settings due to participants reporting greater sensations during the longer individual contractions. This pattern indicates that discomfort perception may be influenced by both contraction duration and frequency. Maffiuletti (2010) has demonstrated that subjective responses to electrical stimulation are multifactorial, involving both peripheral and central mechanisms of sensory processing (25).

The observed relationship between contraction pattern and discomfort can be attributed to the neurophysiological characteristics of mechanoreceptors and nociceptors during electrical stimulation. With longer individual contractions (CPM5/10), the intensity of each stimulation burst needed careful monitoring, while at higher CPM settings (CPM20/40), the cumulative effect of frequent shorter contractions appeared to influence overall session tolerability.
The decline in RPE during sessions suggests that participants adapted to the stimulation protocol over the course of time. This adaptation may have occurred through physiological mechanisms (such as descending pain modulation) or psychological factors (including reduced anxiety with continued exposure) (41). An exception to this adaptation pattern was

observed at 40 CPM, where RPE was elevated throughout the session. This sustained perception of effort at the highest CPM may reflect the cumulative effects of repeated contractions with minimal recovery, though specific physiological markers of metabolic stress were not assessed in this study.

The observed inverse relationship between CPM settings and comfort ratings contrasts the torque-fatigue relationship previously discussed. Our findings indicate that protocols with longer contraction rates (5–10 CPM) were generally better tolerated by participants compared to higher contraction rates (20–40 CPM), likely due to the adequate recovery time between each stimulated contraction. This observation is consistent with research by Kesar and Binder-Macleod (2006), who demonstrated that neuromuscular stimulation protocols incorporating sufficient recovery intervals between contractions resulted in improved force maintenance and reduced subjective discomfort, potentially due to more complete metabolic recovery between activation periods (42).

Synthesizing our findings reveals a consistent pattern: lower CPM settings (5-10 CPM) generally produced greater peak and cumulative torque values compared to higher CPM settings (20-40 CPM). Despite the higher torque values at lower CPM settings, it is important to note that stimulation amplitude often required adjustment during the 5-10 CPM conditions due to the greater intensity of sensation reported by participants during the longer individual contractions.

For practical application, our findings suggest a tiered approach to CPM selection based on training goals. For muscle strengthening and hypertrophy, where sustained force production is paramount, lower CPM settings (5-10 CPM) appear optimal. This recommendation

corresponds with findings from Dudley-Javoroski and Shields (2008) (18), who achieved significant improvements in muscle mass using low-frequency isometric FES training. For cardiorespiratory responses, the absence of significant differences between CPM conditions suggests that parameter selection can be guided primarily by other factors such as torque production and participant comfort, as the metabolic stimulus appears consistent across the tested range.

While our data indicated lower average discomfort ratings at lower CPM settings, the relationship between contraction parameters and subjective comfort proved multifaceted, with some participants reporting increased sensation intensity during the longer individual contractions of the 5-10 CPM protocols. The relationship between stimulation parameters and participant comfort is supported by contemporary research by Maffiuletti et al. (2018), who demonstrated that rest interval characteristics significantly influence both physiological responses and subjective tolerance during electrical stimulation (7). Our findings contribute to the understanding of how contraction timing specifically affects the user experience during isometric FES applications.

Hamstring vs Quadriceps activation:

The co-activation approach employed in this study increased the total muscle mass recruited for metabolic evaluation. However, this creates interpretive limitations for torque data. The dynamometer measured net joint moment, resulting when both quadriceps (extension) and hamstrings (flexion) contract simultaneously. Therefore, measured torque values are significantly underestimated by total force production. If quadriceps generate 30 Nm extension while hamstrings generate 25 Nm flexion simultaneously, only 5 Nm net torque is recorded, yet both muscle groups are mechanically active and metabolically expensive. If the

co-contraction ratio varied across CPM conditions, this could explain the change in net torque despite consistent metabolic reactions.

We cannot determine if quadriceps and hamstrings contributed significantly to cardiorespiratory responses or force production, as we did not accurately measure forces. The relative impact of each muscle group during electrical stimulation depends on electrode placement, current amplitude, and tissue characteristics rather than physiological recruitment order (38). Current penetration depth is affected by subcutaneous adipose tissue thickness (43), and regional differences in fat distribution between anterior and posterior thigh regions could affect relative muscle activation, potentially explaining inter-individual variability in torque responses. Quadriceps and hamstrings have distinct fibre-type compositions and metabolic characteristics, which may respond differently to different recovery periods.

Implications for SCI populations:

While this study established FES parameters in able-bodied individuals, translation to SCI populations requires examining altered muscle characteristics. Following SCI, skeletal muscle undergoes atrophy (40-50% cross-sectional area loss) and fibre-type transformation from slow oxidative to fast glycolytic phenotypes, reducing oxidative capacity and increasing fatigability (18). Dudley-Javoroski and Shields (2008) documented increased type II fibre percentage and reduced oxidative enzyme capacity post-SCI (18). Although fast-twitch dominant muscles may benefit from longer recovery intervals (as opposed to lower CPM), this has not been directly investigated in SCI populations. Recent studies show FES protocols emphasizing force production and adequate recovery produce superior muscle adaptations in SCI (44, 45), supporting potential benefits of lower CPM approaches.

In individuals with complete SCI and sensory impairment below injury level, subjective discomfort reporting cannot guide parameter adjustment (46). Stimulation must be monitored using objective criteria: visual muscle assessment, skin inspection, and temperature monitoring. In our able-bodied participants, particularly at 5-10 CPM, participants reported increased sensation intensity during longer contractions (3.6s) compared to brief contractions (0.45s), likely reflecting temporal summation where longer stimulation duration increases accumulated sensory signals. However, the absence of sensation in SCI populations may lead to greater muscle recruitment, potentially enabling greater muscle recruitment.

Duty Cycle, Contraction Duration, and Long-term Training Implications:

Our protocol maintained constant 30% duty cycle (18 seconds stimulation per minute) across all CPM conditions, varying only the temporal distribution: few long contractions (5 CPM) versus many brief contractions (40 CPM). This isolated contraction-relaxation frequency effects while keeping total stimulation time equivalent. Given the 11.5-fold cumulative torque difference between 5 and 40 CPM, longitudinal investigation is necessary to determine if superior acute force at lower CPM is a result of enhanced chronic adaptations. CPM selection should be individualized, lower CPM (5-10) optimizes force production, while our findings showed similar acute VO_2 across all CPM settings, allowing CPM selection based on force goals or comfort without substantially affecting single-session metabolic stimulation. Additional considerations include skeletal integrity (lower CPM generates higher peak forces) and activity integration.

Limitations

First, this study included only able-bodied male participants to reduce biological variability in this initial assessment of CPM effects. However, this limits the scope of the findings, as

females typically exhibit lower stimulation thresholds and different muscle activation patterns due to variations in subcutaneous adipose tissue and muscle cross-sectional area. These physiological differences may influence torque production, stimulation tolerance, and metabolic responses, implying that the present findings may not directly impact female or clinical populations. In individuals with SCI, the significant changes in muscle fibre type distribution (toward fast-twitch predominance), neuromuscular excitability, and metabolic capacity would likely amplify the differences we observed between CPM conditions. The increased proportion of fast-twitch fibres in chronic SCI muscle would theoretically increase the force advantage of lower CPM settings while potentially reducing fatigue at higher CPMs. Additionally, the altered calcium handling and excitation-contraction coupling that facilitates long-term denervation could alter the relationship between contraction-relaxation cycles and force production (47). Our findings to clinical populations should therefore consider these neurophysiological adaptations, which may require even longer contraction intervals in SCI populations to achieve optimal force production.

Second, a significant limitation was our decision not to include maximal voluntary contraction (MVC) assessments to normalize torque values. While this approach was taken to minimize participant fatigue between conditions, it limited our ability to express torque as a percentage of maximal capacity. The inclusion of MVCs would have provided valuable context for interpreting the relative effort represented by the torques produced across different CPM conditions, particularly for understanding the relationship between maximal force capability and the forces elicited through electrical stimulation. Future studies should incorporate normalized measurements to enhance comparability across different muscle groups and populations.

Third, torque output was the only mechanical outcome observed in this study. While this provided a practical and consistent measure of force across CPM conditions, it does not capture the underlying neuromuscular processes that contribute to force production. Surface EMG, electromechanical delay, and contraction-relaxation dynamics could have provided a greater understanding of activation timing, antagonist co-contraction, and stimulation efficiency. Due to potential interference with stimulation electrodes, participant discomfort from additional sensors, and the need for advanced signal processing to isolate stimulation artefacts, these measures were excluded to minimize protocol complexity and participant burden while remaining focused on the primary research objectives. In addition, this study did not include surface EMG or blood lactate measurements, which limits interpretation of neuromuscular activation patterns and anaerobic contribution. These omissions were intended to reduce protocol complexity and participant burden. However, they restrict physiological insight into mechanisms underlying force production and metabolic response.

This analysis was limited to acute responses following a single session at each CPM setting, rather than chronic adaptations caused by repeated training. Although lower CPM settings resulted in greater acute force production, it is not yet established if this leads to superior long-term training adaptations. Future longitudinal research should investigate the impact of these acute differences on chronic muscular and functional outcomes.

Future Research Directions

Our findings highlight several promising avenues for future research. First, investigating the interaction between CPM and other stimulation parameters (duty cycle, pulse width, amplitude) could yield more comprehensive optimization guidelines. Gregory et al. (2007)

suggested that these parameters exhibit complex interactions that cannot be fully understood by manipulating them in isolation (48).

Second, exploring these effects in populations with neuromuscular impairments would enhance the translational impact of our findings. Martin et al. (2012) demonstrated that FES responses vary significantly between able-bodied individuals and those with neurological conditions, emphasizing the importance of population-specific parameter optimization (2). Assessing both acute responses and longitudinal adaptations in these diverse populations would provide valuable insights for exercise application and training protocols.

Finally, investigating whether these findings extend to dynamic FES applications (e.g., cycling, rowing) would broaden their applicability. Fornusek and Davis (2008) demonstrated that lower cadences during FES cycling produced significantly greater muscle forces and hypertrophy compared to higher cadences despite fewer total contractions (40). The mechanical principles underlying this force-cadence relationship appear consistent across contraction modalities, suggesting that the fundamental biomechanical advantage of longer inter-contraction intervals may extend to cyclic FES applications. Comparative studies across different FES modalities would help develop more comprehensive exercise guidelines and training recommendations.

CONCLUSION

This study provides novel evidence that CPM settings significantly influence muscle force production and subjective comfort during isometric FES, while cardiorespiratory responses remain relatively consistent across tested CPM protocols. Our findings suggest that lower CPM settings (5-10 CPM) offer superior performance for sustained exercise applications by

increasing force output while reducing neuromuscular fatigue, potentially enhancing participant comfort without compromising cardiorespiratory benefits at these stimulation intensities. These results have significant implications for refining FES exercise, indicating that CPM is a key parameter, indicating careful consideration.

The observed relationship between lower CPM and enhanced force maintenance challenges certain techniques in clinical FES applications that emphasize higher CPM. Our data provide a more precise approach to parameter selection that prioritizes sustainable force production over immediate contractile response. Specifically, the inverse relationship between CPM and sustainable force output observed in our study suggests that neural and muscular fatigue mechanisms may be differentially affected by stimulation cadence in ways not previously emphasized in FES protocol design.

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CHAPTER 5

Differential Muscle and Cardiovascular Responses to Duty Cycle Modulation During Isometric Functional Electrical Stimulation Exercise

PREFACE

This chapter extends the investigation of stimulation parameters in isometric FES by focusing on duty cycle, the ratio of contraction to relaxation time, while holding CPM constant. Building on the findings from Chapter 4, this study examines how different duty cycle settings (10%, 20%, 30%, and 40%) influence acute cardiorespiratory, neuromuscular, and subjective responses during isometric contractions. Duty cycle is a key component of FES, as it directly affects the work-to-rest ratio experienced by the muscle, with implications for performance, fatigue, and comfort. By comparing these ratios under a controlled CPM, this study provides critical insights into the physiological trade-offs of varying contraction durations. The comprehensive evaluation of multiple physiological domains allows for a nuanced understanding of how duty cycle adjustments can be tailored to specific clinical or performance goals, whether optimizing force output or improving cardiovascular conditioning. In addition to the findings from CPM modulation, this study supports the development of evidence-based protocols for isometric FES, helping to refine parameter selection for various therapeutic applications in individuals with neuromotor impairments.

Author Attribution Statement

The co-authors of the manuscript *Differential Muscle and Cardiovascular Responses to Duty Cycle Modulation During Isometric Functional Electrical Stimulation Exercise* confirm that Prakash Dhopte had made the following contributions:

- Assisted with concept and design
- Collected the data
- Analysed collected data
- Interpretation of the findings
- Writing the paper and critical analysis of the manuscript

As the primary supervisors for the candidature upon which this thesis is based, I can confirm that the authorship attribution statements above are correct.

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ABSTRACT

Background

Functional Electrical Stimulation (FES) exercise offers a viable alternative for individuals with limited mobility, enabling aerobic and muscular activation without joint movement. The optimization of stimulation parameters, particularly the duty cycle, could be an imperative factor in maximizing efficacy and tolerability, though this requires systematic investigation.

Design

Randomized, repeated-measures crossover

Methods

Twelve able-bodied male participants (mean age ± SD: 25 ± 7 years) completed four sessions of isometric FES, each with a different duty cycle (10%, 20%, 30%, 40%) at a fixed contraction frequency of 10 contractions per minute (CPM) and stimulation period. oxygen consumption (VO_2), heart rate (HR), peak and average torque per contraction perceived exertion (RPE), and discomfort ratings (VAS) were measured.

Results

Heart rate increased significantly with higher duty cycles, with maximum HR reaching 95.55±10.97 bpm at 40% duty cycle compared to 85.82±12.21 bpm at 10% duty cycle ($p=0.001$). Oxygen consumption increased from rest in all sessions ($p<0.001$) but showed no significant differences across duty cycles ($p=0.580$). Peak torque decreased progressively with increasing duty cycle, from 65.35±7.14 Nm at 10% to 49.89±9.20 Nm at 40% ($p=0.036$). Conversely, average torque per contraction increased significantly with higher duty cycles, from 4,070.01±580.37 Nm·s at 10% to 11,065.21±2,236.31 Nm·s at 40% ($p<0.001$). Discomfort levels were significantly higher at 30% and 40% duty cycles compared to lower duty cycles ($p<0.001$), while RPE decreased from mid-session to end-session across all conditions ($p<0.05$).

Conclusion

Duty cycle manipulation during isometric FES significantly affected cardiovascular responses and muscle force responses. Higher duty cycles (30-40%) produced increased heart rates and average torque per contraction, while lower duty cycles (10-20%) better preserved peak force production with less discomfort. Since oxygen consumption did not differ significantly between duty cycles, duty cycle selection should be based on mechanical force objectives and participant tolerance rather than metabolic training goals.

Keywords: Functional Electrical Stimulation (FES), Duty Cycle, Isometric FES, muscle torque

INTRODUCTION

The physiological benefits of exercise for individuals with mobility impairments are well established, yet conventional exercise modes remain inaccessible for many with significant motor limitations (1-3). Functional Electrical Stimulation (FES) has emerged as a valuable intervention that artificially activates muscles to generate functional movements and physiological responses, enabling exercise in those with limited voluntary control (4-6).

Previous research has demonstrated that cardiorespiratory responses remain equivalent between isometric and dynamic FES when stimulation parameters are matched. This finding suggests that simpler isometric protocols can serve as an efficient research model for parameter optimization that translates to more complex FES applications, including FES cycling where duty cycle manipulation is equally critical.

Duty cycle, defined as the proportion of time muscles are actively stimulated within a contraction cycle, represents a particularly promising yet underexplored parameter for optimizing isometric FES (7). Duty cycles can be expressed either as a percentage (e.g., 30%) or as a time ratio (e.g., 10s ON / 30s OFF = 25% duty cycle) (7, 8). The duty cycle directly governs the work-to-rest ratio, fundamentally altering metabolic demands, fatigue development, and ultimately the sustainability of the exercise (9, 10). Higher duty cycles extend the contraction duration relative to recovery time, potentially intensifying metabolic stress and cardiovascular responses but potentially accelerating muscle force reduction (7, 11). Conversely, lower duty cycles provide extended recovery between contractions, potentially enabling greater preservation of muscle force but possibly reducing overall metabolic stimulus (7, 12, 13).

Recent studies have examined the effects of duty cycle and stimulation frequency on energy expenditure during electrical stimulation in individuals with SCI. Ma et al. (2023) investigated duty cycle effects (1:4s vs 1:8s) on energy expenditure using neuromuscular electrical stimulation (NMES) of paralysed lower-limb muscles at 70 Hz with current amplitudes of 35-120 mA, reporting that protocols with shorter rest periods (1:4s duty cycle) produced the highest increase in energy expenditure (+51%; +0.7 kcal/min) compared to rest, though this was accompanied by significant muscle fatigue (14). Woelfel et al. (2017) demonstrated that low-frequency electrical stimulation using single twitches (1 Hz and 3 Hz) at 50-100 mA significantly increased oxygen consumption in people with complete SCI, with 1 Hz stimulation proving more metabolically efficient per stimulus pulse delivered despite requiring longer training duration(15). Their oxygen consumption increased from 195 mL/min to 311 mL/min at 1 Hz (+60%) and 367 mL/min at 3 Hz (+90%). These findings suggest that stimulation intensity (current amplitude and muscle mass recruited), duty cycle (ratio of contraction to rest time), and the absolute duration of these intervals are all key factors in the metabolic and mechanical responses during electrically evoked exercise. Since cardiorespiratory responses are equivalent between isometric and dynamic FES, investigating duty cycle effects using isometric protocols provides a standardized platform for parameter optimization that applies broadly to FES cycling, functional movements, and clinical applications.

This study aimed to investigate how varying duty cycles (10%, 20%, 30%, and 40%) affected cardiorespiratory responses and muscle force responses during isometric FES using a fixed contraction frequency of 10 CPM. Limited research has systematically examined duty cycle effects on the balance between metabolic and mechanical responses during FES exercise. Through comprehensive assessment of cardiorespiratory responses, neuromuscular

performance, and subjective experiences, this investigation sought to characterize the relationships between duty cycle and physiological responses. Given the limited existing evidence, this study adopted an exploratory approach to determine optimal duty cycle selection. These findings are expected to inform duty cycle selection across the broad range of FES applications, providing evidence-based parameter selection for FES cycling protocols, functional training programs, and exercise programs.

METHODS

Participants

Twelve able-bodied male participants (mean age ± SD: 25 ± 7 years, height: 176 ± 7 cm, weight: 81 ± 20 kg, BMI: 26 ± 4) were recruited for this study. Recruitment was conducted via convenience sampling through university advertisements, social media platforms, and departmental newsletters. Inclusion criteria required participants to be physically active, free from neurological or cardiovascular conditions, and either seizure-free or with well-controlled seizures. Exclusion criteria included musculoskeletal impairments, elevating resting blood pressure (>140/90 mmHg), uncontrolled medical conditions, recent lower-limb injuries (within the past six months), sensory impairments affecting response to electrical stimulation, or any contraindication to exercise testing. Participants were screened using the Exercise and Sports Science Australia (ESSA) pre-exercise screening system to ensure suitability for participation. All participants were provided with a detailed explanation of the study's purpose, procedures, potential risks, and benefits before providing written informed consent. The study was approved by the Institutional Review Board of the University of Sydney (Project no. 2024/HE000199).

Study Design

This study employed a randomized, repeated-measures crossover design to assess the effects of different duty cycles on muscle force production, aerobic responses, and discomfort levels during isometric FES. Participants completed six laboratory visits, including two familiarization sessions and four experimental trials. Participants who had already participated in the FES experiment described in Chapter 4 were already familiar with the protocol and therefore were not required to undergo additional familiarization sessions. The four experimental sessions involved different duty cycle conditions (10%, 20%, 30%, and 40%), assigned randomly using a computer-generated concealed randomization schedule to minimize order effects. All sessions were separated by at least 48 hours to ensure adequate recovery and reduce carryover fatigue. Individual stimulation thresholds were established, and electrode placements were precisely marked to maintain consistency across all trials.

Experimental Setup

Physical Setup

Isometric torque, used as an index of knee extensor (quadriceps femoris muscle) was measured with a Cybex HUMAC Norm dynamometer (CSMi, Massachusetts, USA) produced by the FES. The dynamometer was calibrated per the manufacturer's instructions before each session. Participants were seated on the dynamometer with the hip joint at approximately 90° of flexion and the right knee joint at approximately 70° of flexion (0° = full extension). This configuration was chosen as it was comfortable for participants and is close to the 90° knee flexion angle commonly used for assessing isometric quadriceps strength and was consistently replicated throughout all sessions. The anatomical axis of rotation of the knee was aligned with the dynamometer's axis. To ensure stability, the upper body, pelvis, and femoral region were secured using a three-point safety belt and a thigh strap. The right shank of the tested limb was attached to the dynamometer arm just above the

medial malleolus using a Velcro strap, while the non-tested limb was stabilized with a limb support bar. Since this was an isometric protocol, the knee joint was positioned at 90° flexion throughout all tests. Seating positions and joint angles were recorded during the first session and replicated in all subsequent visits.

Before testing, the procedure was thoroughly explained to each participant. They were instructed not to voluntarily move their leg, maintain contact with the backrest, and hold the machine handles throughout the test. Participants completed two familiarization trials, if required, before the actual experiment to enhance adaptability and ensure effective performance.

FES Implementation

Surface electrodes (7.5 × 13 cm, ValuTrode) were placed bilaterally on the quadriceps. The electrodes were positioned over the motor points of the vastus medialis (distal electrode) and vastus lateralis (proximal electrode) using anatomical landmarks, and positions were marked with a marker on the skin.

Electrical stimulation was applied to the quadriceps muscles only, rather than including hamstrings as in Chapter 4, for several practical and methodological reasons. During the CPM experiments in Chapter 4, participants frequently experienced muscle cramps and increased fatigue in the hamstrings, particularly at longer durations. Additionally, the seated position on the Cybex dynamometer (knee at 90° flexion, hip at 90° flexion) placed the hamstrings in a shortened position, which significantly increased discomfort during electrical stimulation and reduced tolerance for sustained contractions. Given that the present study required 20-minute protocols at duty cycles up to 40% (2.4 seconds of continuous stimulation

every 6 seconds), we anticipated that hamstring stimulation would be poorly tolerated and might lead to premature protocol termination.

From a methodological standpoint, stimulating only quadriceps also provided advantages. First, it allowed clearer interpretation of duty cycle effects on a single muscle group without potential confounding from differential fatigue characteristics between quadriceps and hamstrings, which have distinct fibre-type compositions and metabolic profiles. Second, focusing on bilateral quadriceps stimulation reduced the total current amplitude requirements and increased overall participant comfort during the 20-minute protocols.

Electrical stimulation was delivered using a programmable stimulator generating symmetrical biphasic rectangular pulses at 35 Hz with a pulse width of 250 μs. At the beginning of each session, stimulation amplitude was progressively increased from 0 mA until participants reached their maximum tolerable level, with peak amplitude generally achieved between 9-12 minutes. Once maximum tolerance was reached, the amplitude was maintained constant for the remainder of the 20-minute protocol. Stimulation amplitude was individually determined during familiarization sessions, ranging from 60-110 mA, and then held constant across all experimental sessions for each participant, targeting a discomfort below < 7/10 on a numeric discomfort scale.

Experimental trial

Following familiarisation, participants underwent four randomized trials of different duty cycle protocols (10%, 20%, 30%, and 40%) with a fixed 10CPM (period of 6 seconds). Based on the findings from Chapter 4, 10 CPM was selected as it provided effective cardiorespiratory responses while maintaining adequate muscle force output. Each trial

consisted of a 20-minute stimulation time. The duty cycle and period were pre-specified for each condition, resulting in different contraction and rest durations while maintaining a constant 10 CPM. The stimulation parameters are presented in Table 1.

Table 1: Stimulation parameters for Experiment 2 trials

Protocol	CPM	Duty Cycle	Period (s)	Contraction Time (s)
1	10*	10%	6*	0.1×Period
2	10*	20%	6*	0.2× Period
3	10*	30%	6*	0.3×Period
4	10*	40%	6*	0.4×Period

* Contractions Per Minute (CPM) and Period parameters selected from chapter 4. Period = 60/CPM

The protocol began with a 5-minute resting baseline measurement of HR, VO_2, and blood pressure, followed by a 20-minute stimulation period and a 5-minute recovery phase. During each of the four experimental sessions, participants remained in the same position as the stimulator delivered contractions at the predetermined interval.

Metabolic exercise testing

Cardiorespiratory responses including oxygen consumption (VO_2) were measured using a Medgraphics metabolic gas analysis system. HR was continuously monitored using a Polar OH1 arm strap, which was secured via an adjustable arm strap. All cardiorespiratory variables (VO_2, HR) were collected continuously at rest, during the 20-minute exercise session, and during the recovery period. These variables were averaged over 2-minute intervals for time-course analysis, and both average and peak values were extracted for statistical analysis.

Participant reported outcomes

Discomfort was assessed using a 10-cm visual analogue scale (VAS), with 0 representing "no discomfort" and 10 representing "discomfort as bad as possible" (16). Participants marked

their perceived discomfort level anywhere along the continuous line, and scores were determined by measuring the distance from the left anchor to the participant's mark in centimetre's. Participants rated their discomfort level immediately following each electrical stimulation bout, and these assessments were conducted at regular 2-minute intervals throughout the entire 20-minute stimulation period, resulting in 10 discomfort measurements per session. Perceived exertion was recorded using the Borg rate of perceived exertion (RPE) scale (6-20) (17) measured at midpoint (10 minutes) and end (20 minutes) of the stimulation session.

Data Collection and Analysis

Cardiorespiratory responses were extracted from the raw metabolic cart data and averaged to 30-second intervals and were analysed using SPSS (v29, IBM Corp). Torque data from Cybex, were processed using MATLAB R2024a (The MathWorks, Natick, MA, USA). For each duty cycle protocol, average and maximum values of HR and VO_2 were extracted for analysis. Data normality was tested using the Shapiro–Wilk test, and Mauchly's test evaluated sphericity. When sphericity was violated, the Greenhouse–Geisser correction was applied to adjust the degrees of freedom appropriately. Resting baseline values were compared to active exercise conditions using repeated-measures ANOVA, with statistical significance set at $p < 0.05$. If ANOVAs were significant, post-hoc pairwise comparisons were performed with Bonferroni correction to account for multiple testing. Effect sizes were calculated using Cohen's d for pairwise contrasts and partial eta-squared (η^2) to assess the magnitude of effects in the ANOVA models.

Torque data were continuously recorded throughout each trial using the Cybex HUMAC Norm dynamometer at a sampling rate of 100Hz. For each duty cycle protocol, we calculated the following measures:

- Peak torque: the highest force output during each individual contraction, averaging throughout the session.
- Maximum torque: the single highest torque value recorded throughout the entire session.
- Average torque per contraction: calculated as the total time-integrated torque (Nms) summed across all contractions during the 20-minute session, then divided by the number of contractions. This represents the average mechanical impulse per contraction. Since no joint displacement occurred during isometric contractions, no mechanical work was done. Although this measure is sometimes referred to as "work" in the literature, it is more accurate in terms of torque-time integral or mechanical impulse. For consistency with terminology used throughout this chapter and for comparison with previous literature, it is reported as "average torque per contraction".

RESULTS

Cardiorespiratory response

The average cardiorespiratory data across all four duty cycles conditions (10%, 20%, 30%, and 40%) and time points are presented in figures 1A and 1B.

Statistical analysis indicated that duty cycle significantly affected HR but not VO_2 (Table 2). Both average HR ($p = 0.006$, $\eta^2 = 0.333$) and maximum HR ($p = 0.001$, $\eta^2 = 0.417$) increased progressively, peaking at DC40. Pairwise comparisons showed that maximum HR was significantly higher in DC40 than DC10 ($p = 0.040$) and DC30 ($p = 0.048$), while average HR was significantly higher in DC40 than DC30 ($p = 0.014$). In contrast, average VO_2 ($p =$

0.580, $\eta^2 = 0.057$) and maximum VO_2 ($p = 0.480$, $\eta^2 = 0.071$) remained stable across conditions. A significant positive linear relationship between duty cycle and maximum HR was observed ($\eta^2 = 0.477$, $p = 0.013$).

Table 2. Cardiorespiratory responses during duty cycle (10%, 20%, 30%, and 40%) protocols.

	Resting	**DC10%**	**DC20%**	**DC30%**	**DC40%**
VO_2 (mL/min)					
Average - Mean	–	383.3	405.0	393.3	398.4
Average - SD	–	55.0	98.5	79.2	77.4
Maximum - Mean	263.4	522.9	556.4	534.6	562.4
Maximum - SD	69.1	80.4	118.1	101.9	104.8
p-value	Average: 0.580		Maximum: <0.001		
HR (bpm)					
Average - Mean	–	76.4	78.7	79.8	83.5
Average - SD	–	10.7	9.6	10.5	10.0
Maximum - Mean	68.4	85.8	89.6	90.9	95.6
Maximum - SD	9.3	12.2	11.3	11.5	11.0
p-value	Average: 0.006		Maximum: <0.001		

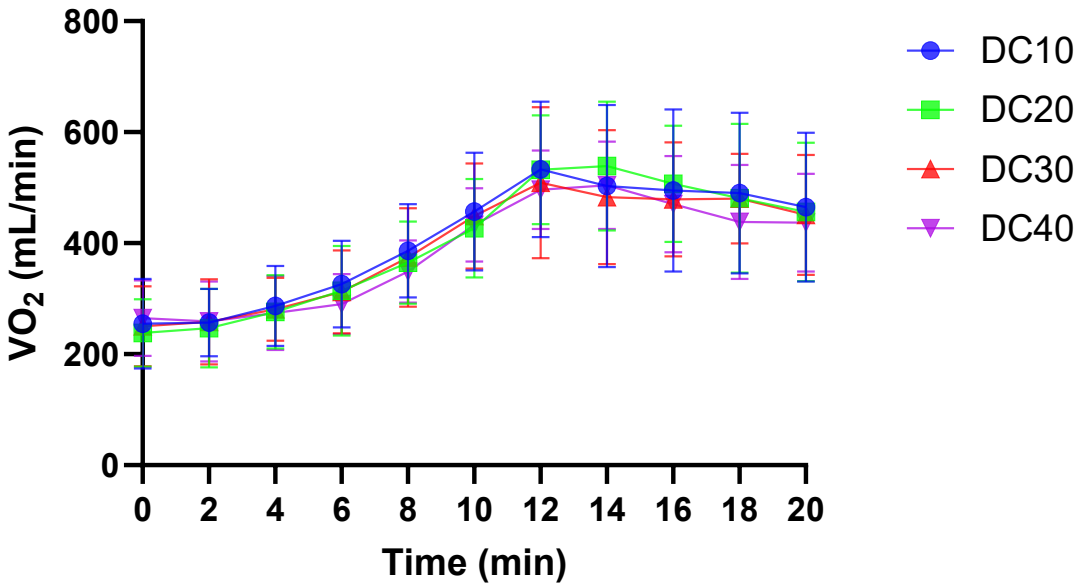

Figure 1A Oxygen consumption rate (VO_2) over time for different duty cycles (10%, 20%, 30%, and 40%).

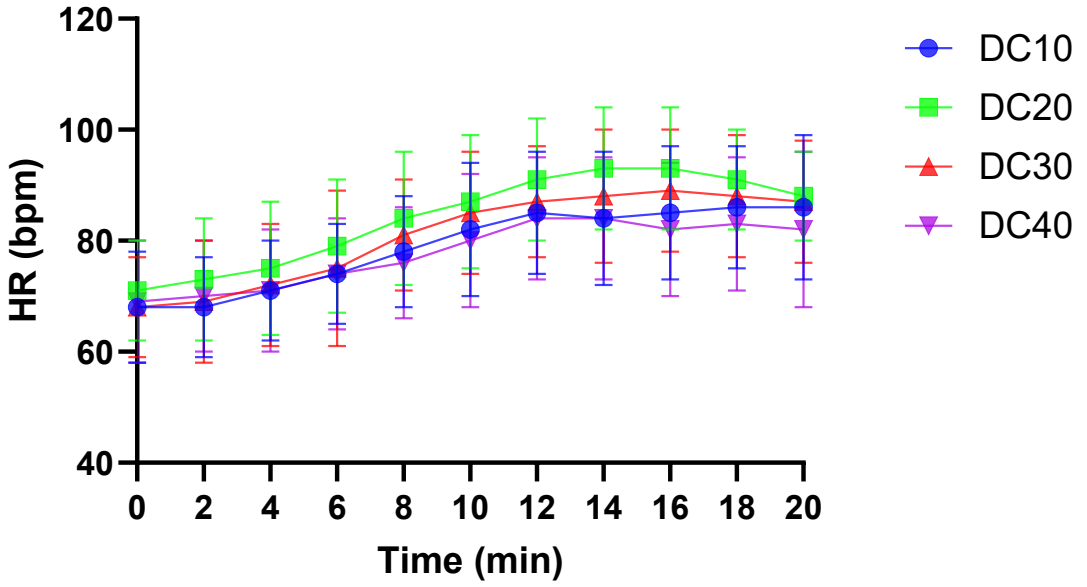

Figure 1B Heart rate (HR) over time for different duty cycles (10, 20, 30 and 40).

Rest Vs Max (VO_2 and HR)

Both maximum VO_2 and HR increased significantly from resting values across all duty cycles ($p < 0.001$). Maximum VO_2 ($\eta^2 = 0.807$) peaked at DC40 (562.42 ml/min), while maximum HR ($\eta^2 = 0.849$) reached 95.55 bpm. However, differences between consecutive duty cycles

were not significant ($p > 0.05$). Although each duty cycle produced significant increases from rest, the differences in response magnitude between different duty cycle conditions were not statistically significant ($p > 0.05$). Maximum HR showed a significant positive linear relationship with increasing duty cycle ($\eta^2 = 0.477$, $p = 0.013$), while VO_2 response remained relatively constant across duty cycle conditions despite the statistically significant increase from rest (Table 2).

Torque Average and Cumulative:

Peak torque and average torque per contraction showed significant differences across duty cycles, while maximum peak torque approached but did not reach statistical significance. Based on repeated measures ANOVA, peak torque ($p = 0.036$, $\eta^2 = 0.794$), average torque per contraction ($p < 0.001$, $\eta^2 = 0.969$) significantly changed across duty cycles, while maximum torque showed a non-significant trend ($p = 0.093$, $\eta^2 = 0.694$). Peak torque showed a decreasing trend with increasing duty cycle, with the highest values observed at DC10% and the lowest at DC40%. Total work output significantly increased progressively. Pairwise comparisons showed significant differences in total torque between DC10% vs. DC30% ($p = 0.029$), DC10 vs. DC40% ($p < 0.001$), DC20% vs. DC40% ($p = 0.015$), and DC30% vs. DC40% ($p = 0.000$), confirming a strong dose-response relationship between duty cycle and total work performed ($\eta^2 = 0.913$, $p < 0.001$). Table 3 summarizes these findings.

Table 3 Comparison of torque-related parameters (Peak Torque and Average torque per contraction) across different four duty cycles.

	DC10%	DC20%	DC30%	DC40%
Peak Torque (Nm)				
Mean (Nm)	65.35[a]	64.72[ab]	56.53[ab]	49.89[b]
SD	7.14	9.31	12.58	9.20
p-value	0.036*			
Average torque (Nm·s)				
Mean (Nm·s)	4,070.01[a]	7,047.65[b]	9,892.57[c]	11,065.21[d]
SD	580.37	981.66	1,938.78	2,236.31
p-value	<0.001*			

*$p < 0.05$ indicates statistical significance. Values with different superscript letters (a, b, c, d) are significantly different from each other based on Bonferroni-corrected pairwise comparisons.

Participant Reported Outcomes:

Discomfort ratings (VAS) showed a significant main effects of duty cycle ($F(3,44) = 8.12$, $p < 0.001$) and time ($F(9,132) = 11.56$, $p < 0.001$). VAS scores increased over time across all duty cycles, with higher duty cycles (DC30%, DC40%) inducing significantly greater discomfort. The highest pain levels were observed in DC40% (3.75 ± 1.48 at 20 minutes, $p < 0.01$ vs. DC10%, $p < 0.05$ vs. DC20%), while DC10 exhibited the lowest discomfort (2.33 ± 1.11 at 20 minutes).

Two-way repeated measures ANOVA revealed a significant main effect of duty cycle on RPE ($p < 0.05$). However, no significant time × duty cycle interaction was observed. RPE significantly decreased from mid to end across all duty cycles ($p < 0.05$). The largest reduction was observed at DC30% (-1.75 points), while other conditions showed similar decreases (approximately -1.00 point).

DISCUSSION

The present study demonstrated the fundamental influence of stimulation duty cycle on both muscle force characteristics and cardiovascular outcomes during isometric FES exercise. The

findings demonstrated that while HR increased with higher duty cycles, oxygen consumption remains unchanged. Subjective measures showed a significant decline in RPE while discomfort with increased duty cycle.

Average and maximum HR values rose consistently, from a 10% duty cycle to 40% duty cycle ($p = 0.001$), likely reflecting the increased CPM (6 seconds at 10% vs. 24 seconds at 40%), not a change in CPM (which was fixed at 10). These results align with earlier reports demonstrating increased cardiovascular load with extended FES-induced contractions (18, 19). Despite significant HR elevation (from 76.36 bpm at 10% DC to 83.45 bpm at 40% DC, $p=0.006$; maximum HR from 85.82 to 95.55 bpm, $p=0.001$), VO_2 did not significantly differ across duty cycles ($p=0.580$) despite cumulative torque impulse increasing nearly 3-fold. This finding was unexpected, as increased contraction duration and total mechanical impulse would usually be associated with increased oxygen consumption. Several mechanisms may explain this counterintuitive HR-VO_2 dissociation. HR elevation strongly paralleled increases in discomfort, with VAS scores rising from 2.33±1.11 at DC10% to 3.75±1.48 at DC40% ($p<0.001$). In individuals with intact sensation, electrical stimulation triggers afferent sensory input activating sympathetic outflow, producing increased HR, peripheral vasoconstriction, and sweating, responses commonly observed during FES amplitude progression that occur independently of oxygen demand. The cumulative torque impulse increased due to longer absolute contraction duration (0.6s at 10% DC vs. 2.4s at 40% DC—4-fold increase) rather than higher force production; peak forces declined from 65.35 Nm to 49.89 Nm.

The VO_2 (383-398 mL/min average; 523-562 mL/min maximum) had modest demands (1.5-2.1 times resting rate), with a narrow rest period variation (3.6-5.4s) likely allowing comparable recovery between contractions. The relatively small muscle mass recruited

(bilateral quadriceps only) may not produce sufficient demand to significantly increase whole-body VO_2 despite increased cardiac work. In addition, breath-by-breath measurement variability during intermittent low-intensity FES may have limited detection of small VO_2 differences, and without stroke volume measurements, cardiac output changes remain uncertain. These findings indicate that duty cycle selection should not be based solely on cardiovascular responses, as HR increases do not reflect the proportional changes in oxygen consumption.

The observed dissociation between HR and VO_2, where HR increased significantly while VO_2 remained stable across duty cycles, may reflect a combination of physiological, perceptual, and methodological factors, and correlation does not necessarily imply causation. A primary explanation is that HR elevation was driven by sympathetically mediated cardiovascular responses to discomfort rather than increased metabolic demand (20). This interpretation is supported by our discomfort data, in which scores progressively increased from 2.33 ± 1.11 at DC10% to 3.75 ± 1.48 at DC40% ($p < 0.001$), closely representing the HR pattern. Prior studies have documented similar HR-VO_2 dissociations during electrical stimulation protocols (19, 21), particularly in individuals with intact sensation where afferent input can drive autonomic activation. Recent studies provide further evidence of HRVO2 dissociation in FES contexts: for example, in a patient undergoing 11 months of FES cycling training, ventilatory patterns shifted despite only modest changes in VO_2 (22). In addition, in a larger study of electrical stimulation exercise in SCI populations, changes in VO_2 did not always align with anticipated cardiovascular outcomes (23). During FES exercise, HR responses may predominantly reflect neural/autonomic activation or discomfort, rather than true aerobic metabolic loading.

However, alternative explanations warrant equal consideration. The relatively small muscle mass recruited during quadriceps FES may not generate sufficient metabolic demand to substantially elevate whole-body VO_2, despite increased cardiac work. Additionally, methodological factors such as metabolic cart sensitivity, mask leakage, or delayed VO_2 kinetic responses during low-intensity intermittent FES, may have affected our ability to detect small metabolic differences. Cardiac efficiency changes or altered cardiovascular regulation in response to FES independent of metabolic demand represent further possibilities.

The clinical significance of this finding is that duty cycle optimization should not be based solely on cardiovascular responses, as HR increases may not reflect the proportional increases in metabolic cost or muscle activation. This indicates that the increased duty cycle does not significantly increase metabolic demand at these parameters, which is crucial for FES prescription. Future studies using longer FES duty cycles (e.g., >60% or continuous stimulation) could improve detection of HR-VO_2 dissociation through sympathetic (heart rate variability, catecholamines) and metabolic (lactate, near-infrared spectroscopy) monitoring.

The cumulative torque impulse increased primarily due to longer contraction duration rather than higher metabolic intensity; each contraction lasted 4 times longer at 40% DC (2.4s vs 0.6s) but peak forces were actually lower (49.89 Nm vs 65.35 Nm). Furthermore, the absolute VO_2 values (383-398 mL/min) were modest metabolic demands (1.1-1.2 times resting rate), indicating that all duty cycles produced low-intensity exercise where muscles met energy demands through similar oxidative rates. The same rest periods across conditions (3.6-5.4s) likely allowed comparable metabolic recovery between contractions, preventing the accumulation of metabolic stress that would increase VO_2. This dissociation between cardiac

and metabolic responses has been observed in other FES studies examining different stimulation parameters (18, 24).

An important design consideration is that while duty cycle varied from 10% to 40%, absolute rest periods between contractions showed relatively modest variation, ranging from 5.4s at 10% DC to 3.6s at 40% DC (a difference of only 1.8 seconds; Table 1), whereas contraction durations varied 4-fold (0.6s to 2.4s). Recovery intervals of 3.6-5.4 seconds may all provide sufficient partial metabolic recovery between contractions, allowing some restoration of high-energy phosphates and clearance of metabolic byproducts (9, 25). However, the rate of fatigue development likely differed across conditions due to the substantially longer absolute contraction durations at higher duty cycles. At 40% DC, each contraction lasted 4 times longer (2.4s vs 0.6s) than at 10% DC, imposing greater contractile stress per contraction despite similar recovery periods. This differential fatigue accumulation may explain why peak torque declined rapidly with increasing duty cycle (from 65.35 Nm at 10% to 49.89 Nm at 40%, $p=0.036$), yet VO_2 remained unchanged throughout the period. The similar rest periods across all duty cycles likely prevented the accumulation of systemic perturbations that would drive elevations in VO_2, while the longer contraction durations at higher duty cycles caused localized muscular fatigue without proportionally increasing whole-body oxygen consumption.

The decline in both peak and maximum torque values as duty cycle increased was not surprising. This observation demonstrated the considerable impact of duty cycle manipulation on neuromuscular performance during isometric FES. Interestingly, the opposite trend was observed for average torque per contraction, which increased significantly with higher duty cycles. At higher duty cycles (30-40%), the shorter relative recovery periods between

stimulations likely provided insufficient time for metabolic recovery and restoration of intracellular ion gradients, resulting in progressive force decline. The significant increase in average torque per contraction with higher duty cycles reflects the greater total contraction time rather than enhanced force production capacity. This measure represents the time-integrated force output (area under the torque-time curve), which naturally increases with longer absolute contraction durations despite declining peak force. At 40% duty cycle, each contraction lasted four times longer than at 10% duty cycle, resulting in greater total impulse despite the reduced peak force capability. This relationship between stimulation duration and total work output has been well-documented in electrical stimulation research, with similar patterns observed in studies examining the effects of prolonged stimulation on neuromuscular performance (26, 27).

While the perceived exertion may have decreased, the same cannot be said about the discomfort levels, which were reflected in increased discomfort scores. This was especially true at 30% and 40% duty cycles. While this may partially be explained by the build-up of metabolic byproducts and limited recovery for the muscle, it does not completely pinpoint how this can be rectified. A study by Ibitoye et al. (2016) found that discomfort was the primary barrier to continuous FES use at higher duty cycles (24). This is important to consider, as certain populations may have lower thresholds of pain or higher nerve sensitivities, and thus the FES must be tailored accordingly to achieve maximum output. Taking the previous recommendations into account, it may be more pertinent to set duty cycles at less than 30%, as they could enhance participant compliance and tolerability without compromising therapeutic efficacy.

While this study used able-bodied participants, several factors are critical for translating these findings to SCI populations. Following SCI, paralysed muscles undergo rapid atrophy, with

cross-sectional area reported to be up to 45% smaller than able-bodied controls within 6 weeks after complete injury (28), and fibre-type transformation from slow oxidative to fast glycolytic phenotypes with reduced oxidative capacity beginning 4-7 months post-injury (29). In our able-bodied cohort, higher duty cycles (30–40%) increased discomfort (VAS 3.75 + 1.48), which may not be a factor in individuals with complete SCI, who typically lack sensation below the lesion. People with SCI often tolerate higher stimulation intensities, enabling a larger muscle volume. However, it is important to note that duty cycle selection is not only about tolerance; it must also consider muscle fatigue, force sustainability, and specific clinical objectives such as cardiovascular conditioning or muscle hypertrophy. Additionally, in individuals with injuries above T6, high-intensity stimulation below the lesion can trigger autonomic dysreflexia (AD), a potentially fatal cardiovascular response (30). While this was not observed in our able-bodied study, our ramp-up protocol, gradual over 10–12 minutes with careful monitoring, may serve as a clinical strategy to mitigate AD risk during FES sessions in high-level SCI.

Our isometric protocol achieved the highest VO_2 values of 522-562 mL/min, lower than typical FES cycling values of 600-1200 mL/min reported in individuals with SCI. This likely reflects cycling's presence of greater total muscle mass (quadriceps, hamstrings, gluteal), compared to bilateral quadriceps-only stimulation in the current study. However, when stimulation parameters and muscle groups are matched, metabolic differences between isometric and FES cycling are minimal. Chapter 3 demonstrated only a 10% metabolic difference between modes, and previous work in individuals with SCI found no significant difference in metabolic responses between isometric quadriceps stimulation and FES cycling when total stimulated muscle mass was equivalent. These findings suggest that muscle mass recruited, and stimulation intensity are the primary determinants of oxygen consumption,

rather than the absence of movement. Isometric FES offers practical advantages: no specialized equipment beyond stimulator and electrodes, no wheelchair transfer, and compatibility with other activities, potentially enhancing adherence.

Limitations and Future Research Directions

Several limitations should be considered when interpreting the findings of this study. Although the inclusion of able-bodied participants limits direct generalization to clinical populations with neuromuscular impairments, the findings still provide valuable insights into the acute physiological responses to FES exercises. These results can serve as a basis for future work targeting therapeutic populations, even if some response patterns may differ. The 9–12-minute progressive ramp-up in stimulation amplitude at each session's start, while essential for safety and comfort, means our "20-minute" protocols actually included 29-32 minutes of total stimulation time. Future research should examine whether shorter warm-up periods (3-5 minutes) or starting at predetermined submaximal intensities could reduce session duration while maintaining safety. The acute experimental design prevents inferences regarding long-term adaptations to various duty cycle procedures, which may significantly differ from immediate responses. The FES amplitude was gradually increased over the first 9–11 minutes of the 20-minute stimulation period, until participants reached their maximum tolerable level. Once this level was achieved, the intensity was constant for the remainder of the session. This progressive ramp-up was implemented to prioritise comfort and safety and reflects standard clinical FES procedures, particularly in cases of sensory impairment or spasticity. However, since the ramp-up occurred within the 20-minute stimulation block, it could have reduced the duration of full-force stimulation and may have influenced the cumulative muscle output. Future studies should examine the effects of different duty cycles in persons with neuromuscular deficits to ascertain population-specific responses and ideal

parameters. Longitudinal research investigating chronic adaptations to various duty cycle regimes would yield significant insights into the long-term physiological and functional effects of isometric FES training.

CONCLUSION

This study illustrated that varying the duty cycle during isometric FES elicited distinct cardiovascular and neuromuscular responses. Higher duty cycles (30-40%) increased heart rates and average torque per contraction, whereas lower duty cycles (10-20%) more effectively maintained peak force production capabilities. The inverse relationship between duty cycle and peak torque, combined with equivalent cardiorespiratory responses between isometric and dynamic FES, indicates that these findings are directly linked to FES cycling applications. This provides a simplified research approach to optimizing duty cycle parameters across FES modalities without requiring complex dynamic testing. For clinical applications, lower duty cycles (10-20%) enhance peak force production, while higher duty cycles (30-40%) enhance total work output despite reduced peak force and increased discomfort. These findings provide evidence-based parameter selection for both isometric interventions and FES cycle protocols. Future research should investigate these relationships using clinical work-to-rest ratios (1:3, 1:5) commonly employed in clinical settings to enhance translational relevance.

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CHAPTER 6

Discussion

6.1 Overview of Main Findings

This thesis investigated the physiological responses of isometric FES exercise in comparison to FES cycling in able-bodied individuals. The systematic review and meta-analysis, along with three experimental studies, specifically examined isometric FES stimulation parameters and their acute physiological effects. The purpose was to examine the magnitude and characteristics of acute cardiorespiratory and force production responses of isometric FES exercise of the lower limbs. In this thesis FES cycling was utilized as a comparative standard. This research consisted of a systematic review and meta-analysis followed by three experimental trials that progressively built upon each other to examine: 1) direct comparison between FES cycling and isometric FES under matched stimulation parameters; 2) exploration of contractions per minute (CPM) ranges; and 3) determination of duty cycle parameters that produced favourable acute responses for isometric FES exercise.

The systematic review and meta-analysis (Chapter 2) identified modest but statistically significant aerobic responses across FES exercise modes, with FES cycling associated with higher mean differences in oxygen consumption compared to isometric FES and other modes. This difference appeared attributable to variations in stimulation intensity and muscle mass activation rather than the movement itself, as FES cycling typically employed higher stimulation doses and activated more muscle groups than other FES exercise modes such as isometric FES. Importantly, both FES exercise modes elicited a significant acute increase in oxygen consumption from baseline, though the magnitude of these responses remained within low-intensity aerobic exercise ranges, providing important context for the clinical application potential. The present findings indicate that both electrical stimulation and mechanical movement contribute to the overall physiological response, with their relative contributions varying based on stimulation parameters and exercise modality.

The first experimental study (Chapter 3) directly compared FES cycling and isometric FES under identical stimulation parameters. FES cycling elicited approximately 10% higher oxygen consumption compared to isometric FES. However, heart rate responses were comparable between modalities, as were discomfort levels, suggesting that while movement contribute to metabolic demand, isometric FES still produced measurable, though relatively modest, substantial cardiorespiratory responses that fall within the lower end of the aerobic exercise intensity spectrum.

The second experimental study (Chapter 4) examined how different CPM settings (5, 10, 20, and 40 CPM) affected muscle torque production and cardiorespiratory responses during isometric FES. Peak torque decreased significantly with increasing CPM, while average torque showed even larger differences. Interestingly, cardiorespiratory responses remained relatively consistent across CPM settings, suggesting that the number of muscle contractions primarily affected force production and fatigue development rather than metabolic demand.

The third experimental study (Chapter 5) investigated the influence of duty cycle (10%, 20%, 30%, and 40%) on isometric FES force production and cardiorespiratory responses at a fixed 10 CPM, which produced the highest average torque while maintaining peak torque in the previous study. Heart rate increased progressively with higher duty cycles, with 40% duty cycle. Conversely, peak torque decreased with increasing duty cycle while average torque showed the opposite pattern, increasing significantly from 10% to 40%. These findings demonstrated that duty cycle manipulation significantly affected cardiovascular responses, muscle force responses, and participant comfort.

Collectively, these findings confirmed three main observations: First, isometric FES could elicit substantial cardiorespiratory responses, comparable though somewhat lower than FES cycling when utilizing identical stimulation parameters. Second, muscle torque responses during isometric FES were significantly influenced by two factors: (1) the number of muscle contractions with lower CPM preserving peak force output, and (2) duty cycle, with lower duty cycle settings preserving peak force while higher duty cycle maximize cumulative muscle work. Third, discomfort levels were affected by both CPM and duty cycle, with higher values of both parameters significantly increasing discomfort while producing similar cardiorespiratory responses, highlighting the need to balance stimulation intensity with participant tolerance when designing FES protocols.

6.2 Physiological Mechanisms and Contextual Significance

6.2.1 Cardiorespiratory Responses to FES Exercise

The observed 10% higher oxygen consumption during FES cycling compared to isometric FES could be attributed to specific physiological mechanisms. First, dynamic contractions during FES cycling engage the skeletal muscle pump, which enhances venous return through cyclical compression and relaxation of blood vessels, potentially improving cardiac preload and consequently stroke volume (1, 2). However, this enhanced venous return primarily affects cardiac output rather than directly influencing oxygen consumption. The rhythmic nature of both exercise modalities provides intermittent muscle pumping, though FES cycling's continuous pedalling motion may create more consistent circulatory assistance compared to the discrete contraction-relaxation cycles in isometric FES.

Second, the energy requirements of dynamic and isometric contractions may differ based on nature of muscle activation. Traditional understanding suggests that dynamic contractions require additional metabolic cost compared to isometric contractions (3)**.** During FES

cycling, muscles are activated in patterns that coordinate joint movements, necessitating ATP expenditure for cross-bridge cycling and calcium handling throughout the movement range. Recent research suggest that dynamic contraction may also require additional energy for muscle coordination, motor unit recruitment patterns, and mechanical work production (4), potentially explaining the lower oxygen consumption observed in the first study.

Claims of FES cycling 'superiority' over isometric FES in the literature require critical re-examination. Chapter 3 demonstrated higher VO2 during FES cycling, but VO2 was already higher before cycling, accounting for nearly 40% of the observed difference. The absence of heart rate differences indicates similar cardiovascular responses to FES exercises. The absolute difference is unlikely to produce differential training adaptations in able-bodied populations; however, it remains untested, if this is true for severely deconditioned SCI individuals. The systematic review concluded that FES cycling protocols in the literature typically utilized higher stimulation doses and recruited larger muscle mass than isometric FES, although these studies were not intended for direct aerobic comparison. The observed VO2 variations likely reflect these parameter variations rather than the characteristic movement advantages. Both modalities provide beneficial physiological responses when implemented with adequate stimulation intensity and duration. The selection should be guided by equipment accessibility, FES exercise objectives, and participant preference rather than assumptions about one modality being physiologically superior to other.

The relatively stable oxygen consumption across different CPM and duty cycle settings, despite significant differences in stimulation parameters, likely reflects several physiological aspects. In Chapter 4, stimulation of both the quadriceps and hamstrings provided a more substantial metabolic response. In contrast, Chapter 5 limited stimulation to the quadriceps,

which likely resulted in reduced total oxygen demand and constrained systemic cardiorespiratory responses. This difference in muscle recruitment may be due to the absence of variation in VO_2, particularly in Chapter 5. It is essential to note that aerobic responses are not the only outcomes of interest in FES studies. Although VO_2 differences were not observed, changes in stimulation parameters significantly contributed to torque production, fatigue resistance, and discomfort. These factors are essential to muscle preservation and bone loading in clinical applications. Oxygen consumption during FES exercise appears to be more closely associated with total active contraction time, defined as the cumulative duration of electrically induced muscle activity, and stimulation amplitude, rather than with contraction frequency or duty cycle alone.

The findings extend previous research by Fornusek et al. (2014), who found no significant differences in VO_2 or heart rate between FES cycling and isometric FES in individuals with SCI (5). However, their study employed a relatively small sample size (n=8) and focused exclusively on participants with chronic paraplegia (T4-T11), who typically exhibit muscle atrophy and altered cardiovascular regulations (6). In contrast, in this study, larger cohort of able-bodied participants (n=20) may have experienced different physiological responses due to several factors: potential involuntary co-contraction during stimulation, differences in muscle condition and fibre composition compared to those with SCI, and importantly different stimulation approach. Specifically, Fornusek et al. used a standardized protocol with stimulation fixed at 140 mA for all participants, while the present study employed individualized stimulation intensities based on each participant's maximum tolerated level. Additionally, Fornusek's study found no significant differences between modalities, whereas the present study detected measurable differences favouring cycling. These methodological differences might explain the discrepancies between our findings and those of Fornusek et al.,

highlighting the importance of considering participant characteristics when interpreting FES response patterns.

Murillo et al. (2022) found that FES cycling significantly increased oxygen uptake (VO_2), carbonic gas production (VCO_2), and cardiac output compared to NMES and passive cycling, highlighting the benefits of dynamic contractions (7). However, several methodological differences limit direct comparison with the present study First, they utilized significantly lower stimulation intensities (20–35 mA) and much shorter stimulation duration (only two minutes per condition) compared to the current study's parameters (60-110 mA for 20 minutes). Second, their study utilized a smaller sample size (n=10) than the current thesis, which utilized 20 participants in a randomized crossover design, providing greater statistical power and control for individual variability. Third, while Murillo's NMES condition did involve isometric contractions, it was not designed as a systematic comparison with matched stimulation parameters. Their NMES protocol utilized different stimulation settings and a 1:1 ON/OFF ratio, which was fundamentally different from the isometric FES protocol employed in Chapter 3 of this thesis.

6.2.2 Neuromuscular Performance and Muscle Fatigue

The investigation of muscle torque production, discomfort, and fatigue under various stimulation parameters (Chapters 4 and 5) revealed important insights into the neuromuscular effects of isometric FES exercise. The findings demonstrated that peak torque decreased significantly with increasing CPM, while cumulative torque also declined, reflecting the reduced force-generating capacity per contraction at higher stimulation frequencies.

The observed VO_2 differences between FES cycling and isometric FES may be due to multiple interacting mechanisms. During dynamic contractions, the cyclical lengthening-

shortening of muscle fibres requires additional ATP expenditure for excitation-contraction coupling across varying muscle lengths, whereas isometric contractions maintain relatively constant sarcomere lengths (8). FES cycling may recruit additional stabilizing muscles (such as hip flexors, trunk stabilizers, and antagonist muscles) beyond those directly stimulated by electrode placement. The muscle fatigue patterns observed across CPM and duty cycle variations reflect both peripheral and central mechanisms. Accumulation of metabolic byproducts such as hydrogen ions, inorganic phosphate, and ADP gradually reduce cross-bridge cycling and reduce calcium sensitivity of contractile proteins (9). Repeated high-frequency stimulation compromises sarcoplasmic reticulum calcium release and handling capacity (10), while potassium efflux from contracting muscle fibres accumulates in t-tubules, reducing membrane excitability and action potential propagation (11). Additionally, electrical stimulation can cause a gradual failure of neuromuscular transmission, particularly under high-frequency protocols (12). The discomfort responses likely arise from activation of group III/IV muscle afferents responsive to mechanical and metabolic stimuli, with higher duty cycles producing greater afferent feedback due to sustained intramuscular pressure and metabolite accumulation.

The progressive decrease in peak torque with increasing CPM observed in Chapter 4 is consistent with the findings of Dreibati et al. (2010), who demonstrated that higher frequencies resulted in stronger muscle contractions, but also a stronger decline in muscle force and faster muscle fatigue (13). This suggests that stimulation parameters significantly impact force preservation during electrically stimulated exercise. Our study furthers these findings by examining a wider range of CPM specifically in an isometric FES protocol that is relevant to clinical application.

The data in chapter 5 revealed distinct mechanical effects of duty cycle manipulation. While peak torque decreased with increasing duty cycle, average torque increased significantly. This pattern reflects the temporal trade-off inherent in duty cycle adjustment: higher duty cycles extend the contraction duration relative to total cycle time, increasing the time under tension despite reducing peak force capacity (14). Physiologically, this represents a shift in the stimulus from maximal force responses to enhanced total work output, as longer activation periods (4 seconds versus 1 second) allow for greater average torque despite the reduction in peak values.

The observed interactions between stimulation parameters and neuromuscular performance have important implications for isometric FES protocol design. The findings suggest that lower CPM settings (5-10 CPM) optimize force production by allowing more complete recovery between contractions, resulting in higher peak torque output across repeated contractions. Moderate duty cycles (20-30%) may provide the best balance between peak force preservation and cumulative work output as they enable sufficient contraction duration to generate meaningful muscular tension.

6.2.3 Subjective Responses and Tolerability

Participant-reported outcomes, including discomfort ratings and perceived exertion, provided insights into the subjective experience of different FES exercise modes and stimulation parameters. In the first experimental study (Chapter 3), discomfort scores measured using a VAS were comparable between FES cycling and isometric FES, suggesting similar tolerability despite differences in FES exercises. However, the sources of discomfort varied, with isometric FES more frequently associated with electrical stimulation sensation and cramping, whereas FES cycling induced more fatigue and muscle tightness.

In the subsequent studies examining stimulation parameters, discomfort increased with both higher CPM and higher duty cycle values. These trends indicate that perceived discomfort during FES exercise tended to rise with the duration of contractions, likely due to greater sensory nerve activation and increased muscle fibre recruitment, as previously described by Maffiuletti (15).

The progressive rise in discomfort with increasing CPM and duty cycle likely stems from several physiological mechanisms. Electrical stimulation at rapid intervals with limited recovery time may lead to greater metabolite accumulation, which can activate muscle chemoreceptors, contributing to perceived discomfort (16). Additionally, frequent or sustained contractions may cause mechanical stress on muscle tissue and surrounding structures, further increasing sensory feedback (17).

6.3 Optimization of Stimulation Parameters

The focus of parameter optimization in this thesis is on the timing and duration of muscle contractions, CPM and duty cycle, rather than the fundamental electrical stimulation parameters. Throughout all experimental studies (Chapters 3-5), the core electrical stimulation parameters were intentionally standardized (biphasic rectangular waveform, 35 Hz, 250 μs, and amplitude individualized to 7/10 tolerance) to isolate the effects of contraction timing and duration on physiological responses. These values were chosen to achieve effective tetanic contractions (defined here as sustained muscular contractions at or above 30 Hz) while maintaining participant comfort, based on preliminary testing and established FES practice. By holding these parameters constant, the experimental design could systematically examine how CPM and duty cycle, the timing and duration patterns of contractions, influenced acute cardiorespiratory during isometric FES exercise. This investigation addresses a critical gap by experimentally manipulating contraction timing and

demonstrating that lower CPM with longer contraction durations increases torque and metabolic load, whereas higher CPM protocols may better engage cardiovascular responses without proportionate increases in force output.

6.3.1 Contractions Per Minute (CPM)

The optimization of CPM represents a significant advancement in isometric FES protocol design. The finding that cardiorespiratory responses remained consistent across CPM settings despite significant differences in force production presents an intriguing physiological paradox. This apparent dissociation between mechanical and metabolic responses may reflect the inherent physiological limits on oxygen consumption in small muscle mass, non-volitional isometric exercise. Elder et al. (2006) reported similar findings, demonstrating that when normalized to recruited muscle mass, oxygen consumption did not differ significantly between dynamic and isometric electrical stimulation despite substantial differences in mechanical output (18). This suggests that the metabolic cost of electrical stimulation may be largely independent of the mechanical outcomes.

The optimization of CPM has direct clinical relevance for isometric FES applications. Our findings indicate that lower CPM settings (5-10 CPM) reduce fatigue, resulting in higher torque production without compromising cardiorespiratory benefits, offering an efficient parameter range for FES based exercise strategies. This aligns with recommendations from Taylor et al. (2018), who emphasized the importance of adequate recovery periods for optimizing FES training responses (19).

6.3.2 Duty Cycle

The examination of duty cycle effects in Chapter 5 demonstrated that duty cycle significantly impacts both cardiovascular responses and neuromuscular performance during isometric FES. Unlike CPM, duty cycle manipulation produced progressive increases in heart rate with higher settings, while simultaneously affecting peak torque (decreasing with higher duty cycles) and cumulative torque (increasing with higher duty cycles).

The progressive increase in heart rate with higher duty cycles likely stems from enhanced sympathetic activation driven by both metabolic and mechanical feedback from working muscles (20). Extended contraction durations at elevated duty cycles increase intramuscular pressure and afferent nerve activation, stimulating group III/IV afferents that trigger chemoreceptor and mechanoreceptor feedback loops, augmenting sympathetic outflow (20).

The inverse relationship between duty cycle and peak torque parallels the CPM findings, supporting the importance of adequate recovery for force preservation. At 10 CPM, increasing the duty cycle from 30% to 40% extended contraction time while reducing rest periods, likely exacerbated excitation-contraction process. As Allen et al. (2008) note, muscle fatigue involves reduced sarcoplasmic reticulum calcium release and and impaired cross-bridge function, contributing to force decline (21).

6.3.3 Integrated Parameter Optimization

The combined insights from the CPM and duty cycle investigations enable a more nuanced approach to isometric FES parameter optimization. Rather than treating these parameters in isolation, their interactions should be considered when designing protocols for specific physiological objectives. Based on these findings, several parameter combinations can be recommended for different clinical goals:

- **Strength Development Focus**: Lower CPM (5-10) combined with lower duty cycles (10-20%) maximized peak torque production and minimized fatigue, potentially optimizing conditions for muscle hypertrophy. This approach aligns with principles established in resistance training literature, where maximizing mechanical tension is critical for strength development (22).
- **Endurance-Oriented Protocols**: Moderate CPM (10-20) with higher duty cycles (30-40%) increased cumulative work and a significant elevation in HR and VO_2 remaining relatively unchanged, cardiovascular demand while maintaining sustainable contractions, potentially enhancing muscular endurance and aerobic adaptations. This approach resembles traditional endurance training principles, where accumulated volume rather than peak intensity drives adaptations (23).
- **Cardiovascular Focus**: Higher duty cycles (30-40%) with any CPM setting effectively elevated heart rate, potentially enhancing cardiovascular training effects. However, the relatively unchanged oxygen consumption across parameter settings may reflect methodological limitations such as insufficient stimulation intensity, brief intervention duration, or measurement sensitivity issues, rather than indicating that duty cycle primarily affects heart rate independent of metabolic demand.
- **Early Exercise Strategies**: Lower CPM (5-10) with moderate duty cycles (20-30%) balanced force production, lower fatigue development, and cardiovascular responses. In these trials, this combination maintained a higher peak torque and was associated with lower discomfort ratings than higher-intensity protocols. These settings may be especially suitable for individuals in the initial phases of structured FES exercise, such as those with recent-onset SCI or neuromuscular impairment
- **Comfort-Prioritized Approach**: Lower CPM (5-10) and duty cycles (10-20%) minimized discomfort and lower perceived exertion, making them suitable for individuals with low pain

tolerance or limited prior experience to FES. While these settings resulted in lower cumulative torque, they still provided basic neuromuscular engagement, helping maintain muscle excitability, prevent disuse, and support initial familiarization with electrical stimulation. These benefits, however modest, may enhance adherence and facilitate gradual progression towards more intensive protocols in clinical or home-based FES programs. These parameter combinations represent evidence-based starting points rather than rigid prescriptions, and individual tailoring remains essential for optimizing specific physiological outcomes. Factors including muscle condition, fibre type distribution, neuromuscular status, and individual tolerance will influence optimal parameters in specific populations (24).

6.3.3 Synthesis of Torque Findings

A summary of stimulation parameter effects on muscle torque and their clinical applications in isometric FES exercise are provided in Table 1. The findings revealed that lower CPM (5-10) maximized torque and reduced fatigue, moderate duty cycles (10-20%) balanced force production with comfort for early exercise strategies, while higher duty cycles (30-40%) enhanced cardiovascular responses.

Table 1: Summary of stimulation parameter effects on muscle torque and their clinical applications in isometric FES exercise

Parameter	**Effect on Muscle Torque**	**Clinical Relevance**
Lower CPM (5–10)	Higher peak and cumulative torque, less fatigue	May preserve force output and comfort
Moderate Duty Cycle (10–20%)	Preserved peak force, less discomfort	Balance torque production and comfort, and may be for early-stage FES exercise

High Duty Cycle (30–40%)	Higher cardiovascular stimulus, but faster fatigue	Appropriate for short-term cardiovascular goals

6.4 Potential Benefits for Clinical Populations

While the experimental work was conducted in able-bodied individuals, considerable caution is required when analysing these findings to clinical populations. FES research has repeatedly demonstrated that able-bodied findings often fail to translate accurately to individuals with SCI, with documented instances of significant and unexpected differences in responses. These include marked atrophy and modifications in muscle fibre composition, reduced perfusion capacity, impaired autonomic regulation, and altered sensory feedback during stimulation (25-27). These factors can significantly alter the tolerance, fatigue rate, and metabolic response to FES. However, the value of able-bodied participant data is based on its ability to isolate specific stimulation effects without the confounding influence of spinal injury or associated changes in autonomic and muscular physiology. For example, understanding how CPM and duty cycle independently affect torque and HR in intact muscle provides a clean experimental framework to guide future SCI-specific adaptation of these parameters. Therefore, the research provides a useful foundational model, particularly in designing progressive FES protocols for early rehabilitation stages, where objective torque output and tolerability are essential.

Isometric FES as an Accessible Alternative

The findings demonstrate that isometric FES produced clear cardiorespiratory responses, including increased heart rate and modest rises in oxygen uptake, though these were approximately 10% lower than those observed with FES cycling under identical stimulation conditions. Advantages include accessibility, reduced equipment needs, joint protection, and simplified application, making isometric FES a viable exercise option for individuals without

access to specialized cycling equipment, particularly in resource-limited settings, home-based rehabilitation, or early intervention stages.

Cardiovascular Conditioning

The significant increases in oxygen consumption and heart rate during isometric FES observed across our studies suggest potential cardiovascular benefits for clinical populations. While the absolute exercise intensity (~20-30% of typical maximal capacity in able-bodied individuals) might appear modest by conventional exercise standards, it exceeded the physiological threshold required for cardiovascular adaptations in deconditioned individuals (28). For individuals with spinal cord injury, who experience a significant reduction in active muscle mass affecting oxygen consumption (VO_2) during exercise (29), even moderate intensity levels of functional electrical stimulation-assisted exercise may represent substantial relative challenges capable of inducing meaningful cardiorespiratory adaptations and health benefits.

Muscular Health and Strength Preservation

The findings from this thesis provide practical guidance for using isometric FES to support muscle force maintenance in individuals with paralysis. Lower CPM (5-10) and duty cycle (10-20%) settings were shown to maximize peak torque, suggesting their suitability for protocols aimed at slowing discus-related declines in force capacity.

Muscle atrophy constitutes a significant secondary complication following SCI, with notable reductions in muscle cross-sectional area evident within the first six months post-injury. Castro et al. (1999) documented decreases of 24% in gastrocnemius and 12% in soleus muscles, while the tibialis anterior showed no significant change (30). At 24 weeks post-

injury, the most affected muscles measured only 54-68% of the cross-sectional area observed in age-matched controls.

FES exercise has demonstrated effectiveness for counteracting muscle atrophy in clinical populations. Mahoney et al. (2005) (31) reported significant increases in muscle cross-sectional area following 12 weeks of FES resistance training in individuals with chronic SCI, while Ryan et al. (2013) (32) observed 35% increases in quadriceps volume after 16 weeks of neuromuscular electrical stimulation. The optimization of stimulation parameters used in this thesis could potentially enhance these outcomes by maximizing mechanical loading while minimizing premature fatigue, creating more favourable conditions for muscle protein synthesis and hypertrophic adaptations.

With chronic paralysis, muscle fibre composition typically shifts toward fast-twitch, glycolytic phenotypes with reduced fatigue resistance. Multiple studies have documented this shift in fibre types following spinal cord injury (30, 33). This transformation begins relatively early, as early as 4-6 weeks post-injury and progresses through a transitional period where fibres co-express both slow and fast myosin heavy chain isoforms before reaching a predominantly fast-twitch state by approximately 70 months post-injury (33). Functionally, these changes contribute to the low force output and rapid fatigue seen during FES (Levy et al., 1990). By optimizing stimulation parameters to balance force production with sustainable activation, properly timed FES protocols might help attenuate this adverse transformation and maintain more diverse fibre type distributions, potentially preserving greater functionality for recovery.

6.4.2 Integration with Existing FES Exercise Approaches

Isometric FES has long been recognised as a valuable exercise modality, particularly in populations with limited voluntary motor control. The current findings provide new insights into how parameter selection, particularly CPM and duty cycle can be strategically adjusted to optimize neuromuscular and cardiovascular outcomes. Instead of framing isometric FES as merely an early-stage exercise option, it should be viewed as a distinct modality capable of providing physiological benefits comparable or superior to FES cycling in certain situations. While home-based FES cycling devices are now available and increasingly affordable, isometric FES remains a highly adaptable alternative, particularly in programs prioritizing safety, simplicity, or progressive familiarization. Furthermore, the controlled nature of isometric contractions allows for precise workload modulation, an advantage when designing exercise protocols for individuals with high fatigue sensitivity, severe spasticity, or orthopaedic limitations. These strengths position isometric FES not just as a starting point, but as a complementary or standalone option in multimodal exercise programs. Integrating these findings into existing FES frameworks allows exercise professionals to design protocols more precisely, aligning with modern exercise prescription principles that emphasise personalised and evidence-based approaches.

6.5 Limitations and Methodological Considerations

Despite the robust experimental design and comprehensive analysis employed in this thesis, several limitations warrant acknowledgment when interpreting the findings and their clinical implications.

First the population studied was able-bodied. Paralysed muscles differ from able-bodied ones in several critical aspects: they undergo fibre-type transformation toward fast-twitch glycolytic phenotypes, exhibit significant atrophy (30-60% reduction in cross-sectional area), display altered neuromuscular junction integrity, lack normal autonomic cardiovascular

regulation, and present different sensory experiences during stimulation (6, 30, 34). These physiological distinctions suggest that while the fundamental parameter relationships identified likely translate to clinical populations, the specific optimal values and magnitude of responses may differ substantially. Therefore, the parameter ranges identified should be considered preliminary frameworks for clinical applications rather than definitive prescriptions.

Second. the experimental studies focused exclusively on acute responses to FES rather than chronic adaptations following extended training periods. This approach allowed precise examination of immediate physiological effects across different FES exercise modes and parameters, but limits conclusions regarding long-term training outcomes, which represent the ultimate goal of clinical FES applications.

Acute responses do not necessarily predict chronic adaptations with precision (35). For example, while the study observed that lower CPM settings preserved force production and reduced fatigue, it remains unclear whether these parameters would optimize muscle hypertrophy or strength development over extended training periods. Similarly, while higher duty cycles increased heart rate acutely, this does not guarantee superior cardiovascular adaptations chronically, as other factors including session frequency, progression, and total volume contribute to long-term outcomes.

Thus, the experimental design explored specific ranges of stimulation parameters: CPM from 5 to 40 contractions per minute and duty cycles from 10% to 40%. While these ranges encompass commonly used clinical parameters, they do not exhaustively evaluate all possibilities. Extremely low CPM settings (<5), very high duty cycles (>40%), or unique

combinations beyond the tested matrix might yield different or even superior outcomes for specific applications. Additionally, while key stimulation variables were controlled including pulse width (300 μs), frequency (35 Hz), and amplitude (individualized to tolerance). The different values for these fundamental stimulation characteristics might interact with CPM and duty cycle effects. These parameter limitations reflect necessary experimental constraints but suggest caution when generalizing the findings beyond the specific conditions tested. Future studies systematically exploring broader parameter ranges and interactions would complement our findings and potentially identify specialized parameter combinations for specific clinical applications.

Beyond parameter selection, three methodological implementation factors need discussion. First, contraction duration varied significantly across experimental trials, likely affecting fibre recruitment patterns, metabolic stress through blood flow occlusion, and sensory responses through differential afferent activation. Second, the 9–12-minute ramp-up at each session served safety purposes but created explanatory complexities: nominal '20-minute' protocols involved total stimulation time per session closer to 30 minutes, and averaging VO_2 across ramp-up and steady-state phases may obscure true metabolic costs. This gradual progression may not be necessary in sensory-impaired SCI populations from a comfort perspective; however, it may still serve important safety functions such as allowing cardiovascular adjustment and monitoring for autonomic dysreflexia. Third, muscle group selection significantly affected outcomes, as quadriceps-only stimulation (Chapter 5) simplified torque interpretation but reduced metabolic stimulus compared to combined quadriceps-hamstrings stimulation (Chapter 3). The seated position at 90° hip/knee flexion (Chapter 3 and 4) placed hamstrings in a shortened, cramping-prone position, resulting in this selection. Future research should independently manipulate contraction duration from CPM/duty cycle,

compare ramp-up protocols to enhance efficiency while maintaining safety, and determine whether parameter-response relationships are muscle-specific or generalizable across different muscle groups and multi-muscle configurations.

6.6 Future Research Directions

Building on the findings and limitations of this thesis, several key research directions emerge as priorities for advancing the understanding and clinical application of isometric FES exercise.

The most immediate research priority involves validating and refining the findings in relevant clinical populations, particularly individuals with SCI and other conditions causing lower limb paralysis. Future work should also examine discomfort ratings, perceived exertion, and qualitative experiences across FES exercise modes and parameters in clinical populations to identify optimal approaches for maximizing adherence. These studies would address the primary limitation of our current work and provide directly applicable clinical guidance for implementing isometric FES protocols in practice.

To bridge the gap between acute and chronic responses, longitudinal training studies should examine the effects of different isometric FES parameters on key physiological outcomes over extended intervention periods. These studies should evaluate cardiorespiratory responses, muscle hypertrophy following 8-12 weeks of isometric FES training using different parameter combinations. Developing and comparing different progression approaches for advancing stimulation parameters throughout training periods would maximize physiological adaptations while managing fatigue and discomfort. These longitudinal investigations would clarify whether optimizing parameters for acute responses effectively predicts optimal training adaptations, providing essential guidance for clinical prescription.

CONCLUSION

This thesis presents a systematic and experimental investigation into the physiological effects of different Functional Electrical Stimulation (FES) modalities and parameter optimizations. The systematic review confirmed that FES cycling elicits greater cardiorespiratory adaptations than isometric FES, while isometric modes offer localized musculoskeletal benefits. Experimental findings in able-bodied participants demonstrated that FES cycling produced significantly higher oxygen consumption than isometric FES, even under identical stimulation parameters, highlighting the importance of FES exercise mode in determining aerobic outcomes. Further, CPM and duty cycle were shown to critically modulate mechanical output and perceived effort during isometric FES. Lower CPMs maximized torque production while minimizing discomfort, with no additional metabolic advantage at higher CPMs. Conversely, increasing duty cycle elevated cardiovascular responses and average torque output but reduced peak torque and comfort levels.

Collectively, these studies emphasize the physiological interplay between stimulation parameters and exercise outcomes, illustrating that precise modulation of FES settings can strategically optimize both cardiometabolic demand and neuromuscular performance. The findings inform evidence-based guidelines for tailoring FES protocols in exercise programs, particularly for individuals with limited mobility. Future research should explore translation of these findings to clinical populations and assess long-term adaptations to optimized FES protocols.

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APPENDICIES

Appendix 1: Chapter 2 Systematic Review Keywords used in the search strategy in

Appendix 2: Chapter 2 Systematic Review Risk of Bias

Appendix 3: Chapter 3 (Study 1) Human Research Ethics Committee Letters of Approval

Appendix 4: Chapter 3 (Study 1) Participant Information Statement and Consent Forms

Appendix 5: Chapter 3 (Study 1) Participant questionnaire about their experiences during FES cycling and Isometric FES

Appendix 6: Chapter 4 and 5 (Study 2 and 3) Human Research Ethics Committee Letters of Approval

Appendix 7: Chapter 4 and 5 (Study 2 and 3) Participant Information Statement

Appendix 8: Chapter 4 (Study 2) Participant Consent Form

Appendix 9: Chapter 5 (Study 3) Participant Consent Form

Appendix 1 for keywords used in the search strategy

1 Spinal Cord Injuries/ (42275)

2 Spinal cord injur*.mp. (55722)

3 SCI.tw. (39118)

4 ((spine or spinal) adj3 (fracture* or wound* or trauma* or injur* or damag*)).tw. (64180)

5 (spinal cord adj3 (contusion or laceration or transaction or trauma or injur* or ischemia)).tw. (48071)

6 exp Multiple Sclerosis/ or Multiple Sclerosis*.mp. (93707)

7 Paraplegia/ (13048)

8 (paraplegi* or paraparesis).tw. (23110)

9 Quadriplegia/ (8303)

10 (quadriplegi* or quadriparesi*).tw. (5922)

11 (tetraplegi* or tetraplagi* or tetraparesis).tw. (5927)

12 exp Stroke/ or Stroke*.tw. (326798)

13 Neurological disorder*.tw. (32101)

14 1 or 2 or 3 or 4 or 5 or 6 or 7 or 8 or 9 or 10 or 11 or 12 or 13 (563188)

15 functional electrical stimulation*.mp. (2700)

16 FES.tw. (6143)

17 Electric Stimulation/ (115923)

18 Electric* stimulation*.mp. (156842)

19 hybrid functional electrical stimulat*.mp. (22)

20 Arm cranking.mp. (375)

21 15 or 16 or 17 or 18 or 19 or 20 (161497)

22 Acute Aerobic*.mp. (404)

23 aerobic exercis*.mp. (11877)

24 Muscle hypertroph*.mp. (3459)

25 Blood Circulation/ (20436)

26 Blood circulation*.mp. (33731)

27 Blood flow*.mp. (243263)

28 Spasm/ (7228)

29 Spasm*.mp. (39403)

30 Muscle Spasticity/ (9980)

31 Muscle spasticit*.mp. (10307)

32 Bone Density/ (58694)

33 Bone density.mp. (77072)

34 Muscle mass*.mp. (22881)

35 Muscle Strength/ (24624)

36 Muscle strength*.mp. (43467)

37 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29 or 30 or 31 or 32 or 33 or 34 or 35 or 36 (466790)

38 14 and 21 and 37

Appendix 2. Overall scores using KMET (Kmet, Cook, & Lee, 2004) quality assessment [Quantitative articles]

Study	1. Question / objective sufficiently described?	2. Study design evident and appropriate?	3. Method of subject/comparison group selection *or* source of information/input variables described and appropriate?	4. Subject (and comparison group, if applicable) characteristics sufficiently described?	5. If interventional and random allocation was possible, was it described?	6. If interventional and blinding of investigators was possible, was it reported?	7. If interventional and blinding of subjects was possible, was it reported?	8. Outcome and (if applicable) exposure measure(s) well defined and robust to measurement/misclassification bias? Means of assessment reported?	9. Sample size appropriate?	10. Analytic methods described/justified and appropriate?	11. Some estimate of variance is reported for the main results?	12. Controlled for confounding?	13. Results reported in sufficient detail?	14. Conclusions supported by the results?	Total Score	Maximum Possible Score (2x14=28)	Percentage Score	Range
Arija-Blazquez 2014 [1]	2	2	2	1	2	1	1	2	2	2	2	2	2	2	25	28	89	
Arnold 1992 [2]	2	2	2	2	N/A	N/A	N/A	1	2	1	1	N/A	1	1	15	28	54	

Ashe 2010 [3]	2	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2	2	8	28	29
Ashley 1993 [4]	2	2	2	2	N/A	N/A	N/A	1	2	2	2	N/A	2	2	19	28	68
Baldi 1998 [5]	2	2	2	2	1	0	0	1	2	1	1	N/A	2	2	18	28	64
Barr 1989 [6]	2	1	2	1	N/A	N/A	N/A	1	1	0	0	N/A	2	2	12	28	43
Barstow 1995[7]	2	1	1	1	N/A	N/A	N/A	2	2	2	2	N/A	2	2	17	28	61
Barstow 1996 [8]	2	1	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	1	18	28	64
Barstow 2000 [9]	2	2	2	2	N/A	N/A	N/A	1	2	2	1	N/A	2	2	18	28	64

BeDell 1996 [10]	2	1	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	19	28	68
Bhambhani 2000 [11]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71
Block 1989 [12]	2	1	1	1	N/A	N/A	N/A	2	1	0	0	N/A	2	2	12	28	43
Bloomfield 1996 [13]	2	2	1	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	19	28	68
Bochkezanian 2018 [14]	2	1	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	19	28	68
Bremner 1992 [15]	2	2	2	2	N/A	N/A	N/A	2	2	0	0	N/A	1	1	14	28	50
Brurok 2011 [16]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	1	19	28	68

Chen 2005 [17]	2	1	2	2	N/A	N/A	N/A	2	2	2	1	N/A	2	2	18	28	64
Deley 2017 [18]	2	2	N/A	1	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2	2	9	28	32
Demchak 2005 [19]	2	1	2	2	N/A	N/A	N/A	2	2	2	1	N/A	2	2	18	28	64
Dolbow 2014 [20]	2	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1	1	6	28	21
Dolbow 2018 [21]	2	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	1	1	6	28	21
Dudley 1999 [22]	1	1	1	1	N/A	N/A	N/A	2	1	1	0	N/A	2	2	12	28	43
Duffell 2008 [23]	2	1	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	19	28	68

Duffell 2010 [24]	2	1	2	1	N/A	N/A	N/A	2	2	2	2	N/A	2	2	18	28	64
Eser 2003 [25]	2	1	1	1	N/A	N/A	N/A	2	2	2	2	N/A	2	2	17	28	61
Everaert 2021 [26]	2	2	2	1	N/A	N/A	N/A	1	1	0	0	N/A	1	1	11	28	39
Faghri 1989 [27]	2	1	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	19	28	68
Faghri 1992 [28]	2	2	2	2	N/A	N/A	N/A	2	2	1	1	N/A	2	2	18	28	64
Figoni 1991 [29]	2	1	1	1	N/A	N/A	N/A	2	2	2	2	N/A	2	2	17	28	61
Figoni 1993 [30]	2	1	2	2	N/A	N/A	N/A	N/A	N/A	N/A	N/A	N/A	2	2	11	28	39

Fornusek 2008 [31]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71
Fornusek 2013 [32]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71
Fornusek 2014 [33]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71
Fornusek 2014 [34]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71
Frotzler 2008 [35]	2	2	1	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	19	28	68
Gerrits 2001 [36]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71
Gorgey 2017 [37]	2	2	2	2	2	N/A	N/A	2	2	2	2	N/A	2	2	22	28	79

Griffin 2009 [38]	2	1	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	19	28	68
Groah 2010 [39]	2	2	1	1	1	1	0	2	2	2	1	1	2	2	20	28	71
Hamzaid 2012 [40]	2	1	2	2	N/A	N/A	N/A	2	2	1	1	N/A	2	2	17	28	61
Hooker 1990 [41]	2	1	2	2	N/A	N/A	N/A	1	1	2	1	N/A	1	2	15	28	54
Hooker 1992 [42]	2	1	2	2	N/A	N/A	N/A	2	2	2	2	N/A	1	2	18	28	64
Janssen 2008 [43]	2	2	2	2	2	2	2	2	2	2	2	2	1	2	27	28	96
Janssen 2008 [44]	2	1	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	19	28	68

Johnston 2016 [45]	2	2	2	2	1	0	0	2	2	2	2	1	2	2	22	28	79
Kjaer 2001 [46]	1	1	1	1	N/A	N/A	N/A	2	2	2	2	N/A	2	2	16	28	57
Krauss 1993 [47]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71
Kuhn 2014 [48]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71
Lai 2010 [49]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71
Laskin 1993 [50]	2	1	2	1	N/A	N/A	N/A	1	2	2	2	N/A	2	2	17	28	61
Leeds 1990 [51]	2	1	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	1	18	28	64

Liu 2007 [52]	2	1	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	19	28	68
Mahoney 2005 [53]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71
Mate 2021 [54]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71
Mohr 1997 [55]	2	1	1	1	N/A	N/A	N/A	2	2	1	1	N/A	2	2	15	28	54
Mohr 1997 [56]	2	1	1	1	N/A	N/A	N/A	2	2	2	2	N/A	2	2	17	28	61
Muraki 2007 [57]	2	2	1	1	N/A	N/A	N/A	2	2	2	2	N/A	2	2	18	28	64
Mutton 1997 [58]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71

Pacy 1987 [59]	1	1	2	2	N/A	N/A	N/A	2	N/A	0	0	N/A	2	2	12	28	43
Pacy 1988 [60]	1	1	1	1	N/A	N/A	N/A	2	N/A	2	1	N/A	2	1	12	28	43
Penis set 2020 [61]	2	2	2	1	2	0	2	2	2	2	2	2	2	2	25	28	89
Perrett 2009 [62]	2	1	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	19	28	68
Petrofsky 1992 [63]	2	1	1	1	N/A	N/A	N/A	2	2	2	2	N/A	2	1	16	28	57
Petrofsky 2000 [64]	2	1	2	2	N/A	N/A	N/A	2	2	1	1	N/A	2	2	17	28	61
Pollack 1989 [65]	1	1	2	2	N/A	N/A	N/A	2	2	1	1	N/A	2	2	16	28	57

Ralston 2013 [66]	2	2	2	2	2	2	0	2	2	2	1	2	2	2	25	28	89
Raymond 2000 [67]	2	2	1	1	N/A	N/A	N/A	2	2	2	2	N/A	2	2	18	28	64
Raymond 2002 [68]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71
Robinson 1988 [69]	2	1	2	1	N/A	N/A	N/A	2	2	2	2	N/A	2	2	18	28	64
Rodger 1991 [70]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71
Ryan 2013 [71]	2	2	2	1	N/A	N/A	N/A	2	2	2	1	N/A	2	2	18	28	64
Sabatier 2006 [72]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71

Scremin 1998 [73]	2	2	2	2	N/A	N/A	N/A	2	2	1	0	N/A	2	2	17	28	61
Scremin 1999 [74]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71
Skiba 2021 [75]	2	2	2	2	2	0	0	2	2	2	2	N/A	2	2	22	28	79
Skold 2002 [76]	2	1	1	1	N/A	N/A	N/A	2	1	2	2	N/A	2	2	16	28	57
Sloan 1994 [77]	1	1	1	2	N/A	N/A	N/A	2	1	2	2	N/A	2	2	16	28	57
Stoner 2007 [78]	2	2	2	1	N/A	N/A	N/A	2	2	2	2	N/A	2	2	19	28	68
Thomas 1997 [79]	2	2	2	0	N/A	N/A	N/A	1	1	1	1	N/A	2	1	13	28	46

Verellen 2007 [80]	2	2	2	2	N/A	N/A	N/A	2	2	2	2	N/A	2	2	20	28	71	
Vodovnik 1984 [81]	1	0	1	2	N/A	N/A	N/A	1	1	0	0	N/A	1	1	8	28	29	
Yoshida 2013 [82]	2	2	1	2	N/A	N/A	N/A	2	2	2	1	N/A	2	2	18	28	64	
																	62	75

Scoring: 2 = yes, 1 = partial, 0 = no, n/a = not applicable

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Research Integrity & Ethics Administration
Human Research Ethics Committee

Monday, 9 October 2023

Dr Che Fornusek
Exercise Health and Performance; Faculty of Medicine and Health
Email: che.fornusek@sydney.edu.au

Dear Che,

The University of Sydney Human Research Ethics Committee (HREC) has considered your application.

After consideration of your response to the comments raised your project has been approved.

Approval is granted for a period of four years from **09/10/2023** to **09/10/2027.**

Project No.: **2023/548**

Project Title: **Comparison of Cardiorespiratory Exercise Response from FES cycling and Isometric exercise in abled bodied persons**

Authorised Personnel: **Fornusek Che; Dhopte Prakash; Hiller Claire**

First Annual Report due: **09/10/2024**

Documents Approved:

Date Uploaded	Version number	Document Name
07/09/2023	Version 1.1	Flyer 2023_548 Version 1.1
07/09/2023	Version 1.1	PIS 2023_548 Version 1.1
16/06/2023	Version 1	Questionnaire on FES Experience Version_1
16/06/2023	Version 1	PCF Version_1

Condition/s of Approval

- Research must be conducted according to the approved proposal.
- An annual progress report must be submitted to the Ethics Office on or before the anniversary of approval and on completion of the project.
- You must report as soon as practicable anything that might warrant review of ethical approval of the project including:
  - Serious or unexpected adverse events (which should be reported within 72 hours).
  - Unforeseen events that might affect continued ethical acceptability of the project.
- Any changes to the proposal must be approved prior to their implementation (except where an amendment is undertaken to eliminate *immediate* risk to participants).
- Personnel working on this project must be sufficiently qualified by education, training and experience for their role, or adequately supervised. Changes to personnel must be reported and approved.

Research Integrity & Ethics Administration
Level 2, Margaret Telfer Building (K07)
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CRICOS 00026A

- Personnel must disclose any actual or potential conflicts of interest, including any financial or other interest or affiliation, as relevant to this project.

- Data and primary materials must be retained and stored in accordance with the relevant legislation and University guidelines.

- Ethics approval is dependent upon ongoing compliance of the research with the *National Statement on Ethical Conduct in Human Research*, the *Australian Code for the Responsible Conduct of Research*, applicable legal requirements, and with University policies, procedures and governance requirements.

- The Ethics Office may conduct audits on approved projects.

- The Chief Investigator has ultimate responsibility for the conduct of the research and is responsible for ensuring all others involved will conduct the research in accordance with the above.

- The Clinical Trials Support Office has been notified as outlined in the University's Clinical Trials Policy where a clinical trial is being undertaken.

This letter constitutes ethical approval only.

Please contact the Ethics Office should you require further information or clarification.

Sincerely,

Associate Professor Stephen Fuller
Chair
Human Research Ethics Committee (HREC 2)

The University of Sydney HRECs are constituted and operate in accordance with the National Health and Medical Research Council's (NHMRC) current National Statement on Ethical Conduct in Human Research (2018) and the NHMRC's current Australian Code for the Responsible Conduct of Research (2018).

Participant Information Statement

Research Study: Comparing the Aerobic Response from Isometric and Cycling FES Exercise

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Mr Prakash Dhopte (PhD student) | Email: pdho8030@uni.sydney.edu.au

1. What is this study about?

We are conducting a research study about functional electrical stimulation (FES) exercise. FES uses brief electric pulses to make muscles contract. The electric pulses are delivered through electrodes which are placed on the skin above the muscles. FES can be used to exercise weak muscles in people with paralysis. In this study, we wish to investigate two different forms of FES exercise to see whether they produce different aerobic exercise responses: FES cycling and FES isometric exercise. During FES isometric exercise the limbs don't move but contract rhythmically from the FES. In FES cycling the muscle contractions are timed to pedal a stationary bicycle."

We will collect aerobic exercise data (heart rate and oxygen consumption) from participants while they perform each mode of exercise. The results of this study will allow us to improve the design of exercise equipment for persons with paralysis. Taking part in this study is voluntary.

Please read this sheet carefully and ask questions about anything that you don't understand or want to know more about.

2. Who is running the study?

The study is being carried out by the following researchers:

- Dr Ché Fornusek, Senior Lecturer, The University of Sydney
- Dr Claire Hiller, Associate Professor, The University of Sydney
- Mr Prakash Dhopte, PhD student, The University of Sydney

Prakash Dhopte is conducting this study as the basis for the degree of PhD at The University of Sydney.

3. Who can take part in the study?

We are seeking male and female able-bodied participants aged 18-50 years old.
Participants must have sufficient vision and ability to follow simple instructions, be able to communicate pain or discomfort directly with the researcher and be seizure free.

We will screen all participants with a pre-exercise screening form from Exercise Sports Science Australia. This pre-screen will ensure that participants are safe to perform FES exercise and the low intensity aerobic exercise it induces. Participants will be excluded from participating if they have conditions/characteristics which could raise the chance of an adverse event. The main exclusion criteria are sensitivity to muscle stimulation, epilepsy, reduced normal knee and hip joint range of motion, unstable cardiovascular conditions, arrhythmia or blood pressure conditions, unhealed wounds or pressure sores, joint instability, recent history of lower limb bone fracture, injury or advanced osteoporosis, or pregnancy.

4. What will the study involve for me?

If you wish to take part in this study, you will be screened prior to participation to make sure that you meet the criteria and that it is safe for you to participate. If you are able to participate you will be asked to attend 6 sessions at the Susan Wakil Health Building (The University of Sydney) which will take up to one hour each. This will require you attending the lab on 6 days.

To ensure safety we will monitor your heart rate, your perceived exertion, and blood pressure before, during and after all the sessions. We will also monitor how you are feeling and signs and symptoms of illness during sessions. If you feel poorly at any stage you should inform us.

During the first 4 sessions you will perform and become familiar with FES cycling exercise and FES isometric exercise. Familiarisation is important to allow you to become accustomed to the stimulation and allow us to determine your stimulation tolerance. The electrical stimulation will be applied via gel electrodes placed on the quadriceps and hamstrings muscles on both legs.

During sessions 5 & 6, you will perform one session with FES cycling and one session with FES isometric; the exercises will be performed in randomized order. We will monitor your heart rate, oxygen consumption, stimulation levels tolerated, quadriceps muscle activation and how uncomfortable the stimulation is during these 2 sessions. Quadriceps muscle activation will be measured by surface EMG electrodes that will be applied to your quadriceps muscles. Preparation for this involves shaving the electrode sites, applying abrasive gel then applying the electrodes and fixing with medical adhesive tape.

After session 6, you will complete a short questionnaire on your experiences of FES cycling and FES isometric exercise.

You will need to bring your own shoes, loose clothes that you are comfortable in and use for physical activity.

5. Can I withdraw once I've started?

Being in this study is completely voluntary. Your decision will not affect your current or future relationship with the researchers or anyone else at The University of Sydney.

If you decide to take part in the study and then change your mind later, you are free to withdraw at any time. You can do this by contacting any of the researchers via email or telephone expressing your wish to withdraw from the study. Your personal details and all information provided in the questionnaires will be shredded and not used in the study. Your information can be removed from our study records and not included in the study results, up to the point that we have analysed and published the results.

6. Are there any risks or costs?

Below, we have outlined the possible risks associated with your participation in the study.

Muscle Soreness and Injury:
As with any exercise testing, there are possible risks of injury or a heart attack. To minimise any risks, you will undergo preparticipation screening prior to any testing procedures being conducted.

The exercise assessments may cause some muscle soreness and fatigue which is transient and will settle over a couple of days. There is also a small risk of musculoskeletal soreness or injury during the exercise assessments, we will carefully monitor you throughout the testing to maximise your safety. If you have any questions or concerns about muscle soreness or injury, please contact the principal investigator Dr Ché Fornusek on 02 9351 9200.

Electrical Stimulation exercise:
Some people may experience discomfort during the application of functional electrical stimulation. The electrical stimulation levels will be kept to within limits you find tolerable, and we will ask you to let us know if the intensity is too high and in this case the intensity will be reduced to levels you can tolerate. The functional electrical stimulation applied may also result in some muscle soreness and fatigue once the electrical stimulation has stopped. There is a minor risk of skin irritation at the electrode sites following functional electrical stimulation, however this is uncommon. Some pink marks may be left on the skin; however, these generally fade within a short

time. We will check your skin at the beginning and end of each session to identify any irritation.

Adverse Effects:
We are not expecting any side effects during this study but you need to inform us of any that you may experience. It is important that you contact the study staff immediately if there are any unusual health experiences, injury or bad effects. This notification should take place whether you believe that the problem is related to the testing or from some other cause. In the event of any adverse effect, you will be able to contact the principal investigator Dr Ché Fornusek on 93519200.

Participation in this study will not cost you anything, and you will receive a $60 gift card after final completion of the trial.

7. Are there any benefits?

You will not receive any direct benefits from being in the study.

8. What will happen to information that is collected?

By providing your consent, you are agreeing to us collecting information about you for the purposes of this study.

Any information you provide us will be stored securely and we will only disclose identifiable information with your permission unless we are required by law to release information. We are planning for the study findings to be published. You will not be individually identifiable in these publications.

The information about you will be stored on a secure server at The University of Sydney and will be password protected. All materials will be kept for five years from the publication of results, as per national requirements, and then disposed of by erasure of computer−generated data.

9. Will I be told the results of the study?

You have a right to receive feedback about the overall results of this study. You can tell us that you wish to receive feedback by ticking the box regarding receiving feedback on the consent form or by contacting the researchers at any time. This feedback will be in the form of a brief 1-page lay summary. You will receive this feedback after the study is finished.

10. What if I would like further information?

When you have read this information, Mr Prakash Dhopte will be available to discuss it with you further and answer any questions you may have. If you would like to know more at any stage during the study, please feel free to contact Dr Che Fornusek (Senior Lecturer), or Dr Claire Hiller (Associate Professor).

11. What if I have a complaint or any concerns?

The ethical aspects of this study have been approved by the Human Research Ethics Committee (HREC) of The University of Sydney [2023/548] according to the *National Statement on Ethical Conduct in Human Research (2007).*

If you are concerned about the way this study is being conducted or you wish to make a complaint to someone independent from the study, please contact the University:

Human Ethics Manager
human.ethics@sydney.edu.au
+61 2 8627 8176

This information sheet is for you to keep

Participant Consent Form

Research Study: Comparing the Aerobic Response from Isometric and Cycling FES Exercise

Dr Che Fornusek (Responsible Researcher)
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Mr Prakash Dhopte (PhD student) | Email: pdho8030@uni.sydney.edu.au

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Participant Name _____

I agree to take part in this research study. In giving my consent, I confirm that that:

- The details of my involvement have been explained to me, and I have been provided with a written Participant Information Statement to keep.
- I understand the purpose of the study is to investigate the aerobic exercise responses elicited by two different modes of FES: cycling and isometric contraction.
- I acknowledge that the risks and benefits of participating in this study have been explained to me to my satisfaction.
- I understand that in this study I will be required to participate in 6 electrical stimulation exercise sessions which may be uncomfortable; however, I will be able to terminate any session whenever I wish.
- I understand that being in this study is completely voluntary.
- I am assured that my decision to participate will not have any impact on my relationship with the research team or the University of Sydney.
- I understand that I am free to withdraw from this study at any time and that I can choose to withdraw any information I have already provided (unless the data has already been de-identified or published).
- I have been informed that the confidentiality of the information I provide will be protected and will only be used for purposes that I have agreed to. I understand that information identifying me will only be told to others with my permission, except as required by law.

- I understand that the results of this study may be published, and that publications will not contain my name or any identifiable information about me.

- I confirm the following:

I consent to being contacted for future studies	Yes ☐	No ☐
I consent to my data being used in future research	Yes ☐	No ☐
I would like feedback on the overall results of this study	Yes ☐	No ☐

If you answered **yes**, please provide your preferred contact details (email/telephone/postal address):

_____

_____

_____

_____

- I understand that after I sign and return this consent form it will be retained by the researcher, and that I may request a copy at any time.

Participant Name _____

Signature _____

Date _____

Participant questionnaire about their experiences during FES cycling and Isometric FES

Post FES cycling session questions:

Now that you have completed the FES cycling session, we would like to ask you about your experience with this exercise mode through a short questionnaire.

1. With Zero being no discomfort and 10 being maximal discomfort possible? How uncomfortable was the session on scale of 0 to 10?

2. What was the primary reason for this discomfort? For example, the electrical stimulation sensation, muscle tightness, cramping, joint pain, fear of injury?

3. Were there any other uncomfortable sensations?

Post Isometric FES cycling session questions:

Now that you have completed the isometric session, we would like to ask you about your experience with this exercise mode through a short questionnaire.

1. With Zero being no discomfort and 10 being maximal discomfort possible? How uncomfortable was the session on scale of 0 to 10?

2. What was the primary reason for this discomfort? For example, the electrical stimulation sensation, muscle tightness, cramping, joint pain, fear of injury?

3. Were there any other uncomfortable sensations?

Participant questionnaire about their experiences during FES cycling and Isometric FES

Questions asked upon completing both the FES cycling and Isometric FES session:

Now that you have completed both the experimental sessions, i.e. FES cycling and Isometric FES exercise, we would like to ask you about your opinion of the two different stimulation exercise sessions.

1. Did the two exercise trials feel similar?
   Yes ☐ No ☐

2. If different (Yes in Question 1), how were they different?

3. Did you prefer one of the exercise trials over the other? If so which one?
   Yes, FES cycling ☐ Yes, Isometric FES exercise ☐ No, both were the same ☐

4. If one was preferred. Why did you prefer this exercise trial?

HUMAN RESEARCH ETHICS APPROVAL

The University of Sydney confirms that this project meets the requirements of the National Statement on Ethical Conduct in Human Research.

Project identifier:	2024/HE000199
Project title:	Optimizing Isometric Electrical Stimulation Exercise
Version:	0.01
Chief Investigator:	Che Fornusek
Authorised project team:	Claire Hiller Prakash Dhopte
Date of approval:	Wednesday, 1 May, 2024
Project end date:	01 May 2028

Provisos *(if applicable)*

Project summary

We seek to gain knowledge on the most effective stimulation parameters to use with isometric electrical stimulation exercise for improving aerobic fitness and muscle health. We will measure the aerobic exercise response and muscle forces during different muscle stimulation exercise protocols. Two experiments will be performed: The first will determine the best contractions per minute for muscle contraction force and the second will confirm what contraction duration elicits the greatest aerobic response. Apparently healthy able-bodied individuals will be used as experimental subjects. The measures will be aerobic response (sub-maximal) elicited, the muscle forces produced, and the discomfort induced by each stimulation protocol. Participants will also be asked questions on their experience with each protocol.

Documents approved

Filename	Document type	Document version	Application version
PCF 2024_199 Expt 1 Contractions per minute Project Version_1.1 02_02_2024 - Clean.docx	Participant Consent Form (PCF)	v.1.1	0.01 - Initial Application
PCF 2024_199 Expt 2 Duty Cycle Project Version_1.1 02_02_2024 - Clean.docx	Participant Consent Form (PCF)	v.1.1	0.01 - Initial Application
PIS 2024_199_Version1.1 - Clean.docx	Participant Information Statement (PIS)	v.1.1	0.01 - Initial Application

Filename	Document type	Document version	Application version
Flyer Project 2024_199 Version_1.1.pdf	Recruitment or advertising material	v.1	0.01 - Initial Application
20240204_Methodology.docx	Other	v.1	0.01 - Initial Application

Conditions of Approval

- Research must be conducted according to the approved proposal.
- An annual progress report must be submitted on or before the anniversary of approval and a final report on completion of the project.
- You must report as soon as practicable anything that might warrant review of ethical approval of the project including:
  - Serious or unexpected adverse events (which should be reported within 72 hours).
  - Unforeseen events that might affect continued ethical acceptability of the project.
- Any changes to the proposal must be approved prior to their implementation (except where an amendment is undertaken to eliminate *immediate* risk to participants).
- Researchers working on this project must be sufficiently qualified by education, training, and experience for their role, or adequately supervised. Changes to the project team must be reported and approved.
- Researchers must disclose any actual, potential of perceived conflicts of interest, including any financial or other interest or affiliation, as relevant to this project.
- Research data and primary materials must be retained and stored in accordance with relevant legislation and University guidelines.
- Ethics approval is dependent upon ongoing compliance of the research with the *National Statement on Ethical Conduct in Human Research*, the *Australian Code for the Responsible Conduct of Research*, applicable legal requirements, and with University policies, procedures, and governance requirements.
- If your research project is a clinical trial and is being sponsored by the University or is to be conducted on a University of Sydney site, you must comply with additional University governance requirements prior to commencing your Clinical Trial.
- The University may conduct audits on approved projects.
- The Chief Investigator has ultimate responsibility for the conduct of the research and is responsible for ensuring all others involved will conduct the research in accordance with the above.

Ethics Committee Representative

Professor Stephen Fuller
Chair
On behalf of the University of Sydney

The University of Sydney HRECs are constituted and operate in accordance with the National Statement on Ethical Conduct in Human Research and the Australian Code for the Responsible Conduct of Research (NHMRC). All personnel named on the project should be acquainted with these documents.

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Level 3, Michael Spence Building (F23)
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CRICOS 00026A

Participant Information Statement

Research Study: Investigating the Aerobic and Muscle Responses Elicited By Isometric Exercise

Dr Che Fornusek (Responsible Researcher)
Discipline of Exercise and Sport Science
The Sydney School of Health Sciences
Faculty of Medicine and Health
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The University of Sydney
NSW 2006

Phone: +61 2 93519200 | Email: Che.Fornusek@Sydney.edu.au
Mr Prakash Dhopte (PhD student) | Email: pdho8030@uni.sydney.edu.au

1. What is this study about?

We are conducting a research study about functional electrical stimulation (FES) exercise. FES uses brief electric pulses to make muscles contract. The electric pulses are delivered through electrodes which are placed on the skin above the muscles. FES can be used to exercise weak muscles in people with paralysis. In this study, we wish to investigate whether the stimulation can be changed to enhance the aerobic exercise responses and muscle forces produced. We will use isometric FES exercise of the thigh muscles for this study. During isometric FES exercise the limbs don't move but contract rhythmically from the FES.

We will collect aerobic exercise measurements (heart rate and oxygen consumption) and muscle force data from participants while they perform isometric exercise. The results of this study will allow us to improve the design of electrical stimulation exercise equipment for persons with paralysis. Taking part in this study is voluntary.

Please read this sheet carefully and ask questions about anything that you don't understand or want to know more about.

2. Who is running the study?

The study is being carried out by the following researchers:

- Dr Ché Fornusek, Senior Lecturer, The University of Sydney
- Dr Claire Hiller, Associate Professor, The University of Sydney
- Mr Prakash Dhopte, PhD student, The University of Sydney

Prakash Dhopte is conducting this study as the basis for the degree of PhD at The University of Sydney.

3. Who can take part in the study?

We are seeking male and female able-bodied participants aged 18-50 years old.
Participants must have sufficient vision and ability to follow simple instructions, be able to communicate pain or discomfort directly with the researcher and be seizure free.

We will screen all participants with a pre-exercise screening form from Exercise Sports Science Australia. This pre-screen will ensure that participants are safe to perform FES exercise and the low intensity aerobic exercise it induces. Participants will be excluded from participating if they have conditions or characteristics which could raise the chance of an adverse event. The main exclusion criteria are sensitivity to muscle stimulation, poorly controlled epilepsy (not controlled by drugs or seizures within last 3 months), reduced normal knee and hip joint range of motion, unstable cardiovascular conditions, arrhythmia or blood pressure conditions, unhealed wounds or pressure sores, joint instability, recent history of lower limb bone fracture, injury or advanced osteoporosis, or pregnancy.

4. What will the study involve for me?

If you wish to take part in this study, you will be screened prior to participation to make sure that you meet the criteria and that it is safe for you to participate. If you are able to participate you will be asked to attend 6 sessions at the Susan Wakil Health Building (The University of Sydney) which will take up to one hour each. This will require you attending the lab on 6 days.

To ensure safety we will monitor your heart rate, your perceived exertion, and blood pressure before, during and after all the sessions. We will also monitor how you are feeling and signs and symptoms of illness during sessions. If you feel poorly at any stage, you should inform us.

There are two sub-studies in this research - one for contraction length or 'Duty Cycle' and one for 'Contractions Per Minute'. You can volunteer for one or both studies. With each study you will need to sign a separate participant consent form. Each study will require 6 sessions at the laboratory.

During the first 2 sessions you will perform FES isometric exercise and become familiar with the sensation of FES. Familiarisation is important to allow you to become accustomed to the stimulation and allow us to determine your stimulation tolerance. The electrical stimulation will be applied via gel electrodes placed on the quadriceps and hamstrings muscles of both legs.

During sessions 3-6, you will perform the experimental trials with isometric FES contractions. Each session the stimulation delivered will be slightly different – the

contractions could be of different lengths or the rate of contractions could vary. You will be seated on a Cybex Dynamometer (see figure 1 below). We will monitor your heart rate, oxygen consumption, the stimulation levels , quadriceps muscle contraction forces and how uncomfortable the stimulation is during these sessions. Quadriceps muscle forces will be measured by the Cybex Dynamometer.

You will need to bring your own shoes, loose clothes that you are comfortable in and use for physical activity.

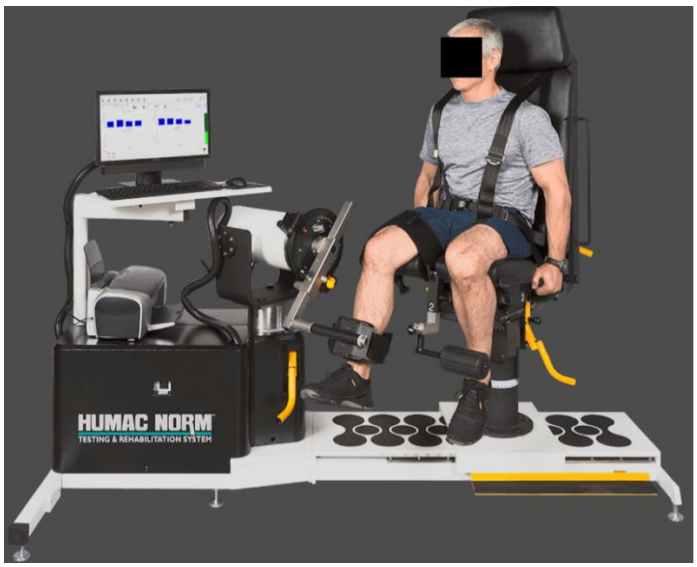

Figure 1: Seating position and Cybex Dynamometer equipment for the research sessions

5. Can I withdraw once I've started?

Being in this study is completely voluntary. Your decision will not affect your current or future relationship with the researchers or anyone else at The University of Sydney.

If you decide to take part in the study and then change your mind later, you are free to withdraw at any time. You can do this by contacting any of the researchers via email or telephone expressing your wish to withdraw from the study. Your personal details and all information provided in the questionnaires will be shredded and not used in the study. Your information can be removed from our study records and not included in the study results, up to the point that we have analysed and published the results.

6. Are there any risks or costs?

Below, we have outlined the possible risks associated with your participation in the study.

Muscle Soreness and Injury:

As with any exercise testing, there is some risk of injury with exercise, including musculoskeletal injury or cardiovascular event, but these risks are low. To minimise any risks, you will undergo preparticipation screening prior to any testing procedures being conducted.

The exercise assessments may cause some muscle soreness and fatigue which is transient and will settle over a couple of days. There is also a small risk of musculoskeletal soreness or injury during the exercise assessments, we will carefully monitor you throughout the testing to maximise your safety. If you have any questions or concerns about muscle soreness or injury, please contact the principal investigator Dr Ché Fornusek on 02 9351 9200 or Che.Fornusek@sydney.edu.au.

Electrical Stimulation exercise:

Some people may experience discomfort during the application of functional electrical stimulation. The electrical stimulation levels will be kept to within limits you find tolerable, and we will ask you to let us know if the intensity is too high and in this case the intensity will be reduced to levels you can tolerate. The functional electrical stimulation applied may also result in some muscle soreness and fatigue once the electrical stimulation has stopped. There is a minor risk of skin irritation at the electrode sites following functional electrical stimulation, however this is uncommon. Some pink marks may be left on the skin; however, these generally fade within a short time. We will check your skin at the beginning and end of each session to identify any irritation.

Adverse Effects:

We are not expecting any side effects during this study, but you need to inform us of any that you may experience. It is important that you contact the study staff immediately if there are any unusual health experiences, injury, or bad effects. This notification should take place whether you believe that the problem is related to the testing or from some other cause. In the event of any adverse effect, you will be able to contact the principal investigator Dr Ché Fornusek on 93519200 or Che.Fornusek@sydney.edu.au.

Participation in this study will not cost you anything, and you will receive a $20 gift card after completion of the trials.

7. Are there any benefits?

You will not receive any direct benefits from being in the study.

8. What will happen to information that is collected?

By providing your consent, you are agreeing to us collecting information about you for the purposes of this study.

Any information you provide us will be stored securely and we will only disclose identifiable information with your permission unless we are required by law to release information. We are planning for the study findings to be published. You will not be individually identifiable in these publications.

The information about you will be stored on a secure server at The University of Sydney and will be password protected. All materials will be kept for five years from the publication of results, as per national requirements, and then disposed of by erasure of computer−generated data.

9. Will I be told the results of the study?

You have a right to receive feedback about the overall results of this study. You can tell us that you wish to receive feedback by ticking the box regarding receiving feedback on the consent form or by contacting the researchers at any time. This feedback will be in the form of a brief 1-page lay summary. You will receive this feedback after the study is finished.

10. What if I would like further information?

When you have read this information, Mr Prakash Dhopte will be available to discuss it with you further and answer any questions you may have. If you would like to know more at any stage during the study, please feel free to contact Dr Che Fornusek (Senior Lecturer), or Dr Claire Hiller (Associate Professor).

11. What if I have a complaint or any concerns?

The ethical aspects of this study have been approved by the Human Research Ethics Committee (HREC) of The University of Sydney [2024/199] according to the *National Statement on Ethical Conduct in Human Research (2007).*

If you are concerned about the way this study is being conducted or you wish to make a complaint to someone independent from the study, please contact the University:

Human Ethics Manager
human.ethics@sydney.edu.au
+61 2 8627 8176

This information sheet is for you to keep

Participant Consent Form

Research Study: Investigating the Aerobic and Muscle Responses Elicited By Isometric Exercise – Experiment 1 Contractions Per Minute

Dr Che Fornusek (Responsible Researcher)
Discipline of Exercise and Sport Science
The Sydney School of Health Sciences
Faculty of Medicine and Health
D18 - Susan Wakil Health Building
The University of Sydney
NSW 2006

Phone: +61 2 93519200 | Email: Che.Fornusek@Sydney.edu.au
Mr Prakash Dhopte (PhD student) | Email: pdho8030@uni.sydney.edu.au

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Participant Name _____

I agree to take part in this research study. In giving my consent, I confirm that that:

- The details of my involvement have been explained to me, and I have been provided with a written Participant Information Statement to keep.
- I understand the purpose of the study is to investigate the aerobic exercise and muscle responses elicited from isometric electrical stimulation when the frequency of contraction is altered.
- I acknowledge that the risks and benefits of participating in this study have been explained to me to my satisfaction.
- I understand that in this study I will be required to participate in 6 electrical stimulation exercise sessions which may be uncomfortable; however, I will be able to terminate any session whenever I wish.
- I understand that being in this study is completely voluntary.
- I am assured that my decision to participate will not have any impact on my relationship with the research team or the University of Sydney.
- I understand that I am free to withdraw from this study at any time and that I can choose to withdraw any information I have already provided (unless the data has already been de-identified or published).
- I have been informed that the confidentiality of the information I provide will be protected and will only be used for purposes that I have agreed to. I understand that information identifying me will only be told to others with my permission, except as required by law.

- I understand that the results of this study may be published, and that publications will not contain my name or any identifiable information about me.

- I confirm the following:

  I consent to being contacted for future studies Yes ☐ No ☐

  I consent to my data (non-identifiable) being used in future research.
  Yes ☐ No ☐

  I would like feedback on the overall results of this study Yes ☐ No ☐

  If you answered **yes**, please provide your preferred contact details (email/telephone/postal address):

  _____

  _____

  _____

  _____

- I understand that after I sign and return this consent form it will be retained by the researcher, and that I may request a copy at any time.

Participant Name _____

Signature _____

Date _____

Participant Consent Form

Research Study: Investigating the Aerobic and Muscle Responses Elicited By Isometric Exercise – Experiment 2 Duty Cycle

Dr Che Fornusek (Responsible Researcher)
Discipline of Exercise and Sport Science
The Sydney School of Health Sciences
Faculty of Medicine and Health
D18 - Susan Wakil Health Building
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NSW 2006

Phone: +61 2 93519200 | Email: Che.Fornusek@Sydney.edu.au
Mr Prakash Dhopte (PhD student) | Email: pdho8030@uni.sydney.edu.au

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Participant Name _____

I agree to take part in this research study. In giving my consent, I confirm that that:

- The details of my involvement have been explained to me, and I have been provided with a written Participant Information Statement to keep.
- I understand the purpose of the study is to investigate the aerobic exercise and muscle responses elicited from isometric electrical stimulation when the duration of contraction is altered.
- I acknowledge that the risks and benefits of participating in this study have been explained to me to my satisfaction.
- I understand that in this study I will be required to participate in 6 electrical stimulation exercise sessions which may be uncomfortable; however, I will be able to terminate any session whenever I wish.
- I understand that being in this study is completely voluntary.
- I am assured that my decision to participate will not have any impact on my relationship with the research team or the University of Sydney.
- I understand that I am free to withdraw from this study at any time and that I can choose to withdraw any information I have already provided (unless the data has already been de-identified or published).
- I have been informed that the confidentiality of the information I provide will be protected and will only be used for purposes that I have agreed to. I understand that information identifying me will only be told to others with my permission, except as required by law.

- I understand that the results of this study may be published, and that publications will not contain my name or any identifiable information about me.

- I confirm the following:

  I consent to being contacted for future studies Yes ☐ No ☐

  I consent to my data (non-identifiable) being used in future research
  Yes ☐ No ☐

  I would like feedback on the overall results of this study Yes ☐ No ☐

  If you answered **yes**, please provide your preferred contact details (email/telephone/postal address):

  _____

  _____

  _____

  _____

- I understand that after I sign and return this consent form it will be retained by the researcher, and that I may request a copy at any time.

Participant Name _____

Signature _____

Date _____