Chapter One

Introduction

1.1 Background

1.1.1 Spinal cord injury

A spinal cord injury (SCI) may result in catastrophic and devastating consequences to the survivor. Trauma to the spinal cord results in the death of neural cells, severance/lesion of spinal tracts resulting in demyelination of descending and ascending axons, and consequently, loss or change of motor, sensory and/or autonomic function. These changes can be temporary or permanent depending on the severity of the injury. In many cases, endogenous repair efforts fail to repair the spinal cord resulting in permanent functional impairments (Dumont et al., 2001; McDonald & Sadowsky, 2002; Nandoe Tewarie, Hurtado, Bartels, Grotenhuis, & Oudega, 2010; Wyndaele & Wyndaele, 2006). There is good evidence that persons with SCI have a variety of secondary medical consequences of paralysis and/or the consequences of extreme inactivity (Bauman et al., 2012).

1.1.2 Physical activity and exercise in spinal cord injury

Physical activity has long been demonstrated to have beneficial effects on health and longevity in the general population, with physically active individuals showing lower risk for many chronic diseases when compared to their more sedentary peers (Fernhall, Heffernan, Jae, & Hedrick, 2008). Most persons with SCI are forced to adopt sedentary lifestyles resulting in poor cardiovascular health and low functional fitness, increasing their risk of cardiovascular morbidity and mortality (Jacobs & Nash, 2004). Buchholz and colleagues' noted low physical activity levels and reduced total daily energy expenditure in persons with SCI (Buchholz, McGillivray, & Pencharz, 2003).

Regular exercise and active lifestyles should be encouraged to prevent the sequelae of negative secondary health conditions that follow SCI. People with SCI who exercise gain physical and metabolic benefits as well as reporting less stress, reduced feelings of depression and improved quality of life (Hicks et al., 2003). In people with SCI, however, the sensorimotor neurological impairments, autonomic nervous system deficiencies, and impaired or altered systemic blood flows significantly affect the cardiorespiratory and peripheral vascular physiologic responses during exercise (Dela et al., 2003; Lavis, Scelza, & Bockenek, 2007).

For many persons living with SCI, physical activity and exercise is limited to upper body activities. Upper body exercise, such as arm crank ergometry (ACE) and wheelchair propulsion are commonly prescribed for this population, but due to the relatively small muscle mass in their upper limbs, such exercises are not always as beneficial as lower limb exercise (Glaser, 1989). In addition, arm exercise can also produce mechanical strain in the upper extremities and can further exacerbate problems associated with early shoulder pain and injuries, as well as overuse syndromes in SCI wheelchair users (Figoni, 2009; Powers, Newsam, Gronley, Fontaine, & Perry, 1994).

In the past three decades, functional electrical stimulation (FES) has increasingly been used to elicit rhythmic muscle contractions and purposeful movements of the paralysed lower limbs of SCI individuals both as a therapeutic approach and an exercise modality. Davis and colleagues in their review of the health and fitness benefits of FES leg exercise concluded that there were significant trends for altered muscle size and morphology, enhanced metabolism, including aerobic fitness, greater functional exercise capacity and improved psychological outlook after FES leg exercise (Barstow et al., 2000; Davis, Hamzaid, & Fornusek, 2008). However, FES-leg cycle exercise (FES-LCE) alone has often resulted in significantly lower submaximal oxygen uptakes compared to ACE (Raymond, Davis, Climstein, & Sutton, 1999). To further enhance exercise dose-potency, FES-LCE has been combined with ACE to augment submaximum oxygen uptake, as the larger muscle mass utilised during the combined arm and leg exercise has demonstrated greater cardiorespiratory demands and enhanced venous return (Davis, Servedio, Glaser, Gupta, & Suryaprasad, 1990; Raymond et al., 1999).

1.2 Purpose

The purpose of this work was to investigate cardiorespiratory responses during acute and chronic hybrid FES cycling exercise in individuals with SCI. Three main experiments were undertaken to achieve this purpose. Each experiment represented separate objectives, but the experiments were in continuum, highly linked and progressive.

1.3 Objectives

1.3.1 Exercise responses during FES cycling in individuals with spinal cord injury

Concurrent voluntary ACE and FES-LCE, termed "hybrid exercise", can be deployed in the form of an adapted stationary arm crank ergometer mounted over a FES-leg cycling system, FES rowing ergometers or roadworthy integrated hybrid FES bikes (Heesterbeek et al., 2005; Raymond et al., 1999; Verellen, Vanlandewijck, Andrews, & Wheeler, 2007). With hybrid exercise, increased muscle mass is activated, with augmented sympathetic outflow, reduced venous pooling in the legs, higher cardiac outputs and elevated oxygen uptakes, providing better whole body exercise benefits (Hettinga & Andrews, 2008b; Mutton et al., 1997b; Raymond et al., 1999).

Exercise training using the integrated hybrid FES bike which can be used indoors and outdoors, has resulted in improvement of physical fitness after only four weeks of training (Heesterbeek et al., 2005). Previous studies have compared the acute exercise responses in arm crank exercise, FES-LCE and FES-rowing but not with the hybrid FES bike.

The **first objective** of this manuscript was to compare the acute cardiorespiratory and metabolic exercise responses during maximal and submaximal ACE, FES-LCE and two modes of arm+FES-leg cycling in individuals with SCI. This study also investigated whether indices of cardiac performance (cardiac output and stroke volume) during both types of hybrid FES cycling would be greater than that elicited during arm cranking exercise or FES-leg cycling alone. It was deemed useful to investigate submaximal cardiorespiratory exercise responses since these represent an intensity that can be sustained over prolonged periods of time, and which might represent "real world" utility to the SCI individual undertaking fitness training using arms or/and legs. The findings of this experiment are presented in Chapter 3.

1.3.2 Exercise responses during outdoor versus virtual reality indoor Arm+FES-leg cycling in individuals with spinal cord injury

High intensity and high volume exercise programmes can sometimes provide superior health and fitness benefits, but might cause compliance problems in some users. Hettinga et al (Hettinga & Andrews, 2008b) has suggested virtual reality (VR) to promote training compliance in individuals with SCI. Virtual reality technologies are increasingly being used as a rehabilitation strategy in recent years. The rationale is based on a number of unique attributes of this technology, such as enabling safe and ecologically valid environments, control of task-specific level of performance and the provision of enjoyable and motivating experiences to the user (Riva et al., 1999; Schultheis & Rizzo, 2001). In the SCI population, Chen and co-workers (Chen, Jeng, Fung, Doong, & Chuang, 2009) investigated the effect of virtual rehabilitation on the psychology of 30 patients and observed that a virtual-reality-based rehabilitation programme could ease patients' tension and induce calm. Currently there is an increasing trend for people to undertake outdoor physical activity and exercise. To date, the outcomes of indoor versus outdoor exercise in terms of physiological or psychological responses after SCI has not been investigated.

Therefore, the **second objective** of this manuscript was to compare the acute exercise responses and the perceptual-psychological perceived experiences between outdoor hybrid-FES-cycling and indoor VR-enhanced hybrid FES-cycling in persons with spinal cord injury. The findings of this experiment are presented in Chapter 4.

1.3.3 A six-week high-intensity interval training virtual-reality hybrid FES cycling exercise programme in individuals with spinal cord injury

Regular physical activity has been shown to improve lipid profiles and other risk factors in persons with SCI (Jacobs & Nash, 2004; Washburn & Figoni, 1998b). Exercise programmes are important in the primary and secondary prevention of diabetes mellitus. Exercise has been proven to be effective in improving muscular, adipose tissue and insulin sensitivity (de Groot, Hjeltnes, Heijboer, Stal, & Birkeland, 2003; Griffin et al., 2009; Warburton, Nicol, & Bredin, 2006; Wheeler et al., 2002). Previous studies have demonstrated that participation in physical activity and exercise is able to help improve fitness levels and exercise capacity in people with SCI (Tordi et al., 2001). Cardiorespiratory endurance, an important component of physical fitness must receive priority for people with SCI as improved physical fitness can potentially decrease risk factors for coronary artery disease (Glaser, 1989; Krauss et al., 1993b). Stefanizzi and Overend concluded in their review that hybrid exercise training apears to hold promise for improvement of cardiovascular fitness in people with SCI (Stefanizzi & Overend, 1998). There is limited data however on training protocols, dose response and training intensity in order to achieve favourable training effects.

Therefore, the **third objective** of this manuscript was to investigate the effect of high-intensity interval training using "hybrid" exercise (arm and FES-leg cycling) on aerobic fitness, lipid profiles, glucose tolerance and psychosocial perception in individuals with chronic spinal cord injury (SCI). The findings of this experiment are presented in Chapter 5.

1.4 Hypotheses

To satisfy the objectives of this study, the following hypotheses were proposed:

h1: Submaximal steady-state and peak cardiorespiratory responses during exercise would be higher than those elicited during ACE alone or FES-LCE alone

h2: There would be no differences of cardiorespiratory and perceptual-psychological responses during steady-state submaximal exercise between indoor VR-enhanced "hybrid" exercise versus outdoor overground "hybrid" exercise

h3: Six weeks of indoor 'hybrid' high-intensity interval training would produce greater aerobic fitness and other beneficial physiological and psychological adaptations compared to pre-training

1.5 Rationale

The clinical experience in the rehabilitation management of persons with spinal cord injury in a specialized rehabilitation unit within a university hospital in Kuala Lumpur has led the investigator to question "what's next for the "SCI patient" beyond the "traditional" established rehabilitation programmes. The realization that despite advances in SCI rehabilitation, persons with SCI still die at younger ages compared to the general population because of medical complications and secondary health conditions, has spurred these series of investigation to assess the effects of exercise and technology use in health promotion in persons with SCI.

Recognizing that cardiovascular disease is a recognized leading cause of morbidity and mortality in SCI and that promotion of physical activity and structured exercise as well as identification of and judicious treatment of lipids and insulin resistance are important components in the long-term management of SCI, the experiments in this manuscript have been planned such that the acute physiological response of FES-assisted exercise was first assessed comparing the different exercise modalities specifically including hybrid FES cycling that are available for persons with SCI. Based on the findings of the first experiment, the acute physiological and psychological responses to hybrid FES cycling was then further assessed in different exercise environment i.e. natural outdoor environment and simulated virtual reality enhanced indoor environment. Following these experiments on acute responses, the third experiment comprised the outcome of a short-term hybrid FES cycling training study.

The collective results of the experiments in this manuscript will contribute to the available knowledge on the benefits and complexities of FES-assisted exercise in the rehabilitation of persons with SCI. The results of the experiments will provide insights into the cardiovascular and metabolic responses during acute FES-assisted exercise and following training. In addition, the results from these experiments will provide useful information to clinicians with regards to the uniqueness of cardiorespiratory responses during exercise in persons with SCI, the types of exercise and rationale in choosing type of exercise intervention as well as the benefits of integrating assistive technology such as functional electrical stimulation and virtual reality into rehabilitation programmes. It is the author's hope that there will be a paradigm shift amongst rehabilitation practitioners to extend their roles beyond improving and restoring function, and prevention of SCI-related complications towards encouraging health promotion and prevention of secondary health conditions through exercise and assistive technology.

Chapter Two

Review of literature: Exercise after spinal cord injury

2.1 CONSEQUENCES OF SPINAL CORD INJURY

A spinal cord injury (SCI) may result in catastrophic and devastating consequences to the survivor. An insult to the spinal cord results in the death of neural cells, severance and demyelination of descending and ascending axons, and consequently, loss or change of motor, sensory and/or autonomic function and these changes can be temporary or permanent depending on the severity of the injury. In many cases, endogenous repair efforts fail to repair the spinal cord resulting in permanent functional impairments (Dumont et al., 2001; McDonald & Sadowsky, 2002; Nandoe Tewarie et al., 2010; Wyndaele & Wyndaele, 2006).

The current chapter concerns a review of the medical consequences and physical outcomes after spinal cord injury and how these pertain to in exercise in individuals who have that condition. It will thoroughly review cardiovascular fitness, physical fitness and training and how these may change the parameters of cardiovascular disease risk factors.

2.1.1 Pathophysiological Consequences

The pathophysiology of acute SCI involves primary and secondary mechanisms of injury. The primary injury involves mechanical trauma, which includes impact of trauma, traction and compression forces resulting in the damage of bone, disc, ligament, nervous and vascular elements within the spine (Dumont et al., 2001; Nandoe Tewarie et al., 2010). The secondary mechanism involves a sequence of molecular and cellular inflammatory events leading to additional nervous tissue injury and loss (Dumont et al., 2001; McDonald & Sadowsky, 2002; Nandoe Tewarie et al., 2010). Subsequently, this chain of events manifests itself as neurological deficits below the level of the lesion due to the disruption or lack of innervation below the level of the lesion.

2.1.2 Clinical and Functional Consequences

The severity of injury is assessed using the International Standards for Neurological and Functional Classifications of Spinal Cord Injury (ISNCSCI) which assess motor function in ten muscle groups (arms, C5-T1; legs, L2-S1) and sensation (light touch and pinprick) in 28 dermatomes (C2-S4/5) on both sides of the body. The neurological level of injury can then be determined. The neurological level refers to the most caudal segment of the cord with intact sensation and antigravity muscle function strength, provided that there is normal sensory and motor function rostrally. The results are used in combination with evaluation of anal sensory and motor function as a basis for the determination of the American Spinal Injury Association (ASIA) Impairment Scale (Kirshblum et al., 2011). The ASIA Impairment Scale (AIS) designation is used to grade the degree of impairment into complete and incomplete injuries. An ASIA A injury indicates no sensory or motor function is preserved in the sacral segments S4-S5. ASIA B injury is when there is sensory but not motor function is preserved below the neurological level of injury (NLI) and includes the sacral segments S4-S5, and no motor function is preserved more than three levels below the motor level on either side of the body. In an ASIA C injury, motor function is preserved below the neurological level, and more than half of key muscle functions below the single NLI have a muscle grade less than 3 (Grades 0–2). In an ASIA D injury, motor function is preserved below the neurological level, and at least half (half or more) of key muscle functions below the NLI have a muscle grade more than 3. If sensation and motor function as tested are graded as normal in all segments, and the patient had prior deficits, then the AIS grade is E (Kirshblum et al., 2011).

Functionally, persons with spinal cord injury can present as tetraplegia or paraplegia. Tetraplegia refers to impairment or loss of motor and/or sensory function due to damage of the neural elements within the cervical segments of the spinal cord. Tetraplegia presents as impairment of function in all four limbs as well as the trunk and pelvic organs. Paraplegia refers to impairment or loss of motor and/or sensory function due to damage of the neural elements within the thoracic, lumbar or sacral segments of the spinal cord. With paraplegia, arm function is spared but lower limbs, trunk and pelvic organs may be involved. The tetraplegia and paraplegia clinically present as complete or incomplete paralysis of the limbs depending on the AIS.

Nearly all spinal cord injuries damage both upper and lower motor neurons. Therefore additionally, it is important to distinguish between upper motor neuron (UMN) and lower motor neuron (LMN) dysfunction (McDonald & Sadowsky, 2002). This has important prognostic, therapeutic and research implications for bowel, bladder and sexual function as well as mobility. This cannot be determined just on the basis of the NLI. A detailed clinical examination including sacral reflexes is required. UMN dysfunction involves damage to the descending motor tracts, which results in paralysis and spasms since spinal reflex circuits below the lesion are preserved. LMN dysfunction results in denervation of the sensori-motor function and gives rise to paralysis and areflexia (Doherty, Burns, O'Ferrall, & Ditunno, 2002; McDonald & Sadowsky, 2002).

2.1.3 Medical Consequences

SCI adversely affects the physiological functions of most organ systems and may result in the disturbances of the functioning of the pulmonary, cardiovascular, haematological, skin, gastrointestinal and genitourinary systems (Chen, Apple, Hudson, & Bode, 1999; Nandoe Tewarie et al., 2010). This occurs early following the SCI and may impact recovery and rehabilitation. Previous reports show that while there have been declines in the incidence of several complications, most notably deep vein thrombosis and pulmonary embolus, other common complications, especially pressure ulcers, atelectasis/pneumonia, bradycardia, arrhythmias and hypotension still occur with relative frequency in the acute phase and during rehabilitation (Aito & Gruppo Italiano Studio Epidemiologico Mielolesioni, 2003; Chen et al., 1999; Grossman et al., 2012). The long-term impact of these medical consequences leads to the development of secondary health conditions in persons with chronic SCI.

2.1.4 Physical Consequences

Physical consequences associated with SCI include loss of muscle mass, increase in body fat, physical inactivity / low level of activity and general decrease in the ability to maintain cardiovascular or aerobic fitness (Myers, Lee, & Kiratli, 2007; Warburton, Eng, Krassioukov, & Sproule, 2007). Numerous studies suggest that persons with SCI have significantly lower levels of regular physical activity than the able-bodied population.

Depending on the level of the lesion and the completeness of the injury, SCI impacts the physical functioning of the survivor. SCI renders most of its survivor wheelchair dependent as a result of lower limb paralysis. The higher the level of the lesion, the greater the impact on the physical function of the various areas of basic mobility, self-care, fine motor function, ambulation and wheelchair mobility (Ragnarsson, Adam, Stein, Spungen, & Bauman, 2004; Tulsky et al., 2012). The limited physical functioning lead to reduced activity and physiological deconditioning which subsequently affect the health of persons with SCI and further leads to a debilitative cycle (Grange, Bougenot, Groslambert, Tordi, & Rouillon, 2002). Most persons with SCI are “forced” to adopt a sedentary lifestyle as a result of their wheelchair confinement, environmental barriers and possible psychological issues which further complicate the consequences of SCI leading to deconditioning, poor physical fitness, and cardiovascular health outcomes (Fernhall et al., 2008; Tremblay, Colley, Saunders, Healy, & Owen, 2010; Warburton et al., 2007).

2.2 SECONDARY HEALTH CONDITIONS FOLLOWING SPINAL CORD INJURY

It has been described in the literature that persons with SCI have secondary medical consequences of paralysis and/or consequences of extreme inactivity (Bauman et al., 2012). People with SCI are at risk not only for increased secondary conditions but also for increased medical utilisation and higher rehospitalisation rates related to those secondary conditions. For secondary conditions, prevention is the most desired outcome (Bauman et al., 2012; Wyatt & White, 2000). Some of the most common secondary conditions include pressure ulcers, respiratory problems (e.g. pneumonia), genitourinary problems (e.g. urinary tract infections), spasticity, pain, and circulatory problems including autonomic dysreflexia (Chiodo et al., 2007; Hitzig et al., 2008; Johnson, Gerhart, McCray, Menconi, & Whiteneck, 1998; Kalpakjian, Scelza, Forchheimer, & Toussaint, 2007; McKinley, Jackson, Cardenas, & DeVivo, 1999; Noreau, Proulx, Gagnon, Drolet, & Laramee, 2000).

2.2.1 Cardiovascular disease in persons with spinal cord injury

Cardiovascular disease (CVD) is the leading cause of mortality in both able-bodied persons and persons with SCI (Whiteneck et al., 1992). The literature also shows that an earlier onset of CVD and increased prevalence of CVD in persons with SCI (Bauman, Kahn, Grimm, & Spungen, 1999; Devivo, Krause, & Lammertse, 1999b; Garber et al., 2011; Whiteneck et al., 1992). A review by Myers and colleagues indicated 30-50% prevalence of symptomatic CVD in persons with SCI compared to 5-10% prevalence in able-bodied population (Myers et al., 2007). More alarming is that, Bauman and colleagues reported a prevalence of 60-70% of asymptomatic CVD based on cardiac testing and nuclear imaging of SCI subjects (Bauman, Raza, Chayes, & Machac, 1993; Bauman, Raza, Spungen, & Machac, 1994). Notably, Groah and co-workers reported that the risk of developing CVD was associated with both the neurological level and extent of injury in a study of 545 persons with SCI surviving at least 25 years of injury (Groah, Weitzenkamp, Sett, Soni, & Savic, 2001).

Nash and Mendez found that the combination of abdominal obesity, elevated fasting triglycerides (TG), low levels of fasting high-density lipoprotein cholesterol (HDL), hypertension, and fasting hyperglycemia was observed in more than 30% of young, healthy persons with paraplegia, qualifying for lipid-lowering therapeutic lifestyle intervention (Nash & Mendez, 2007).

2.2.2 Risk factors for cardiovascular disease

Changes in body composition and lower levels of physical activity are the key risk factors for cardiovascular disease in persons with SCI (Lavis et al., 2007). These include changes in lipid and carbohydrate metabolism, obesity and lack of physical fitness (Bauman, Adkins, Spungen, & Waters, 1999; Demirel, Demirel, Tukek, Erk, & Yilmaz, 2001; Myers et al., 2007; Phillips et al., 1998).

2.2.2.1 Lipid metabolism

Abnormal lipid-lipoprotein profiles have been associated with an increased risk for CVD (Warburton et al., 2007; Warburton et al., 2006). Low-density lipoproteins (LDL) is believed to have artherogenic effect and there is a positive association between LDL and the increased risk of CVD. Conversely, HDL is believed to be an inhibitor of artherogenesis and have CVD protective effects (National Cholesterol Education Program Expert Panel on Detection & Treatment of High Blood Cholesterol in, 2002). Therefore elevation in LDL and depression in HDL are two important main risk factors for CVD. Serum TG is not an independent risk factor for CVD however it is associated with non-lipid risk factors of CVD such as diabetes, sedentary lifestyle, obesity, hypertension and cigarette use (National Cholesterol Education Program Expert Panel on Detection & Treatment of High Blood Cholesterol in, 2002). Bauman and colleagues reported an inverse correlation with HDL levels and TG levels (Bauman et al., 1992).

In persons with SCI, previous studies have shown worsened lipid profiles in this population presenting with increased total cholesterols, elevated LDL and lower levels of HDL (Bauman, Kahn, et al., 1999; Bauman et al., 1992; Krum et al., 1992; Phillips et al., 1998). According to Bauman and colleagues, those with tetraplegia are shown to have lower levels of HDL, suggesting decreased physical activity is a major contributor to lower HDL levels (Bauman, Adkins, Spungen, Kemp, & Waters, 1998).

2.2.2.2 Glucose intolerance and diabetes mellitus

Impaired glucose tolerance and diabetes mellitus are more prevalent in persons with SCI. Previous findings show that people with SCI have a three to five times higher risk of developing diabetes mellitus than able-bodied control group (Bauman, Kahn, et al., 1999; Bauman & Spungen, 1994, 2000; Lavela et al., 2006). The high prevalence of diabetes mellitus and impaired glucose tolerance has been attributed to changes in body composition and muscle characteristics after the injury (Burnham et al., 1997; Spungen, Bauman, Wang, & Pierson, 1995). Following SCI, atrophy of skeletal muscle below the NLI ensues decreasing muscle mass. The loss of muscle mass is crucial because insulin acts peripherally on the individual's muscle mass for the metabolism of glucose (Lavis et al., 2007). This results in glucose intolerance as higher plasma levels of insulin are required to maintain normal blood glucose levels giving rise to hyperinsulinemia predisposing these persons with SCI to an atherogenic condition, increasing the risk for CVD (Bauman & Spungen, 2008). Bauman and Spungen also found that those with complete tetraplegia have the highest incidence of impaired glucose metabolism, stressing the importance of muscle mass and immobility (Bauman & Spungen, 1994).

2.2.2.3 Physical activity and fitness

The level of fitness is established by the aerobic capacity, for which the peak oxygen uptake (VO_{2peak}; $l \cdot min^{-1}$) is the gold standard and by the maximal maintainable workload, which is determined by the peak power output (*ACSM's Guidelines for Exercise Testing and Prescription*, 2006; Haisma et al., 2007). It has been reported that nearly one in four healthy young persons with paraplegia fails to achieve levels of oxygen uptake on an arm exercise test sufficient to perform many essential activities of daily living (ADL) (Noreau, Shephard, Simard, Pare, & Pomerleau, 1993). Janssen and colleagues described how persons with SCI have limited physical fitness which impact on their physical ability resulting in physical strain during ADL. This in turn decreases activity level exacerbating the already low physical fitness. They concluded that the physical strain arising from ADL is not sufficient to maintain or improve physical fitness (Janssen, van Oers, van der Woude, & Hollander, 1994). In a review by Glaser, he stated that normal daily wheelchair activity may not provide sufficient exercise to train the cardiopulmonary system and that supplemental arm exercise training is necessary to stimulate fitness improvement (Glaser, 1989). Previous studies also showed that while those with paraplegia have far greater capacities for activity and more extensive choices for exercise participation than persons with tetraplegia, they are only marginally more fit (Bostom et al., 1991; Dearwater et al., 1986).

Majority of persons with SCI report virtually no physical activity (Dearwater et al., 1986; Tasiemski, Bergstrom, Savic, & Gardner, 2000; Washburn, Zhu, McAuley, Frogley, & Figoni, 2002). Buchholz and colleagues found that total daily expenditure is reduced in persons with SCI through measurements using doubly labeled water (Buchholz et al., 2003). It has been established that physical inactivity is a major independent risk factor for cardiovascular disease and premature mortality (Warburton et al., 2007). As a result of their physical limitations, most individuals with SCI are forced to adopt sedentary lifestyles resulting in poor cardiovascular and functional fitness, increasing the risk of cardiovascular morbidity and mortality (Jacobs & Nash, 2004).

Inactivity, independent of lipid values or other risk factors for CVD, may be an independent risk factor for CVD. Therefore, persons with SCI should be strongly encouraged to reach and maintain the highest level of daily activity, compatible with their neurological level of injury (Bauman et al., 2012). Regular physical activity has been shown to improve lipid profiles and other risk factors in persons with SCI (Jacobs & Nash, 2004; Washburn & Figoni, 1998a). Physical activity has also shown positive effects on glucose metabolism (Thompson, 2003).

2.2.3 Physical fitness

Previous studies have demonstrated that participation in physical activity and exercise is able to help improve fitness levels and exercise capacity in people with SCI (Kraus et al., 2002; Tordi et al., 2001). Cardiorespiratory endurance, an important component of physical fitness must receive priority for people with SCI. Improved physical fitness can potentially decrease risk factors for coronary artery disease (Glaser, 1989; Krauss et al., 1993b). It has been been shown that increased levels of cardiopulmonary fitness elevate levels of HDL in persons with SCI and the able-bodied population (Bauman et al., 1992; Kraus et al., 2002; Thompson, 2003).

2.3 EXERCISE FOR HEALTH PROMOTION IN SPINAL CORD INJURY

2.3.1 Health promotion

The aims of a health promotion programme for people with disabilities are to reduce secondary health conditions, to maintain functional independence, to provide an opportunity for leisure and enjoyment and to enhance the overall quality of life. Rimmer opined that health promotion for those with disabilities, including those with SCI, has historically been directed at primary prevention of disability rather than prevention of secondary health conditions (Rimmer, 1999). Njoki and colleagues found that SCI participants in their study were involved in health-risk behaviours, which are associated with development of secondary conditions such as cardiovascular disease. The authors concluded that health promotion strategies are necessary to encourage participation in physical activity (Njoki, Frantz, & Mpofu, 2007). Warms reported that people with SCI were more concerned with health promotion services than disability–related services, specifically with access to services relating to exercise, nutrition and stress management (Warms, 1987).

2.3.2 Exercise participation

In a cross-sectional survey of 72 persons with SCI, Scelza et al reported that less than half (45.8%) were currently active in an exercise programme and less than half (47.2%) had exercise recommended for them by their physician. The subjects reported barriers such as lack of motivation, lack of energy, lack of interest, cost of exercise programme, not knowing what to exercise and inaccessibility to facilities and knowledgeable instructors. More individuals with tetraplegia reported concerns over exercise being too difficult and that health issues kept them from exercising (Scelza, Kalpakjian, Zemper, & Tate, 2005). Kehn and Kroll conducted a quantitative exploration of exercise and physical activity patterns on 26 persons with SCI and inferred from their study that most people with SCI, despite many obstacles and barriers to performing exercise, are principally motivated to engage in exercise to maintain health and secondary conditions (Kehn & Kroll, 2009).

2.3.3 Exercise benefit

There is very good evidence that physical activity and exercise is effective in improving physical fitness and general health in the SCI population (Jacobs & Nash, 2004; Nash, 2005; Washburn & Figoni, 1998a). Physical activity and exercise have been shown to assist in reducing complications of SCI including pressure ulcers, urinary tract infections, respiratory illness, pain and depression (Johnson et al., 1998; Martin Ginis et al., 2010). In addition, physical activity can help persons with SCI manage SCI-associated problems such as spasticity, weight gain and chronic pain (Martin Ginis et al., 2010).

Previous studies have reported numerous exercise benefits for persons with SCI which include improvement in functional capacity, increased bone density, endurance, muscle strength, pain and psychological well-being (Dallmeijer & van der Woude, 2001; Duran, Lugo, Ramirez, & Eusse, 2001; Jones, Legge, & Goulding, 2002; Noreau et al., 1993). However, a recent systematic review by Hicks and colleagues of 82 studies on the effects of exercise training on physical capacity, strength, body composition and functional performance among adults with SCI, found insufficient evidence to conclude that exercise can affect body composition, reduce body weight and improve functional performance in these individuals. There was mixed evidence on the effects of exercise on muscle and fat mass. However they were able to conclude that exercise training increases physical capacity. There was also strong evidence to conclude that exercise training increases muscle strength (Hicks et al., 2011). Jacobs and colleagues observed increased peak oxygen consumption, peak power output and improved muscle strength following 12-week circuit training in ten paraplegic subjects (Jacobs, Nash, & Rusinowski, 2001).

Moderate intensity exercise interventions have been shown to improve serum HDL levels and reduce CVD risk (Nash, Jacobs, Mendez, & Goldberg, 2001; Rader, 2002). High-intensity training showed increased levels of HDL and decreased TG, LDL and total cholesterol levels (de Groot et al., 2003).

2.3.4 Exercise training for persons with SCI

The American College of Sports Medicine (ACSM) recommends that most adults engage in moderate-intensity cardiorespiratory exercise training for ≥30 min·d^{-1} on ≥5 d·wk^{-1} for a total of ≥150 min·wk^{-1}, vigorous-intensity cardiorespiratory exercise training for ≥20 min·d^{-1} on ≥3 d·wk^{-1} (≥75 min·wk^{-1}), or a combination of moderate- and vigorous-intensity exercise to achieve a total energy expenditure of ≥500-1000 MET·min·wk^{-1} (Garber et al., 2011). As these recommendations also apply to adults with chronic diseases or disabilities, recommendation for exercise training for those with spinal cord injuries is not very different from the able-bodied population. The recommended exercise prescription for persons with SCI for the commonly employed exercise modes are three to five weekly exercise sessions of 20-60 minutes at moderate exercise intensities of 50-80% maximal oxygen uptake.

Most exercise training following SCI employs upper extremity exercise modes such as arm crank ergometry, wheelchair pushing and wheelchair ergometry. These training modes have been found to improve oxygen uptake with the magnitude of improvement inversely proportional to the neurological level of injury (Davis, Shephard, & Jackson, 1981; Franklin, 1985; Hooker & Wells, 1989; Jacobs & Nash, 2004; Jacobs et al., 2001). Other modes of exercises are swimming, resistance training, wheelchair sports and functional electrical stimulation (FES)-assisted exercise.

Devillard and co-workers reviewed 62 literature on the effects of training programmes for people with SCI and concluded that reconditioning training programmes after SCI have a direct impact on function and quality of life, permitting participation in physical activities in addition to ADL (Devillard, Rimaud, Roche, & Calmels, 2007). Hicks and colleagues conducted a systematic review of effects of exercise on physical fitness in people with SCI. Using the SCIRE (Spinal Cord Injury Rehabilitation Evidence) level of evidence, the authors concluded that there is strong evidence that a combination of resistance and arm crank ergometry training, performed twice to thrice weekly at moderate intensity (60-80% HRmax or 60-65% VO2peak) improve physical capacity. The evidence of the effectiveness of wheelchair ergometry for improving physical capacity was weaker. For FES-assisted exercise, there is strong evidence for the effectiveness of FES-assisted exercise for muscle strength but the authors could not conclude on type and intensity of FES-assisted exercise as well as its effect on increasing muscle mass or decreasing fat mass (Hicks et al., 2011).

2.4 EXERCISE AND SPINAL CORD INJURY

2.4.1 Reduced exercise capability of persons with spinal cord injury

Following SCI, there is loss of voluntary motor function in the large muscle groups in the lower limbs. The higher the level and the more complete the SCI, the greater the loss of motor function as well as muscle mass. As described earlier, neurological lesions in the thoracic and lumbar area result in paraplegia, whereas lesions in the cervical region results in tetraplegia where all four limbs and the trunk are involved. The greater the paralysis the lower is the exercise capability resulting in lower cardiorespiratory fitness level that can be achieved through exercise training. With higher lesions involving more than half of the intercostal muscles, the pulmonary ventilation will also be limited further reducing the exercise capability (Glaser, 1991; Lavis et al., 2007). Furthermore, with loss of motor function in the trunk, truncal stability is affected, also limiting the ability to exercise in persons with tetraplegia. The loss of the lower limbs large muscle groups limits exercise capability to the smaller muscle groups in the upper limbs. Shephard and colleagues described peak oxygen uptake as directly related to the active muscle mass which may be recruited for exercise (Shephard, Bouhlel, Vandewalle, & Monod, 1988).

In addition to the paralysis of muscles and loss of motor control in the lower limbs, there are also significant alterations in the blood flow and distribution throughout the cardiovascular system in persons with SCI. There is loss of the venous pumping action in the muscles of the lower limbs resulting in pooling of blood in the lower limbs and consequently reduced venous return. These two factors i.e. muscle paralysis and impaired blood flow are considered as mechanical factors affecting exercise capability in persons with SCI.

The other important factor affecting exercise capability is neurally-related factors. Persons with higher level thoracic and cervical injures may also experience a partial or complete dissociation of the autonomic nervous system from central control. This autonomic dysfunction affects the cardiac response to exercise and lead to impairment in cardiac output during exercise (Lavis et al., 2007). Sympathetic stimulation is required for cardiovascular reflex responses to exercise. These reflexes redistribute blood flow to metabolically active skeletal muscles to provide more oxygen and fuel substrates. The cardiovascular reflex responses include vasoconstriction in the relatively inactive tissues (gut, skin, kidneys), vasodilatation of skeletal muscle arterioles, venoconstriction in the skeletal muscles, increased heart rate, stroke volume and cardiac output (Glaser, 1991; Lavis et al., 2007). In persons with SCI however, the ability to redistribute blood from the lower limbs is impaired and compounded with the impaired cardiovascular reflex responses results in limited cardioacceleration, myocardial contractility, stroke volume and cardiac output (Glaser, 1991; Hopman, Verheijen, & Binkhorst, 1993; Kinzer & Convertino, 1989). Additionally in neurological lesions within or above T1-T5 spinal cord level, there is blunted heart rate response to increasing levels of exercise as the sympathetic fibres supplying the heart arise from these levels.

In the absence of leg exercise capability, most people with SCI undertake upper body exercise. However, the combination of mechanical and neural factors above can contribute further to the high fatigability of the relatively small muscle mass in the arms. This restriction in exercise performance results in poor physical and psychological fitness gains and consequently poor motivation to maintain physical activity and exercise, further exacerbating reduced functional and exercise capability (Davis, 1993; Glaser, 1989).

2.4.2 Acute physiological responses to exercise in persons with spinal cord injury

The damage to the somatic and autonomic nervous system results in significantly different exercise responses to SCI survivor from those of able-bodied persons (Hopman, 1994; Jehl et al., 1991). The different exercise modes also render unique cardiorespiratory and cardiovascular responses in persons with SCI.

2.4.2.1 Upper body exercise

As presented earlier, due to the lower limb paralysis, most people with SCI undertake arm exercises but normal daily wheelchair activity may not provide sufficient exercise to train the cardiopulmonary system and that supplemental arm exercise training is necessary to stimulate fitness improvement (Glaser, 1989).

Upper body exercise such as arm crank ergometer (ACE), wheelchair propulsion and wheelchair sports are usually prescribed for the SCI population, but because of the relatively small muscle mass in their upper limbs, such exercise is not as beneficial as lower limb exercise (Glaser, 1989). Because of the smaller muscle mass, muscle fatigue can occur first before endurance training targets are met. Upper body exercise elicits greater cardiorespiratory stresses when compared with similar workloads during leg exercise (Davis, 1993; Davis et al., 1990). Previous studies have shown lower stroke volumes and reduced cardiac outputs in people with SCI performing upper body exercise (Glaser, 1991; Hopman, Oeseburg, & Binkhorst, 1992; Kaprielian, Plyley, Klentrou, Goodman, & Goodman, 1998). This has been attributed to “circulatory hypokinesis” a term described by Hjeltness whereby the leg venous return is reduced because of impaired muscle pump in the paralyzed limbs resulting in reduced cardiac outputs for a given oxygen uptake (Hjeltnes, 1977), and impaired autonomic cardiovascular control below the level of the spinal lesion (Davis & Shephard, 1988;

Glaser, 1989; Jacobs, Mahoney, Robbins, & Nash, 2002). Kinzer and Convertino, in their study comparing the cardiovascular dynamics of able bodied, spinal cord injured and bilateral amputee subjects suggest that an active muscle pump in the legs contribute significantly to elevated venous return and stroke volume during arm cranking exercise, further describing the legs of the paraplegics as reservoir for fluid accumulation, which may limit cardiac filling (Kinzer & Convertino, 1989). The combination of these mechanisms explains the findings of investigations which reported lower peak oxygen uptakes in subjects with paraplegia, compared to able-bodied population performing arm crank ergometry testing (Hooker et al., 1993; Hopman et al., 1992; Price & Campbell, 1999).

Previous literature reported that when people with untrained arms perform arm cranking exercise, their maximal oxygen uptake corresponds to approximately 70% of the value reached during leg exercise (Glaser, 1991; Secher, Ruberg-Larsen, Binkhorst, & Bonde-Petersen, 1974; Secher & Volianitis, 2006). The power output capability during arm exercise in the SCI population is also limited (Glaser, 1991). Earlier investigations have shown that peak oxygen uptake values are usually lower in persons with tetraplegia than those with paraplegia and nondisabled persons during arm exercise and much lower than nondisabled persons performing large-muscle group exercise (Coutts, Rhodes, & McKenzie, 1983; Figoni, 1993; Gass & Camp, 1979; Van Loan, McCluer, Loftin, & Boileau, 1987). In an investigation of a hundred recently injured SCI individuals, Hjeltnes found that peak oxygen uptake was closely correlated to the neurological level of injury and that peak oxygen uptake in females with mid-level thoracic paraplegia was on the average lower than in males with corresponding injury levels (Hjeltnes, 1986).

In addition to injury level factor, existing fitness level factor also impacts on the peak oxygen uptake during arm crank exercise where trained or highly active paraplegics demonstrated greater peak oxygen uptake, higher maximal cardiac output and increased stroke volume (Burkett, Chisum, Stone, & Fernhall, 1990; Davis & Shephard, 1988). Despite its popularity and convenience, it is obvious that alternatives to the arm crank exercise mode must be investigated further to enable greater cardiorespiratory fitness gains as well as its associated long-term health benefits with regular exercise training in persons with SCI.

2.4.2.2 Lower limb exercise

Passive leg cycling is one of the methods used by persons with SCI as an exercise mode. In most persons with SCI, there is muscle paralysis and loss of motor control resulting in the inability of volitional leg cycling. In many rehabilitation settings this mode of exercise is still prescribed and is done via hand-driven leg ergometers or motorized leg ergometers. Muraki and colleagues reported that passive leg cycling can be used as a method to promote venous return through the lengthening and shortening actions in the muscles that mimic muscle pump activity. In their experiment comparing able-bodied and spinal cord injured subjects, they found that passive cycling exercise led to an increase in stroke volume without a rise in heart rate suggesting the promotion of venous return from the paralyzed limbs during passive cycling (Muraki, Ehara, & Yamasaki, 2000). Other studies however did not find any significant changes in oxygen uptake, stroke volume and heart rate responses with passive leg exercises (Figoni et al., 1990; Nash et al., 1995). The increases in oxygen uptake during passive cycling attributed to rhythmic lengthening and shortening of the paralysed muscles was also found not comparable to increases in oxygen uptake during electrical stimulation induced exercise (Figoni et al., 1990; Glaser et al., 1988; Nash et al., 1995).

In a study examining arterial blood flow during passive leg exercise and passive leg cycling, it was found that there was no alteration in arterial peripheral circulation (changes in leg blood flow, vascular resistance or blood pressure) during these two modes of passive leg exercises (Ter Woerds, De Groot, van Kuppevelt, & Hopman, 2006). A study by Ballaz and colleagues however found that acute passive leg cycling exercise increases femoral artery blood flow velocity in paralyzed legs of people with paraplegia (Ballaz, Fusco, Cretual, Langella, & Brissot, 2007). Even though there seems to be no cardiovascular benefit and the results do not support the use of passive leg exercises for the prevention of cardiovascular disease-related secondary complications, passive leg exercises still have its place in addressing musculoskeletal concerns in people with SCI (Ter Woerds et al., 2006).

2.5 ASSISTIVE TECHNOLOGY FOR EXERCISE FOR PERSONS WITH SPINAL CORD INJURY

2.5.1 Functional electrical stimulation-assisted leg exercise

The use of electrical current to initiate purposeful movement in people with SCI dates to 1963, when Kantrowitz used “electrical stimulation” to contract the paralyzed quadriceps of a person with T3 paraplegia (Nash, 2005). Since then, in the past three to four decades, functional electrical stimulation (FES) has increasingly been used to elicit rhythmic muscle contractions and purposeful movements of the paralysed lower limbs of persons with SCI. FES leg exercises can be performed either as static muscle contractions, dynamic knee extension or rhythmic cycling exercise (Hettinga & Andrews, 2008a; Ragnarsson, 2008). Static FES-evoked muscle contractions usually involve simultaneous contractions of the agonist-antagonist muscle groups such as the quadriceps-hamstrings complex. Dynamic FES-evoked muscle contractions result in programmed desired movements most commonly rhythmic cycling whereby the quadriceps-hamstring-gluteal muscle complex is pre-programmed to be electrically stimulated sequentially to produce cycling motions. Other forms of FES-assisted exercise are FES-rowing, FES-stepping, FES-standing and FES-walking with or without orthosis. FES can also be applied to the upper extremity in the form of static FES contractions, dynamic flexion-extension movements or FES-assisted arm cycle ergometry to facilitate upper body exercise.

The electrical stimulation to the target muscle groups is delivered via electrodes, usually carbon-backed gel electrodes. The electrodes used are usually large enough to cover the width of the muscles to enable as much muscle recruitment as possible.

2.5.1.1 Mechanism of action

The pre-requisite for successful FES is upper motor neuron injury of the paralyzed muscles with intact lower motor neurons as muscle activation occurs via indirect electrical stimulation of the intact peripheral nerve and not muscle (Phillips, 1987). The electrically evoked muscle contraction is independent of central nervous system control. When electrically stimulated, the motor neurons and units excite simultaneously with preferential activation of motor units in closer proximity to the stimulation source and limited activation occurring in motor units further away from the stimulation source (Faghri & Trumbower, 2005). With FES, there is selective activation of the larger diameter motor neurons as these are easier to stimulate, which is the opposite of normal muscle fibre recruitment. These reversal of normal muscle recruitment and synchronous activation of motor units result in less efficient and less effective contraction leading to faster muscle fatigue (Faghri & Trumbower, 2005; Jacobs et al., 1997; Ragnarsson, 2008).

2.5.1.2 Clinical consideration

Prior to initiating an FES programme, a thorough medical examination is essential. This should include neurological assessment using the ISNCSCI recording the ASIA impairment scale and neurological level of injury. Distinguishing between upper and lower motor neuron dysfunction is also crucial. The existence of stretch reflex activity and spasticity indicate that the SCI individual is a potential candidate for FES. The individual should also be evaluated for residual sensation that could impact the tolerance to electrical stimulation. Other assessment includes lower limb radiographs. All potential candidates should be informed regarding the benefits and risks of FES exercise. In persons with SCI above T6, electrical stimulation may provoke autonomic dysreflexia, electrical stimulation should be introduced gradually and blood pressure monitored closely in the early phase of training (Faghri & Trumbower, 2005).

2.5.1.3 Cardiorespiratory responses

Previous authors had demonstrated that FES-assisted leg cycling increases oxygen uptake above levels produced by passive leg cycling (Figoni et al., 1990; Glaser et al., 1988). Other investigators showed increases above resting or baseline levels (Barstow et al., 1996; Goss, McDermott, & Robertson, 1992; Gurney, Robergs, Aisenbrey, Cordova, & McClanahan, 1998; Hjeltnes et al., 1997; Hooker et al., 1992b; Hooker, Scremin, Mutton, Kunkel, & Cagle, 1995; Kjaer, Mohr, Biering-Sorensen, & Bangsbo, 2001; Krauss et al., 1993b; Mohr et al., 1997; Mutton et al., 1997b; Pollack et al., 1989). These findings concur with the review by Davis and co-workers whereby the effects of FES on cardiorespiratory, metabolic and biochemical responses supported the view that FES-evoked leg exercise promotes positive metabolic responses and enhances aerobic fitness for people with SCI (Davis et al., 2008).

Pollack and colleagues demonstrated that lower extremity FES exercise can safely achieve significant aerobic training effects in persons with SCI but the peak levels of cardiorespiratory performance were low, an average of 1.0 L•min^{-1} similar to those reported for tetraplegic persons performing maximal voluntary upper extremity exercises (Pollack et al., 1989). This finding is in agreement with later studies that show lower peak oxygen uptakes during FES leg cycling than other type of exercise (Barstow et al., 2000; Mutton et al., 1997b; Raymond et al., 1999; Verellen et al., 2007).

A very important feature of FES cycling that needs to be recognized is the low power output levels produced by persons with SCI despite the relatively high oxygen uptake (Duffell, Donaldson, & Newham, 2010). Glaser and colleagues attributed this finding to the mechanical inefficiency of the FES cycling exercise. The inefficiency may be due to non-physiologic recruitment and activation of muscle fibres, disruption in sensory feedback and vasomotor control in paralyzed SCI subjects and inappropriate joint biomechanics. The authors however found this inefficiency a positive exercise effect as higher magnitudes of metabolic and cardiopulmonary responses can be elicited by people with SCI without highly stressing their muscles, bones and joints (Glaser, 1991; Glaser et al., 1988). The mechanical efficiency of SCI subject performing FES cycling has been reportedly low with previous studies reporting values of between four to six percent (Duffell & Newham, 2009; Fornusek & Davis, 2008; Theisen, Fornusek, Raymond, & Davis, 2002).

2.5.1.4 Cardiovascular and haemodynamic responses

Glaser and colleagues demonstrated that rhythmic patterns of FES-induced isometric contractions of calf and thigh muscles can significantly increase stroke volume and cardiac output of able-bodied and SCI individuals during rest in a sitting position

(Glaser, Rattan, & Davis, 1987). FES leg cycling exercise has been shown to promote central and peripheral haemodynamic responses by promoting higher stroke volumes and cardiac outputs (Davis et al., 1990; Figoni et al., 1991; Raymond et al., 1999). This suggests that FES leg exercise may enhance arm exercise capability by increasing blood availability. In a study examining lower limb blood flow, Thomas and co-workers concluded that FES-induced contractions of the lower limbs increase total lower limb blood flow and decrease venous pooling, suggesting that this will potentiate cardiovascular responses which is consistent with previous findings (Thomas, Davis, & Gass, 1992). Total peripheral resistance (TPR) was found to be reduced in individuals with SCI during FES leg exercise; Figoni and colleagues suggested that a normal vasodilator response exists in the exercising muscles (Figoni et al., 1990). Faghri and Yount evaluated the central haemodynamic responses during supine-sitting-standing position changes in able-bodied and SCI subjects and found significant reductions in mean arterial pressure when changing positions from sitting to standing and during prolonged standing, the TPR increased in both groups (Faghri & Yount, 2002). With impaired neural mechanism centrally, local and humoral control may play a role in maintaining the haemodynamics in these individuals.

FES leg cycling exercise performed by people with SCI produce inconsistent heart rate and blood pressure responses. Thomas and colleagues (1997) did not find any change in heart rate response when performing flexion-extension electrical stimulation exercise (Thomas, Davis, & Sutton, 1997). Adams and colleagues; as well as Brice and colleagues found decreased heart rates during FES exercise but other authors had observed increased heart rate response with FES exercise (Adams et al., 1984; Barstow et al., 1995; Brice et al., 1988; Figoni et al., 1990; Hooker et al., 1990; Kjaer et al., 1999). According to Petrofsky, some SCI individuals have a diminished heart rate while others have a diminished or absent blood pressure response to fatiguing isometric exercises (Petrofsk, 2001).

Dela and co-workers compared the cardiovascular responses in paraplegics, tetraplegics and able-bodied subjects during FES leg cycling and found that in all subjects cardiac output and leg blood flow increased but in the SCI subjects they reached a maximal value. In the tetraplegic group, the increase in cardiac output was mainly elicited by an increase in stroke volumes whereas in the paraplegic group, it was by heart rate. The increase in heart rate in SCI subjects was slow compared to the able-bodied subjects. The blood pressure remained stable in the able-bodied group but decreased over time in the SCI subjects especially the tetraplegic group (Dela et al., 2003). The mechanism for cardioacceleration during exercise is not clear. The authors postulated that without central influence on heart rate, neural feedback from working muscles or autonomic influence on the heart, the heart rate increase during exercise could be due to arterial baroreceptors response to low blood pressure and/or due to the role of plasma catecholamine.

2.5.2 Hybrid FES-exercise

Concurrent voluntary ACE and FES-LCE termed "hybrid FES exercise" are available in the form of adapted stationary arm crank ergometers over FES-cycling ergometers, FES rowing ergometers and roadworthy integrated hybrid FES bike. The earliest literature on the combination of arm cranking and FES leg cycling were by Glaser and Hooker and colleagues (Glaser, 1989; Hooker, Glaser, & Figoni, 1989). Glaser reported additive effects upon aerobic metabolism, a 0.5 $L \bullet min^{-1}$ higher oxygen uptake with this combined exercise mode (Glaser, 1991). Hooker and colleagues found significantly higher peak oxygen uptake, heart rate and cardiac output and significantly lower total peripheral resistance in a group of eight tetraplegic subjects compared to arm cranking alone or FES cycling alone (Hooker et al., 1989). Figoni and colleagues also found similar findings of higher magnitudes of cardiorespiratory responses during hybrid exercise in a group of tetraplegic subjects (Figoni, Glaser, & Rodgers, 1989). Glaser postulated that this can be accomplished with the hybrid exercise due to the substantially larger muscle mass utilized, and the enhanced venous return and cardiac output that occurs with lower limb FES exercise (Glaser, 1991). Hybrid exercise appears to provide optimal levels of metabolic and cardiopulmonary responses for aerobic conditioning of people with SCI, while providing training benefits to both the upper and lower body musculature.

Hybrid exercise training is formally defined as FES-induced leg cycling exercise performed simultaneously with arm crank exercise. However, FES has also been used to produce static contractions, knee extension, and gait and these modes have been combined with arm crank exercise to produce hybrid exercise training effects.

Following the discovery by the earlier researchers, numerous studies have shown that with hybrid exercise, it is possible to activate more muscle mass, augment sympathetic outflow, reduce pooling of blood in the legs, increase cardiac volume load and oxygen uptake and provide whole body exercise benefits (Hettinga & Andrews, 2008a; Krauss et al., 1993b; Mutton et al., 1997a; Raymond et al., 1999; Verellen et al., 2007).

2.5.2.1 Cardiorespiratory responses

During hybrid FES leg cycling exercise, several authors found a greater oxygen uptake than during arm cranking alone (Figoni & Glaser, 1993; Hooker et al., 1992a; Raymond, Davis, Fahey, Climstein, & Sutton, 1997). In training studies involving this combined mode, authors have reported hybrid FES leg cycling training result in higher work rate for the legs and improved aerobic capacity (Figoni, Glaser, & Collins, 1996; Krauss et al., 1993b; Mutton et al., 1997b). In recent years, integrated hybrid bikes, which can be used indoors and outdoors, have been made commercially available. A study by Heesterbeek and colleagues showed that training using this hybrid FES-cycle results in significant increase in oxygen uptake and improvement of physical fitness after only four weeks of training (Heesterbeek et al., 2005).

In the other combined modes i.e. arm cranking exercise combined with FES-leg exercise other than cycling, several authors found significant increases in peak oxygen uptake measurements during hybrid exercise. Edwards and Marsolais found the combination of ACE and FES walking produced highest oxygen uptake compared to ACE alone and FES walking alone (Edwards & Marsolais, 1990). Climstein and colleagues found higher heart rate and oxygen uptake in combined FES-induced knee extension/flexion exercise compared to passive leg exercise (Climstein, Davis, & Hunt, 1994). Laskins and co-workers reported increased oxygen uptakes in submaximal tests and Verellen and colleagues reported increased oxygen uptakes in maximal exercise testing comparing FES-rowing to arm exercise and combined arm and FES-rowing (Laskin et al., 1993; Verellen et al., 2007).

There is enough evidence from the available literature to suggest that hybrid exercise provides a greater stimulus to the cardiorespiratory system resulting in increased metabolic, respiratory and cardiovascular responses through the increased active muscle mass or increased blood circulation to active muscles, or a combination of both. There is still insufficient evidence however to determine the relative contribution to the increased physiological responses between FES-mediated increases in muscle mass and muscle blood flow (Stefanizzi & Overend, 1998).

2.5.2.2 Cardiovascular and haemodynamic responses

Hooker and colleagues found increased cardiac output and heart rate during hybrid FES leg cycling exercise than during arm cranking alone whereas Figoni and co-workers did not find any change in peak heart rate, stroke volume, cardiac output and total peripheral resistance in a group of 14 tetraplegics following 15 weeks of hybrid FES leg cycling training (Figoni et al., 1996; Hooker et al., 1992a). Davis and colleagues reported significantly higher cardiac outputs and stroke volumes, and lower total peripheral resistance when isometric FES leg contractions was combined with arm cranking exercise (Davis et al., 1990). Phillips and colleagues found increased blood flow and decreased venous pooling with isometric FES leg contractions during arm cranking exercise (Phillips, Burkett, Munro, Davis, & Pomeroy, 1995). A four-week hybrid FES cycling training leads to vascular adaptations in the exercised tissues but not in the unstimulated areas whereby Doppler studies demonstrated increased thigh peak blood flow, decreased thigh vascular resistance compared to baseline, and increased diameter of the common femoral artery (Thijssen, Heesterbeek, Van Kuppevelt, Duysens, & Hopman, 2005).

The heart rate responses in the hybrid FES literature were found to be inconsistent. Several authors reported increased heart rate response with hybrid FES exercise (Climstein et al., 1994; Figoni & Glaser, 1993; Figoni et al., 1989; Hooker et al., 1992a), some reported decreased heart rate responses (Krauss et al., 1993b; Raymond et al., 1997), and even unchanged heart rate response with hybrid FES exercise (Figoni et al., 1996; Thomas et al., 1992).

These findings are not surprising given the findings of inconsistent heart rate responses in the studies of FES leg exercises only. Without central influence on heart rate, neural feedback from working muscles or autonomic influence on the heart, the heart rate responses during exercise is dependent on several factors including arterial baroreceptors response to blood pressure changes and the role of plasma catecholamine.

2.5.3 Virtual reality technology for exercise

Virtual reality (VR) refers to a range of computing technologies that present artificially generated sensory information in a form that people perceive as similar to real-world objects and events (Wilson, Foreman, & Stanton, 1997). During the mid to late 1990s, VR technologies first began to be developed and studied as potential tools for rehabilitation assessment and treatment intervention (Weiss, Rand, Katz, & Kizony, 2004). The rationale is based on a number of unique attributes of this technology, such as enabling safe and ecologically valid environments, control of task-specific level of performance and the provision of enjoyable and motivating experiences to the user (Riva et al., 1999; Schultheis & Rizzo, 2001). In VR, the focus is shifted from the person's efforts in producing a movement or completing a task to that of interacting within a virtual environment. Virtual environments are usually experienced with the aid of special hardware and software for input and output. Visual information is often displayed using head-mounted displays, projection systems or large flat screen monitors. In addition to specialized hardware, compatible computer software is needed to link perceptual inputs with user performance (Weiss & Katz, 2004).

VR can be used as an enhancement to conventional therapy for patients with conditions ranging from musculo-skeletal problems, to neurological-induced paralysis, to cognitive deficits. This approach is called "VR-augmented rehabilitation" or "VR-assisted rehabilitation". When VR replaces conventional interventions altogether, the rehabilitation is considered "VR-based". If the intervention is done at a distance, it is called "telerehabilitation". VR simulations for rehabilitation differ depending on the particular therapeutic approach such as "teaching by example", "video game like" and "exposure therapy". VR presents significant advantages when applied to rehabilitation of patients with varied conditions. These advantages include patient motivation, adaptability and variability based on patient baseline, transparent data storage, online remote data access, economy of scale and reduced medical costs (Burdea, 2003).

Potential areas for VR applications are in cognitive rehabilitation, driving rehabilitation, activity of daily living skill training, patient and family education, and vocational and social retraining. One area of interest is VR-assisted exercise, whereby VR-enhanced exercises involving visual inputs with motion-tracking enables the individual to interact within the virtual environment and provide a sense of presence and positive involvement. Chuang and colleagues investigated the effect of a virtual reality-enhanced exercise protocol after coronary artery bypass graft surgery, and observed that incorporating a VR environment into cardiac rehabilitation programmes accelerated recovery of patients with cardiovascular impairment (Chuang, Sung, Chang, & Wang, 2006). In an earlier study, Chuang and colleagues found that the maintenance of endurance, increase in target intensity and total energy expenditure in exercise programmes could be assisted by introducing VR technology (Chuang et al., 2003). Sveistrup and colleagues used a VR-based exercise programme in a population of community-living individuals with traumatic brain injury. The group underwent a six-week thrice-weekly exercise intervention, which resulted in clinically significant changes on the Community Balance and Mobility Scale (Sveistrup et al., 2003).

Hettinga and Andrews suggested several strategies to simulate training compliance in people with SCI which includes virtual reality (VR) exercise (Hettinga & Andrews, 2008a). There is a dearth of evidence however, on the potential for FES-exercise combined with VR technology to produce aerobic fitness benefits. Literature on VR rehabilitation in the SCI population is also limited.

In a case report, Riva described a VR-enhanced orthopaedic appliance for gait training a paraplegic subject. The virtual environment used in the study was a simulation of a stroll through a mountain path using actual images of Alpine scenery incorporating sounds of the natural environment (Riva, 1998). The subject reported improved levels of self-confidence, will, relaxation and activity. Additionally there was improvement in the sense of well-being and mood and quality of sleep (Riva, 1998, 2000). Kizony and co-workers investigated the outcome of a VR protocol in 13 paraplegic SCI subjects. They found that interaction with virtual stimuli in functional environments appear to enhance motivation and enjoyment during therapy sessions and found significant correlations between performance within a VE and static balance ability as measured by the Functional Reach Test (Kizony, Raz, Katz, Weingarden, & Weiss, 2005).

VR presents an alternative means of achieving improved psychological well-being. Combining VR with usual exercise machines, such as stationary exercise bikes may serve to enhance the psychological benefits of exercise. In a study of college students involved in a VR exercise programme, the investigators found that female students reported a positive impact on energy and tiredness levels with VR exercise (Smith, Handley, & Eldredge, 1998). Plante and colleagues investigated the psychological outcomes of combining moderate intensity (60-70% maximum heart rate) stationary cycling within a VR environment viewed on a computer comparing it with cycling only and playing a computer bicycle game only in 88 subjects. The results suggest that VR enhances enjoyment, energy and reduces tiredness when paired with exercise (Plante, Aldridge, Bogden, & Hanelin, 2003).

Chen and co-workers investigated the effect of virtual rehabilitation on the psychology of 30 SCI patients (Chen et al., 2009). Their experimental group performed a researcher-designed rehabilitation therapy programme using a VR-based exercise bike, while the control group underwent the same therapy without VR. The researchers observed that the virtual-reality-based rehabilitation programme could ease patients' tension and induce calm.

2.6 EFFECTS OF EXERCISE ON LIPID AND CARBOHYDRATE METABOLISM AND PSYCHOLOGICAL OUTCOMES IN PERSONS WITH SPINAL CORD INJURY

SCI and inactive lifestyle increases the risk of CHD. This risk is expressed in the level of HDL, which correlates positively with physical activity and negatively with the risk of CVD (Dallmeijer, Hopman, & van der Woude, 1997). The lower activity level can result in lower cardiovascular fitness and inferior lipid profile. Results from previous studies indicated that highly trained SCI subjects had better lipoprotein profiles than sedentary individuals. Dallmeijer and colleagues also found that lipid and lipoprotein profiles improve in persons with SCI during the first 2 years post-injury, and that improving the physical capacity or being physically active can improve the lipid and lipoprotein profiles (Dallmeijer, van der Woude, van Kamp, & Hollander, 1999). The literature reveals that FES leg exercises are able to provide stimulus to the cardiorespiratory system resulting in increased metabolic, respiratory and cardiovascular responses through the increased active muscle mass and increased blood circulation to active muscles. There is good evidence that FES hybrid exercise is able to provide a more superior physiological and consequently health and fitness benefit. In their review of oxygen consumption during FES-assisted exercise in people with SCI, Hettinga and Andrews concluded that FES hybrid exercise would be the preferred modality if optimal reduction in the risk for obesity, cardiovascular disease and type 2 diabetes is to be achieved (Hettinga & Andrews, 2008a). There is still limited work however on the outcomes of FES hybrid exercise training on carbohydrate and lipid metabolism.

2.6.1 Effect of exercise on lipid profile

Previous literature evaluating the outcomes of exercise training on lipid profile consisted of programmes involving aerobic, strength training and upper body exercise, FES leg cycling and body weight supported treadmill training.

A study evaluating the effect of training intensity found improvements in physical capacity and lipid profile in response to high-intensity (70-80% heart rate reserve (HRR)) 8-week thrice weekly arm cranking exercise programme compared to low intensity (40-50% HRR) programme in a group of recently injured SCI individuals (de Groot et al., 2003). Nash and colleagues investigated the outcomes of a 3 months upper body circuit exercise training in chronic paraplegia and found increased levels of HDL and reduced levels of LDL, supporting the beneficial effects of circuit exercise training on fitness and lipid profiles which reduces the risk of CVD (Nash et al., 2001). El-Sayed and Younesian compared the acute and training effects of arm cranking exercise on blood lipid profiles in wheelchair bound SCI individuals and able-bodied individuals. They concluded that acute ACE and 12 weeks ACE training in individuals with SCI were associated with favourable effects on HDL, whereas total cholesterols and triglycerides were not altered (El-Sayed & Younesian, 2005). In a recent study, Mitsui and colleagues compared the plasma concentrations of oxidized low-density lipoprotein (oxLDL) and adrenaline during arm crank exercise between persons with SCI and able-bodied individual. The authors found significantly increased plasma adrenaline levels in the able-bodied group and persons with SCI; but with a lower increase in those with SCI, and a significantly increased plasma oxLDL levels in the able-bodied group but not in persons with SCI (Mitsui et al., 2012).

In a mixed aerobic, relaxation, mobility and strength training programme and a training protocol involving a wheelchair aerobic fitness trainer, the investigators did not find any statistically significant change in the lipid profile of their subjects (Duran et al., 2001; Midha, Schmitt, & Sclater, 1999). Stewart and colleagues found that a body weight supported treadmill training programme significantly decreased total cholesterol levels, decreased LDL levels but did not result in any significant increase in HDL levels (Stewart et al., 2004).

In an FES-assisted exercise programmes, Griffin and colleagues did not find any change in triglyceride, total cholesterol and LDL posttraining levels from pre-training levels following 10 weeks of twice to thrice weekly FES cycling in 18 paraplegic subjects but instead found statistically significant reduction of HDL posttraining (Griffin et al., 2009). The authors attributed this finding to the variable HDL response to exercise among individuals as well as genetic variation. Solomonow and colleagues reported significant decreases of total cholesterol and LDL but no change in HDL levels in 28 paraplegic subjects who underwent FES powered reciprocating gait orthosis gait training of 15 weeks duration (Solomonow et al., 1997). Johnston and co-workers compared the outcomes of hourly thrice weekly FES cycling over 6 months versus passive cycling and FES only in 30 children with various levels of SCI (C4-T11). The authors found significant reduction in total cholesterol level in the group receiving electrical stimulation only and significant increase of peak oxygen uptake in the FES cycling group after 6 months of training leading them to conclude that FES cycling led to gains in oxygen uptake, whereas FES alone led to improvements in cholesterol. (Johnston, Smith, Mulcahey, Betz, & Lauer, 2009). In a recent study investigating the effects of 12 weeks twice weekly neuromuscular electrical stimulation resistance training of the paralyzed knee extensor muscle groups in men with SCI, Gorgey and colleagues found significant hypertrophy of knee extensor and flexors and decreased intramuscular fat and visceral adipose tissue, and significant improvements in lipid metabolism (Gorgey, Mather, Cupp, & Gater, 2012).

Even though there is good evidence of increased aerobic fitness benefit following FES-assisted exercise, the literature on improvements of lipid profile following FES-assisted exercise is limited and non-conclusive.

2.6.2 Effect of exercise on carbohydrate metabolism

Increased prevalence of glucose intolerance and diabetes among persons with SCI is well-documented and has been discussed earlier in this chapter. Physical activity, especially regular aerobic endurance exercise has been shown to reduce the incidence and prevalence of diabetes in the general population. The evidence of outcomes of exercise programmes on glucose tolerance and diabetes in the SCI population is still somewhat limited.

de Groot and co-workers in a study which evaluated the effect of training intensity in an arm cranking exercise programme of three times a week for 8 weeks in a group of recently injured SCI individuals, found significant improvement in insulin sensitivity in response to high-intensity (70-80% heart rate reserve (HRR)) compared to low intensity (40-50% HRR) exercise (de Groot et al., 2003). Midha and colleagues however did not find any change in fasting serum glucose in a 10-week fitness training using a wheelchair aerobic fitness trainer in 12 SCI subjects (Midha et al., 1999). Phillips and colleagues investigated the effect of exercise on blood glucose regulation following 6 months of a body-weight supported treadmill training (BWSTT) programme in nine incomplete SCI subjects and found significant decreases of plasma glucose during a 2 hour oral glucose tolerance test (OGTT) from pre-training levels and significant decreases of plasma insulin levels during OGTT at post-training (Phillips et al., 2004).

In exercise programmes employing FES-assisted methods, the outcomes of FES on carbohydrate metabolism have been inconsistent. In several studies, no change was reported on plasma glucose levels, glucose tolerance measured with OGTT and plasma insulin levels, with FES-assisted exercise training (Chilibeck et al., 1999; Mahoney et al., 2005; Mohr et al., 2001). Mahoney and colleagues employed FES-knee extensions resistance exercise training whereas in the other studies, FES-assisted leg cycling training was used (Mahoney et al., 2005).

Three other FES-assisted cycling studies reported favourable changes in glucose metabolism following training. Despite no favourable change in lipid profile from pre-training to post-training, Griffin and colleagues found significant decreases of blood glucose levels and plasma insulin during OGTT from pre-training levels following 10 weeks of twice to thrice weekly FES cycling in 18 paraplegic subjects indicating improved glucose tolerance (Griffin et al., 2009). Hjeltnes and colleagues assessed the effects of 8 weeks FES leg cycling on whole body insulin sensitivity, skeletal muscle glucose metabolism, and muscle fiber morphology in five tetraplegic subjects with complete C5-C7 lesions and concluded that muscle contraction improves insulin action on whole body and cellular glucose uptake in cervical cord-injured persons through a major increase in protein expression of key genes involved in the regulation of glucose metabolism (Hjeltnes et al., 1998). Jeon and colleagues investigated the effect of 30 minutes, thrice weekly FES cycling for 8 weeks, on glucose tolerance and insulin sensitivity in seven persons with motor complete SCI and reported significantly lower glucose levels during OGTT and improved glucose utilization in three subjects and improved insulin sensitivity in two subjects (Jeon et al., 2002).

In a later study, Jeon and colleagues investigated the effect of 3 to 4 times a week FES rowing over a 12 week period, on aerobic fitness, plasma glucose and leptin in six persons with paraplegia and concluded that a 12 week training involving FES rowing improved aerobic fitness and fasting glucose and leptin levels in the absence of significant change to body composition, fasting insulin levels, or calculated insulin sensitivity (Jeon et al., 2010). In addition to favourable body composition changes and lipid metabolism, Gorgey and colleagues also reported significant improvements in insulin metabolism in five SCI individuals following 12 weeks of FES resistance training of the paralyzed knee extensor muscle groups (Gorgey et al., 2012).

Even though there is numerous research on the physiological benefits with FES-assisted exercise with respect to cardiovascular, muscular, pulmonary and hormonal adaptations, there are limited studies and inconsistent evidence on the effects of FES-assisted exercise on glucose tolerance in people with SCI.

2.6.3 Effects of exercise on psychological outcomes

Apart from physiological and metabolic benefits, physical activity and exercise can also play a role in the promotion of positive mental health. Some reported psychological benefits include depression, anxiety, anger and improved mood (Hassmen, Koivula, & Uutela, 2000; Scully, Kremer, Meade, Graham, & Dudgeon, 1998). In addition to enhancing mood and psychological well-being, exercise also improves self-concept and self-esteem (Plante & Rodin, 1990). In the spinal cord injured population, it was shown that those who participated in physical activity and exercise reported significantly less pain, stress and depression after training and had higher scores in indices of satisfaction with physical function, level of perceived health and overall quality of life (Hicks et al., 2003; Latimer, Ginis, Hicks, & McCartney, 2004). Several authors cautioned that it is important to recognize that perceived psychological benefits may occur in the absence of clearly identifiable changes in physiological parameters, just as it is possible to establish physiological changes in the absence of any perceived psychological benefits (McAuley & Courneya, 1994; Scully et al., 1998). From the literature, it is not yet clear how psychological and physiological processes and functions interact in the determination of outcomes.

The mood enhancing properties of exercise have been investigated and showed that exercise training can have a positive influence on mood states (Scully et al., 1998). However, it has also been reported that exercise training did not result in significant improvements in long term mood states among non-clinical samples (Lennox, Bedell, & Stone, 1990). It was suggested that low to moderate levels of aerobic exercise are better than traditionally demanding (anaerobic) exercise programmes in terms of enhancing mood and improving psychological functioning (Moses, Steptoe, Mathews, & Edwards, 1989). Other authors however reported that in the general population, the greatest gains in psychological well-being have been observed with vigorous physical activity that increases aerobic fitness (Greenwood, Dzewaltowski, & French, 1990). Greenwood and colleagues examined perceptions of efficacy toward physical tasks and mood states in wheelchair tennis participants which included individuals with SCI and suggested that sport participation may be an important source of self-efficacy information and psychological well-being improvement for wheelchair mobile populations (Greenwood et al., 1990).

In a review article, Martin Ginis and colleagues suggested that by promoting sports and exercise SCI patients may be motivated by the potential psychosocial outcomes of activity such as reduced pain and stress, or enhanced mood and self esteem (Martin Ginis, Jorgensen, & Stapleton, 2012). In another review, Kawanishi and Greguol concluded that physical activity appears to have an important influence on social relationships, functional independence, psychological factors and physical aspects, which can enhance quality of life and independence in the performance of daily activities (Kawanishi & Greguol, 2013).

Lannem and colleagues investigated the role of physical exercise, perceived exercise mastery and fitness on life satisfaction in people with incomplete spinal cord injury through a cross-sectional survey. They found that participants who exercised regularly experienced a significantly higher life satisfaction and perceived exercise fitness (Lannem, Sorensen, Froslie, & Hjeltnes, 2009). In another cross-sectional survey, Anneken and co-workers reported that SCI individuals who were actively involved in sports have higher employment rate than physically inactive individuals and that physical exercise was identified as the main influencing determinant of quality of life (Anneken, Hanssen-Doose, Hirschfeld, Scheuer, & Thietje, 2010). A recent study by Blauwet and colleagues also found that participation in organized sports programme was positively associated with employment in adults with chronic spinal cord injury (Blauwet et al., 2013).

Most research linking exercise and physical activity to psychological well-being have adopted chronic exercise training as a focus. Several authors however suggested that attention should also be directed toward the effects resulting from acute bouts of physical activity (Gauvin & Rejeski, 1993). Acute aerobic exercise has been shown to be associated with significant positive mood changes in the able-bodied and clinical population including SCI (Hicks & Ginis, 2008; Hicks et al., 2003). A study conducted by Rendi and co-workers revealed that significant improvements occurred even after a 20-min bout of exercise (Rendi, Szabo, Szabo, Velenczei, & Kovacs, 2008). In addition, several authors also concluded that exercising at a self-selected workload yielded positive changes in affect that were not related to exercise intensity (Rendi et al., 2008; Szabo, 2003). A study by Blanchard and colleagues concluded that although exercise intensity and level of fitness did not moderate acute exercise relationship for positive feeling states, fitness level effects may be intensity dependent for negative feeling states (Blanchard, Rodgers, Spence, & Courneya, 2001). In a parallel group RCT, Hitzig and co-workers compared the benefits of FES-assisted walking on various domains pertinent to well-being to a conventional aerobic/resistance training programme and found that both groups reported positive gains in well-being from trial participation (Hitzig et al., 2013).

Participation in physical activities and exercise are not without risk (e.g. overuse injuries, increase risk for autonomic dysreflexia), however, the benefits far outweigh the risks (Hicks et al., 2011). A variety of benefits from participating in exercise and sports include socialization, the acquisition of knowledge from others, the development of greater awareness of health and well-being issues, weight management, functional development and independence (Stephens, Neil, & Smith, 2012). Clinicians need to be aware of these benefits so that they can help their patients find personally meaningful reasons to be active (Martin Ginis et al., 2012). Anneken and co-workers recommend that the improvement of physical and coordinative skills with interaction between individuals with SCI and external sport groups should be an inherent part of the rehabilitation process. SCI individuals should also be given the opportunity to participate in wheelchair mobility courses that may improve their adherence to physical exercise in post-clinical settings (Anneken et al., 2010).

VR presents an alternative means of exercise modality and achieving improved psychological well-being. Combining VR and exercise machines, such as stationary exercise bikes may serve to enhance the psychological benefits of exercise (Plante et al., 2003; Smith et al., 1998). Chen and colleagues investigated the psychological benefits of VR in SCI rehabilitation and reported that a VR-based rehabilitation programme could ease tension and induce calm in SCI individuals undergoing rehabilitation (Chen et al., 2009).

2.7 SUMMARY

People with SCI are amongst the most deconditioned human beings. With the permanence nature of SCI and due to the systemic effect on the organs system as a result of the SCI, people with SCI are at risk of developing a myriad of secondary medical consequences. Further complicating the problems are medical consequences resulting from the effect of paralysis and extreme inactivity. Regular exercise is encouraged to prevent the occurrence of secondary health conditions. This manuscript attempts to investigate the various exercise options and their physiological responses in people with SCI. It also attempts to identify novel ideas on assistive technology assisted exercise and their outcomes for the SCI population.

Chapter Three

Exercise responses during FES cycling in individuals with spinal cord injury

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This chapter is presented in its published form. However, the referencing style has been altered and the paragraphs numbered to maintain to maintain consistency with the overall format of the thesis.

3.1 Abstract

Purpose: This study compared acute exercise responses during arm cranking, functional electrical stimulation (FES)-assisted leg cycling and combined arm and leg ("hybrid") cycling in individuals with spinal cord injury (SCI) during maximal and submaximal exercise.

Methods: Nine male subjects with long-standing neurological lesions from C7-T12 were recruited. All subjects performed arm crank ergometry (ACE), FES-leg cycle exercise (FES-LCE), combined ACE+FES-LCE and cycling on a hybrid FES tricycle (HYBRID). They were assessed for their peak exercise responses in all four modalities. Subsequently, their submaximal heart rates (HR), cardiac outputs (Q), stroke volumes (SV) and arterio-venous oxygen extractions $(Ca\text{-}Cv)O_2$ were measured at 40%, 60% and 80% of mode-specific VO_2peak.

Results: Arm exercise alone and arm+leg exercise resulted in significantly higher VO_2peak and HRpeak compared to FES-LCE ($p<0.05$). Submaximal VO_2 during FES-LCE was significantly lower than all other modalities, across the range of exercise intensities ($p<0.05$). ACE elicited 70-94% higher steady-state VO_2, and HYBRID evoked 99-148% higher VO_2 compared to FES-LCE. Steady-state FES-LCE also produced significantly lower Q, HR, and $(Ca\text{-}Cv)O_2$. ACE evoked 31-36% higher Q and 19-47% greater HR than did FES-LCE. HYBRID elicited 31-49% greater Q and 23-56% higher HR than FES-LCE.

Conclusion: Combined arm and leg exercise can develop a higher oxygen uptake and greater cardiovascular demand compared to ACE or FES-LCE alone. These findings suggested that combined arm+leg FES training at submaximal exercise intensities may

lead to greater gains of aerobic fitness than would arm exercise alone. These data also proffered that FES leg-cycling exercise by itself may be insufficient to promote aerobic fitness in the SCI population.

Key words: hybrid exercise; cardiorespiratory responses, maximal and submaximal tests; oxygen uptake

3.2 Introduction

One of the leading causes of death in the chronic spinal cord-injured population is cardiovascular disease (Frankel et al., 1998; Garshick et al., 2005; Myers et al., 2007). Reduced physical function and chronic immobilization underlie a sedentary lifestyle, and the concomitant lower energy expenditure is a contributing factor to the high morbidity and mortality after spinal cord injury (SCI) (Myers et al., 2007). These low physical activity levels are not only because of reduced muscle mass and impaired motor function, but also due to lack of accessibility and opportunities to undertake exercise (Myers et al., 2007; van den Berg-Emons et al., 2008). There is very good evidence that exercise is effective in improving physical fitness and general health in the SCI population (Jacobs & Nash, 2004; Nash, 2005; Washburn & Figoni, 1998a). However, leg exercise is usually restricted due to paralysis after SCI. Upper body exercise, such as arm crank ergometry (ACE) and wheelchair propulsion are commonly prescribed for this population, but due to the relatively small muscle mass in their upper limbs, such exercise is not as beneficial as lower limb exercise (Glaser, 1989). Upper body exercise elicits greater cardiorespiratory stresses when compared to similar workloads during leg exercise (Davis et al., 1990). Previous studies have demonstrated lower stroke volumes and reduced cardiac outputs in SCI individuals performing upper body exercise (Hopman et al., 1992). This has been attributed to: (i) ‘circulatory hypokinesis’, whereby leg venous return is reduced due to an impaired muscle pump in the paralysed limbs resulting in reduced cardiac outputs for a given oxygen uptake, and, (ii) impaired autonomic cardiovascular control below the level of spinal lesion (Davis & Shephard, 1988; Glaser, 1989; Jacobs et al., 2002).

In the past three decades, functional electrical stimulation (FES) has increasingly been used to elicit rhythmic muscle contractions and purposeful movements of the paralysed lower limbs of SCI individuals. FES leg exercise can be performed either as static muscle contractions, dynamic knee extension or rhythmic cycling exercise (Hettinga & Andrews, 2008a; Ragnarsson, 2008). Previous studies have also demonstrated that activation of the skeletal muscle pump in the lower limbs augments venous return, improves ventricular filling and increases oxygen uptake (Muraki et al., 2000; Muraki, Yamasaki, Ehara, Kikuchi, & Seki, 1996). FES leg exercise has been shown to promote central and peripheral haemodynamic responses by promoting higher stroke volumes and cardiac outputs (Davis et al., 1990; Figoni et al., 1991; Raymond et al., 1999). However, FES leg exercise alone has often resulted in significantly lower submaximal oxygen uptakes compared to ACE (Barstow et al., 2000; Raymond et al., 1999).

FES-LCE has been combined with ACE to augment submaximum oxygen uptake, as the larger muscle mass utilised during the combined arm and leg exercise has demonstrated greater cardiorespiratory demands and enhanced venous return (Davis et al., 1990; Raymond et al., 1999). Concurrent voluntary ACE and FES-LCE, termed “hybrid exercise”, can be deployed in the form of an adapted stationary arm crank ergometer mounted over a FES-leg cycling system, FES rowing ergometers or roadworthy integrated hybrid FES bikes (Heesterbeek et al., 2005; Raymond et al., 1999; Verellen et al., 2007). With hybrid exercise, increased muscle mass is activated, with augmented sympathetic outflow, reduced venous pooling in the legs, higher cardiac outputs and elevated oxygen uptakes, providing better whole body exercise benefits (Hettinga & Andrews, 2008a; Mutton et al., 1997b; Raymond et al., 1999). In recent years, integrated hybrid bikes, which can be used indoors or outdoors, have become commercially available. Exercise training using these hybrid FES-cycles has resulted in improvement of physical fitness after only four weeks of training (Heesterbeek et al., 2005).

This study compared the acute cardiorespiratory exercise responses during ACE, FES-LCE and two modes of arm+FES-leg cycling in SCI subjects. We hypothesized that submaximal steady-state oxygen uptakes and heart rates during both types of hybrid FES exercise would be higher than those elicited during ACE or FES-LCE alone. This study also investigated whether indices of cardiac performance (i.e.. cardiac output and stroke volume) during both types of hybrid FES cycling would be greater than that elicited during arm cranking exercise or FES-leg cycling alone.

3.3 Methods

3.3.1 Subjects

Nine male subjects (aged 40.6 ± 1.1 y, stature 1.73 ± 0.01 m, body mass 73.1 ± 1.0 kg, time since injury 6.6 ± 0.4 y) with traumatic spinal cord injury ASIA A, B and C from C6 to T12 (International Standards for Neurological Classification of Spinal Cord Injury, (Kirshblum et al., 2011)) volunteered to participate in this study (Ref No. 09-2009/12147). The Human Research Ethics Committee of the University of Sydney approved this study, and written informed consent was obtained from all subjects prior to their participation. The subjects were recruited through convenience sampling methodology. They were participants regularly attending a gymnasium catering to persons with disability at the Faculty of Health Sciences, University of Sydney. At the time of subject recruitment, there were no female participants attending the gymnasium. Eligible subjects were those aged between 18 and 65 years old. All subjects underwent a full medical screening which included a physical and neurological examination, a 12-lead resting ECG, measurement of resting blood pressure and lower limb radiographs prior to the study. All subjects were healthy, neurologically stable and had previous experience with FES cycling exercises for at least 8 weeks prior to the study. Previous experience with arm crank exercise was not a pre-requisite for the study.

3.3.2 Protocol

The subjects were assessed on four different exercise modalities presented in a set order: (i) an arm crank ergometer (ACE), (ii) a FES-leg cycle ergometer (FES-LCE), (iii) a combined ACE and FES-LCE system (ACE+FES-LCE), and, (iv) a commercially-available arm and leg tricycle (“HYBRID”; Berkelbike BV, 's-Hertogenbosch, The Netherlands), which incorporated a FES system to recruit the leg musculature. The arm crank ergometer was mounted over the leg cycle ergometer for ACE and ACE+FES-LCE assessments. For all tests, the crank axle of the ACE was positioned at shoulder height with the subject in the seated posture. For FES-LCE and ACE+FES-LCE, the subjects transferred themselves onto the leg cycle ergometer chair and their feet were strapped and held in position by ankle-calf supports to minimize leg movements during cycling. Subjects transferred onto the HYBRID had their feet and legs strapped and held in position by customized carbon-fibre leg supports. HYBRID was then mounted on a stationary cycle resistance trainer (Tacx i-Magic, Tacx BV, Wassenaar, The Netherlands), which calculated external power output during combined arm and leg effort.

Prior to the tests involving electrical stimulation, gel-backed self-adhesive surface electrodes were placed over the bellies of the quadriceps, hamstrings and glutei muscle groups. Electrode placement was kept consistent by measurements to key anatomical landmarks to ensure muscle fibre recruitment was similar between trials. Subject preparation and the experimental set-up were all performed by the primary investigator. During the FES cycling, electrical stimulation was delivered via biphasic rectangular pulses at a frequency of 35 Hz and pulse width of 300 μs. The muscle stimulation 'firing' angles were fixed and the timing of stimulation was pre-set by a computer programme (Fornusek, Davis, Sinclair, & Milthorpe, 2004). The maximum stimulation amplitude was limited to140 mA.

The research design involved 8 sessions of testing over 7 days which were performed on separate days. Testing were conducted in two stages (as described below) with all assessments separated by at least 48 hours.

In the first stage, all participants underwent an incremental power output test to maximal effort in all four different exercise modes. Peak oxygen uptake (VO_2peak) was derived to ascertain the highest physical work capacity for each individual in all four different exercise modes, as described below:

1) Maximal ACE: Subjects were instructed to arm crank at 50 $rev^{\cdot}min^{-1}$ at 0W for 3 min (warm-up). Resistance was subsequently increased by 5-10W every minute until volitional fatigue. The criteria for termination of the test were; subject requested to stop, subject unable to maintain cadence at 50 $rev^{\cdot}min^{-1}$ for at least 15s, or an obvious plateau of oxygen uptake from one minute to the next (Raymond et al., 1999).

2) Maximal FES-LCE: The FES-LCE was set up to enable the subjects to perform passive cycling at 0W (no electrical stimulation) at 50 $rev^{\cdot}min^{-1}$ for 3 min. Resistance was increased via a pre-set programme in the computer system. The cycling cadence was pre-set at 50 $rev^{\cdot}min^{-1}$ throughout the test. The cycle power output was increased by 1-3 W every 2 min. The FES system

microprocessor automatically increased electrical stimulation to match the power output demand (“Feedback” mode; (Fornusek et al., 2004)). The subject was considered to have reached leg-specific VO_2peak when the power output produced by the electrically stimulated muscles could not further increase despite reaching maximum stimulation amplitude of 140 mA.

3) Maximal ACE+FES-LCE: Subjects underwent a combined maximal ACE and maximal FES-LCE test protocol as previously described. The combined test was terminated when the subject stopped arm cranking at volitional fatigue.

4) Maximal HYBRID: The test protocol was performed following the arm and leg loading protocol of Heesterbeek and colleagues (Heesterbeek et al., 2005). The graded hybrid test consisted of a warming up phase at 0W for 3 min followed by increase in workload of 10W every minute. Subjects were instructed to perform voluntary arm cranking and FES-leg cycling simultaneously and to maintain pedaling cadence at 50 $rev \cdot min^{-1}$. The electrical stimulation was increased manually in four increments (minimum contraction, 33%, 66% and 100% of maximum amplitude of 140mA) at equivalent heart rates of resting HR, 33%, 66% and 100% of heart rate reserve. The goal of this protocol was to exhaust the arm and leg muscles simultaneously. The endpoint of the test was determined when cadence fell below 35 $rev \cdot min^{-1}$ or when power output dropped below 70% of the imposed power (Heesterbeek et al., 2005).

In the second stage of testing, cardiorespiratory responses were measured during submaximal steady-state exercise at 40%, 60% and 80% of mode-specific VO_2peak, determined from each of the previous maximal effort tests.

1) Submaximal ACE: Subjects were instructed to arm crank at 50 rev·min^{-1} at 0W for 3 minutes, followed by power output increases of 10W·minute^{-1} until reaching a target power output corresponding to 40% ACE VO_{2peak}. After a short recovery wherein the heart rate and VO_2 were observed to have returned to near pre-exercise levels, subjects then continued arm cranking until reaching target power out corresponding to 60% VO_{2peak}. Finally, after another recovery, they continued arm cranking up to 80% VO_{2peak}. Measurements were taken when the subjects demonstrated a physiological steady-state at each exercise intensity (after 3-5 min).

2) Submaximal FES-LCE: Subjects performed passive leg cycling at 0W (without FES) at 50 rev·min^{-1} for 3 min, followed by power output increments of 1-3 W·min^{-1} every minute until reaching target power output corresponding to 40%, 60% and 80% of FES-LCE specific $VO_{2peak.}$ After each exercise bout a short recovery was provided, followed by incremental power output to the next intensity. Increases of leg power output were achieved by deploying incrementally higher FES current amplitudes. At each fraction of mode-specific VO_{2peak}, physiological measurements were taken in steady state (usually after 3-5 min).

3) Submaximal ACE+FES-LCE: Subjects performed a combined ACE and FES-LCE cycling, incrementing both arm and leg power outputs until reaching a

target power output corresponding to 40% VO_{2peak} of ACE+FES-LCE. The subjects then continued ACE and FES-LCE until reaching target power outputs corresponding to 60% VO_{2peak} and 80% VO_{2peak} in steady-state similar to the ACE and FES-LCE protocols.

4) Submaximal HYBRID: Subjects performed simultaneous arm cranking and leg cycling until reaching target power output corresponding to 40% HYBRID VO_{2peak}. They then continued arm cranking and leg cycling until reaching target power outputs corresponding to 60% VO_{2peak} and 80% VO_{2peak} in steady-state similar to the ACE+FES-LCE protocol.

3.3.3 Physiological measurements and techniques

3.3.3.1 Heart rate and oxygen uptake

Heart rate and cardiorespiratory parameters were measured continuously breath-by-breath by open-circuit spirometry with a metabolic gas analysis system at rest and during the submaximal and maximal effort assessments. The metabolic gas analysis system (Medical Graphics CPX; Medical Graphics Corp, St. Paul, USA) was calibrated before each test. Heart rate (HR), and oxygen uptake (VO_2), carbon dioxide production (VCO_2), expired ventilation (V_E) and respiratory exchange ratio (RER) were smoothed with a three breath rolling average. Subsequently, all measures were averaged over 15-s periods during the third to fourth minute of rest and during the last minute of maximal exercise to derive the resting VO_2, and VO_{2peak} during maximal effort.

3.3.3.2 Cardiac output and stroke volume

Indices of cardiovascular performance during submaximal-state exercise at 40%, 60% and 80% of mode-specific VO_{2peak} comprised of left ventricular stroke volume (SV) and cardiac output (Q). These were determined noninvasively via carbon dioxide (CO_2) rebreathing as described by Collier (Collier, 1956). The subjects breathed from an anaesthetic bag filled with a mixture of approximately 10% carbon dioxide in oxygen. The volume in the bag was fixed at 1.5 times the mean tidal volume of the preceding respirations. The CO_2 rebreathing equilibrium method and calculations of heart rate and stroke volume were performed using the software integrated into the gas analysis system (Medical Graphics CPX metabolic cart). Arteriovenous oxygen difference (Ca-Cv)O_2 was calculated via the Fick principle from Q and VO_2.

3.3.3.3 Lactate

Blood lactates were obtained from finger prick capillary samples before and within 2 minutes after maximal and submaximal tests for the determination of lactate responses (Hooker et al., 1995). Samples were taken at rest and after cessation of exercise. Lactate measurements were made via a portable lactate analyser (Accutrend, Roche Diagnostics, Basel, Switzerland).

3.3.3.4 Power output

Power outputs (PO) during submaximal and maximal tests were recorded from the power output obtained during the last minute of exercise during all four tests modalities. The recorded ACE PO was based on the set workload on the arm ergometer. The PO obtained during the FES-LCE was recorded from a computer programme which was linked to the leg cycle ergometer (Fornusek et al., 2004) and the total PO from the ACE+LCE were derived from the sum of PO of the ACE and FES-LCE. The PO from HYBRID (commercially-available Berkelbike tricycle) was recorded from the software that ran the commercial cycle trainer (Tacx i-Magic) and was a summation of both the arm and leg power outputs. ACE, FES-LCE and HYBRID were calibrated according to manufacturer's instructions before the study was commenced.

3.3.4 Data analysis

Differences of outcome measures obtained during maximal and submaximal exercise amongst the four exercise modalities (i.e. ACE, FES-LCE, ACE+FES-LCE and HYBRID) were contrasted by one-way analysis of variance. For all variables, where there was a significant main effect for exercise modality, a posteriori analyses were performed using Tukey B tests (two-tailed). All statistical analyses were performed using the SPSS 18 statistical package. Data are presented as mean ± standard error (SE), and the level of statistical significance was set to the 95% confidence limit ($p<0.05$).

3.4 Results

3.4.1 Maximal tests

All subjects completed all maximal-effort exercise tests. During maximal effort, there were significant differences in peak absolute and relative oxygen uptakes, expired ventilation, heart rate, lactate concentration and power output between the four modalities. Tukey B post-hoc analyses further revealed that absolute ($ml \cdot min^{-1}$) and relative peak oxygen uptakes ($ml \cdot kg \cdot min^{-1}$), expired ventilation, heart rate and power output were significantly lower during FES-LCE compared to the other exercise modes (Figure 3.1). Power outputs were significantly higher during ACE+FES-LCE compared to ACE only and HYBRID, and lactate concentrations significantly higher during ACE+FES-LCE and HYBRID compared to ACE and FES-LCE (Table 3.1).

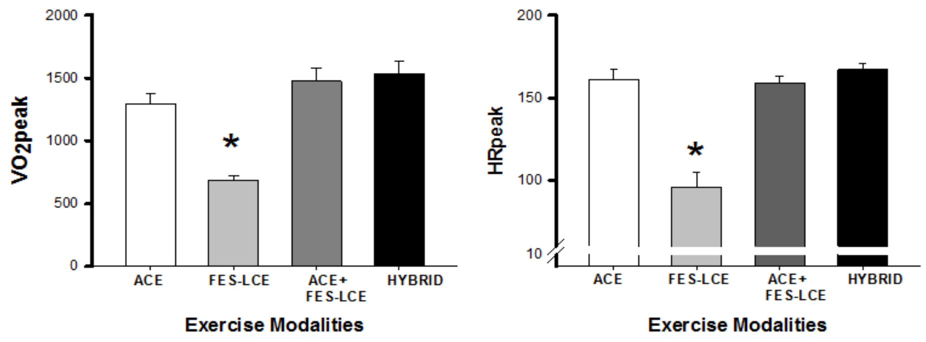

Figure 3.1 Peak oxygen uptake ($ml \cdot min^{-1}$) and peak heart rate ($b \cdot min^{-1}$) during maximal tests across all test modalities: ACE, FES-LCE, ACE+FES-LCE and HYBRID. * denotes $p<0.05$ compared to ACE, ACE+FES-LCE and HYBRID. Abbreviations: ACE = arm crank ergometer; FES-LCE = functional electrical stimulation-leg cycle ergometer; VO_{2peak} = peak oxygen uptake; HR_{peak} = peak heart rate

Table 3.1 Peak exercise responses during arm versus leg exercise

	ACE	FES-LCE	ACE+FES-LCE	HYBRID
PO (W)	74.4 ± 7.5	26.4 ± 3.3*	100.7 ± 8.3 †	75.6 ± 5.0
VO_2 ($ml \cdot kg^{-1} \cdot min^{-1}$)	18.4 ± 1.7	9.6 ± 0.9*	20.8 ± 1.7	21.5 ± 1.6
VE ($L \cdot min^{-1}$)	49.4 ± 2.9	26.7 ± 2.2*	63.7 ± 4.6	64.8 ± 6.6
RER	1.36 ± 0.05	1.38 ± 0.06	1.47 ± 0.06	1.35 ± 0.04
Lactate ($mmol \cdot L^{-1}$)	6.3 ± 0.5	5.2 ± 0.5	9.9 ± 0.9 ‡	9.2 ± 0.6‡

Data refer to power output, body mass-adjusted oxygen uptake, expired ventilation, respiratory exchange ratio and lactate concentration during maximal exercise. * denotes $p<0.05$ compared to the other modes, † denotes $p<0.05$ compared to ACE, FES-LCE and HYBRID, ‡ denotes $p<0.05$ compared to ACE and FES-LCE. Data are Mean ± SE. Abbreviations: ACE = arm crank ergometer; FES-LCE = functional electrical stimulation-leg cycle ergometer; VO_2 = oxygen uptake; VE = expired ventilation; RER = respiratory exchange ratio

3.4.2 Submaximal tests

The resting and submaximal cardiorespiratory data during ACE, FES-LCE, ACE+FES-LCE and HYBRID across all exercise intensities are presented in Table 3.2 and Figure

3.2. All nine subjects completed the submaximal tests at exercise intensities of 40%, 60% and 80% mode-specific VO_2peak, except for one individual wherein equipment failure prevented measurement at 80% HYBRID VO_2peak. Power output for exercise intensities was determined from the mode-specific VO_2 peak, ie. 40%, 60% and 80% of each modality's highest VO_2 during maximal effort.

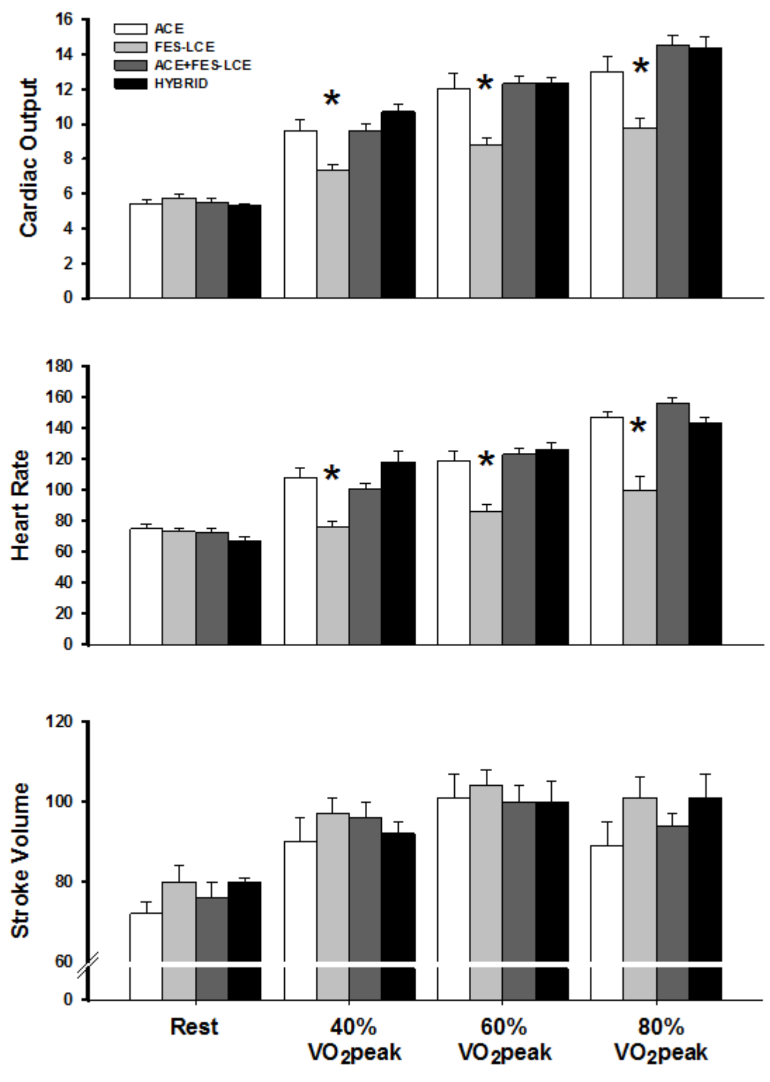

Figure 3.2 Cardiovascular responses during ACE, FES-LCE, ACE+FES-LCE and HYBRID submaximal exercise at different intensities (rest, 40%, 60%, 80% mode-specific VO_{2peak}). Data are presented as mean ± SE for HR ($b \cdot min^{-1}$), SV ($ml \cdot b^{-1}$) and Q ($l \cdot min^{-1}$). * denotes $p<0.05$ compared to ACE, ACE+FES-LCE and HYBRID. Abbreviations: ACE = arm crank ergometer; FES-LCE = functional electrical stimulation-leg cycle ergometer; VO_{2peak} = peak oxygen uptake

Table 3.2 Cardiovascular data during submaximal exercise

Exercise intensity	40% VO_2peak	60% VO_2peak	80% VO_2peak
PO (W)			
ACE	20.1 ± 3.4	37.2 ± 4.9	56.7 ± 6.2
FES-LCE	6.7 ± 0.4*	13.9 ± 1.5*	21.4 ± 2.3*
ACE+FES-LCE	28.2 ± 3.1	49.9 ± 4.9	74.1 ± 5.7‡
HYBRID	20.0 ± 2.9	37.8 ± 2.8	54.4 ± 3.8
VO_2 ($L{\cdot}min^{-1}$)			
ACE	702.1 ± 37.9	889.1 ± 54.9†	1165.6 ± 69.9†
FES-LCE	411.3 ± 35.3*	488.4 ± 30.6*	600.0 ± 45.6*
ACE+FES-LCE	819.4 ± 30.8	1082.1 ± 22.7	1411.6 ± 47.1
HYBRID	912.6 ± 67.8	1210.8 ± 49.3	1392.0 ± 60.3
$(Ca\text{-}Cv)VO_2$ ($ml{\cdot}100min^{-1}$)			
ACE	7.4 ± 0.3	7.5 ± 0.3	19.0 ± 10.0
FES-LCE	5.6 ± 0.4*	5.6 ± 0.4*	6.1 ± 0.3
ACE+FES-LCE	8.6 ± 0.4	8.9 ± 0.3	9.7 ± 0.3
HYBRID	8.4 ± 0.5	9.8 ± 0.3	9.4 ± 0.8
Lactate ($mmol{\cdot}L^{-1}$)			
ACE	2.8 ± 0.2	3.7 ± 0.3	5.7 ± 0.5
FES-LCE	3.4 ± 0.27	4.7 ± 0.4	5.7 ± 0.5
ACE+FES-LCE	3.5 ± 0.3	4.9 ± 0.6	7.4 ± 0.8§
HYBRID	4.4 ± 0.9	5.5 ± 0.9	8.3 ± 0.5§

Data refer to power output, absolute oxygen uptake, expired ventilation, arterio-venous O_2 differences and lactate concentration during submaximal exercise at rest, 40%, 60% and 80% mode-specific VO_2peak . * denotes $p<0.05$ compared to the other modes † denotes $p<0.05$ compared to ACE+FES-LCE and HYBRID ‡ denotes $p<0.05$ compared to ACE and HYBRID § denotes $p<0.05$ compared to ACE and LCE. Data are presented as Mean ± SE. Abbreviations: ACE = arm crank ergometer; FES-LCE = functional electrical stimulation-leg cycle ergometer; PO; power outputVO_2 = oxygen uptake; (Ca-Cv)VO_2 = arterio-venous oxygen extractions.

At 40% VO_2peak, oxygen uptake, heart rate, cardiac output and arterio-venous O_2 differences were significantly lower during FES-LCE than for all the other exercise modalities. ACE elicited 70% greater VO_2 than FES-LCE; ACE+FES-LCE and HYBRID elicited 99% and 122% greater VO_2 than FES-LCE, respectively. ACE evoked a 42% higher HR than FES-LCE; ACE+FES-LCE and HYBRID elicited 33% and 55% higher HR, respectively, compared to FES-LCE. Q was higher by 31% during

ACE and ACE+FES-LCE and 46% greater during HYBRID compared to legs-only exercise. Comparing arm and leg exercise to arms alone, ACE+FES-LCE elicited 17% higher VO_2 and HYBRID exercise elicited 30% greater VO_2.

At 60% VO_2peak, oxygen uptake, heart rate, cardiac output and arterio-venous O_2 differences were significantly lower during FES-LCE than for all the other exercise modalities. Oxygen uptake was also significantly higher during ACE+FES-LCE and HYBRID than ACE alone. ACE elicited 82% higher VO_2 than FES-LCE; ACE+FES-LCE and HYBRID elicited 122% and 148% higher VO_2 than FES-LCE, respectively. ACE evoked a 19% higher HR than FES-LCE, and ACE+FES-LCE and HYBRID elicited 23% and 26% higher HR than legs-only exercise. Q was higher by 36% during ACE and greater by 40% during ACE+FES-LCE and HYBRID. Comparing arm and leg exercise to arms alone, ACE+FES-LCE elicited 22% higher VO_2 and HYBRID exercise elicited 36% greater VO_2.

At 80% VO_2peak, oxygen uptake, heart rate and cardiac output were significantly lower during FES-LCE than for all the other exercise modalities. Oxygen uptake was also significantly higher during ACE+FES-LCE and HYBRID than ACE alone. ACE elicited 94% higher VO_2 than FES-LCE; ACE+FES-LCE and HYBRID evoked 135% and 132% higher VO_2 than FES-LCE, respectively. ACE resulted in 47% higher HR than FES-LCE, and ACE+FES-LCE and HYBRID evoked 56% and 43% higher HR than legs-only exercise. Q was greater by 33% during ACE and 49% during ACE+FES-LCE and 47% during HYBRID exercise. Comparing arm and leg exercise to arms alone, ACE+FES-LCE elicited 21% higher VO_2 and the HYBRID exercise elicited 19% higher VO_2. ACE+FES-LCE elicited 16% higher Q and the HYBRID exercise elicited

10% higher Q. ACE+FES-LCE evoked a 6% higher HR, but the HYBRID exercise did not evoke a higher HR response.

There were no significant differences in stroke volume amongst any exercise modality from 40% - 80% of mode-specific VO_2peak. However we observed at 40% exercise intensity during FES-LCE, that there was 8.3% increase in SV compared to ACE, and at 80% VO_2peak a 13.3% increase in SV compared to ACE.

3.5 Discussion

This study compared the acute cardiorespiratory responses during maximal exercise in people with SCI performing four types of exercise involving arm and legs: ACE, FES-LCE, ACE+FES-LCE (2 separate pieces of equipment used concurrently) and a commercially-available arm and leg hybrid FES tricycle. Based on the peak exercise responses in the maximal exercise testing, we then compared the metabolic and cardiovascular responses during submaximal exercise at 40%, 60% and 80% of mode-specific VO_2peak in all four exercises.

3.5.1 Cardiorespiratory responses during maximal exercise

The results from this study demonstrated lower oxygen uptakes and heart rates during FES-LCE compared to ACE or arm and leg exercise (ACE+FES-LCE and HYBRID). This finding agreed with previous studies that have shown lower peak oxygen uptakes during FES-leg cycling than other type of exercise (Mutton et al., 1997b; Raymond et al., 1999; Verellen et al., 2007). A very early study conducted in the 1980's suggested that ACE alone might be less effective than lower limb exercise for health and fitness promotion in the SCI population due to the relatively small muscle mass in the upper limbs resulting in lower stroke volumes and cardiac outputs (Glaser, 1989). The current investigation highlighted that leg exercise alone is not always superior to arm effort, even when the muscle mass of the legs exceeds that at the arms in SCI individual. Indeed, just because the paralyzed leg musculature can be artificially activated by FES is not evidence that the metabolism is markedly elevated sufficiently to promote enhanced cardiorespiratory fitness. The combination of ACE and FES-LCE, termed "FES-hybrid" exercise, has shown significantly higher peak oxygen uptake, heart rate, cardiac output and stroke volume than arm-only or legs-only exercise (Muraki et al., 1996; Mutton et al., 1997b; Raymond et al., 1999). Findings from the current study revealed 14% - 18% higher peak oxygen uptake during maximal hybrid exercise compared to arm exercise alone. This was likely due to the recruitment of a larger muscle mass with the addition of lower limb FES-evoked cycling to arm exercise. Our findings agreed with Verellen and colleagues (Verellen et al., 2007), in confirming a significantly lower VO_2 peak attained during FES cycling, compared to ACE or FES hybrid exercises (arm+leg cycling and rowing), without much apparent difference between the latter two.

In this study, FES-LCE did not result in the attainment of "centrally-limited" maximal heart rate, since the highest HR observed, was at the time when the electrically stimulated muscles had become fatigued. Consistent with previous studies (Krauss et al., 1993a; Mutton et al., 1997b; Raymond et al., 1999). We did not observe any differences of peak heart rate responses between ACE and ACE+FES-LCE or HYBRID. These findings contrasted with those of Hooker et al. (Hooker et al., 1992a) who observed exercise heart rates during ACE+FES-LCE to be significantly higher than ACE alone. These differences may be explained by a different subject population, since Hooker investigated responses in tetraplegic subjects whereby an increase in heart rate during exercise was driven by predominantly parasympathetic withdrawal (Hooker et al., 1992a). This is in comparison to the current study, where participants were either paraplegics with spinal lesions below T4, or they possessed "incomplete" spinal lesions (ASIA B or C). Raymond and colleagues (Raymond, Davis, van Der Plas, Groeller, & Simcox, 2000) have proposed that FES-LCE lacks a "central command" component of leg exercise and also lacks complete skeletal muscle afferent feedback due to the spinal cord lesion. Thus, the underlying mechanisms for sympathetically-induced exercise cardioacceleration driving such exercise would be blunted or lacking, resulting in the low peak heart rates observed herein.

The RER values in the current study were all above 1.10, indicating maximal effort. However, despite achieving maximal mode-specific effort, the lactate concentration was significantly higher after hybrid exercise compared to ACE alone or FES-LCE. Clearly, the larger muscle mass engendered by arm plus leg exercise and possibly improved circulation, at a maximal intensity resulted in higher lactate production than by arms or legs alone.

3.5.2 Cardiorespiratory responses during submaximal exercise

It is useful to investigate submaximal cardiorespiratory exercise responses since these represent an intensity that can be sustained over prolonged periods of time, and which might represent "real world" utility to the SCI individual undertaking fitness training using arms or legs.

During submaximal exercise, the power output was predetermined based on the results from maximal exercise assessments (i.e. the corresponding mode-specific workload at 40%, 60% and 80% of PO_{peak}). Interestingly, we observed that the VO_2 achieved at the different submaximal intensities performed at the predetermined power outputs were higher than the predicted VO_2 for those intensities. This was attributed to the exercise protocol, whereby the incremental workload (for the given exercise intensity) was ramped up within the first 3 minutes of exercise prior to steady state, as compared to the gradual increment over 8 – 12 minutes during the maximal effort tests. The sudden increase in dynamic exercise had possibly resulted in the quick rise in oxygen uptake (Fletcher et al., 2001) as documented in this study.

In a similar way to maximal exercise, the submaximal VO_2 during FES-LCE was significantly lower than all other exercise modalities from 40% to 80% VO_2peak. Further analysis revealed there were also significant differences in the oxygen uptake between both types of arm and leg exercise compared to arm cranking alone at the highest exercise intensity (i.e. 80% VO_2peak). During steady-state exercise within the 40% to 80% VO_2peak range, ACE elicited up to 90%, the ACE+FES-LCE up to 135% and the hybrid bike up to 150% higher VO_2 than FES-LCE. The ACE+FES-LCE elicited up to 20% and the hybrid bike up to 40% higher VO_2 than ACE. These findings agreed with earlier studies that examined cardiorespiratory responses during FES-hybrid exercise (Barstow et al., 2000; Mutton et al., 1997b; Verellen et al., 2007). The addition of arm exercise to FES-LCE clearly elicits a greater whole-body oxygen uptake supporting the view that hybrid exercise promotes better aerobic fitness potential.

This study also suggested that FES-LCE produced a larger submaximal stroke volume compared to ACE, ACE+FES-LCE or HYBRID by 3% to 13%. This finding however did not achieve statistical significance, although it was obvious by visual inspection of the data (Figure 2). Davis and colleagues (Davis et al., 1990) and Raymond et al. (Raymond et al., 1999) demonstrated significant increases of stroke volume when FES leg exercise was superimposed on ACE. Raymond and co-worker attributed this to an augmented venous return, rather than increased sympathetic neural drive augmenting cardiac contractility, as there was no simultaneous increase of heart rate during FES-leg cycling (Raymond et al., 1999).

In the current study, the heart rate responses during steady-state were significantly lower during FES-LCE across all exercise intensities compared to the other modes of exercise. In addition, there was no significant difference of steady-state heart rate between ACE and the combined arm and leg exercise modes. Only two previous studies that investigated heart rate response during arms exercise, FES leg exercise and hybrid exercise have suggested a lack of difference in steady state heart rates between ACE and hybrid exercise (Davis et al., 1990; Raymond et al., 1997). Interestingly, in one of these, Raymond and colleagues (Raymond et al., 1997) noted significantly lower HR responses during combined arm and leg exercise compared to arm cranking exercise alone, and they concluded that combined arm and leg exercise reduced cardiac stress for a given oxygen uptake. In contrast, Hooker et al (Hooker et al., 1992a) observed that hybrid exercise elicited significantly higher heart rates (up to 33%) compared to ACE or FES-LCE. In that early study, the authors investigated tetraplegic subjects and attributed their findings to a diminished vagal tone in the absence of sympathetic-evoked cardioacceleration.

Cardiac output (Q) during FES-LCE was significantly lower than all other exercise modalities, across the range of effort intensities. There was no significant difference however in the Q between ACE and ACE+FES-LCE at all exercise intensities. During steady-state exercise within the 40% to 80% VO_2peak range, ACE elicited up to 36%

and ACE+FES-LCE and HYBRID up to 50% higher Q than FES-LCE. The ACE+FES-LCE and HYBRID elicited 10% higher Q than ACE.

3.5.3 Cardiorespiratory responses during hybrid FES cycling

Some studies have noted a lower cardiac output during maximal or submaximal arm exercise in paraplegic individuals compared to able-bodied subjects. This has been due to a greater increase in heart rate in the paraplegic individuals, which was largely responsible for their increase in cardiac output while the stroke volume was not significantly altered (Hjeltnes, 1977; Jehl et al., 1991; Phillips & Burkett, 1995). Arm exercise alone may not be capable of stressing the cardiovascular system for a sustained period of time to enable a beneficial training effect to occur. Active lower limb exercises in spinal cord injured paralyzed limbs via electrical stimulation enable improvement of central and peripheral circulation by activation of venous muscle pumps in the lower limbs. However electrical stimulation of the lower limbs alone does not result in substantial elevation of oxygen uptake or cardiac output (Hooker et al., 1992b). As demonstrated in this study, combined arm and leg exercises result in a higher cardiac output with no significant difference in heart rate responses compared to arm exercise alone. Davis and co-workers (Davis et al., 1990) suggested that elevated central haemodynamic responses during submaximal hybrid exercise may make blood more available to the working upper body musculature for improved exercise performance.

There is still sparse literature on the acute cardiovascular responses during hybrid FES cycling in individuals with traumatic SCI, and the findings of heart rate changes corresponding to increases in oxygen consumption and cardiac output have been conflicting. This perhaps can be attributed to the difference in exercise testing protocols, electrical stimulation procedures, the different subject profile whether high paraplegics or low paraplegics or tetraplegics which can all influence the outcomes of cardiovascular and cardiorespiratory responses in the maximal and submaximal exercise testing.

The current study has provided insights into the cardiovascular and metabolic responses during different exercise modalities by measuring cardiac output, stroke volume (Figure 2) and arteriovenous oxygen extractions during arm, FES-leg or arm plus leg exercise in a SCI cohort (Table 2). Taken together, these variables clearly showed that lower submaximal exercise power outputs during FES leg cycling exercise could be seen as the end point in a chain of ablated underlying physiological variables. During steady-state FES-LCE from 40%-80% of mode-specific VO_2peak, lower heart rates resulted in reduced cardiac outputs, and this played a role in lower submaximal oxygen consumptions. Even a slightly greater stroke volume during FES-LCE could not compensate for a ‘lower heart rate on cardiac output’ effect. However in addition, lower whole body arteriovenous oxygen extractions also contributed to lower VO_2 during legs-only exercise. In contrast, when voluntary exercise using musculature above the spinal cord lesion was added (e.g. ACE+FES-LCE, HYBRID) these differences of physiological responses were eliminated. The “real world” utility of these findings to the SCI individual undertaking fitness training using arms or legs is that legs-only training may not always provide sufficient intensity for promotion of whole body aerobic fitness. Conversely, some component of upper body exercise may be needed to achieve sufficient intensity to increase aerobic fitness for cardiovascular health in this population.

3.6 Conclusion

This study demonstrated that the cardiorespiratory demands during submaximal ACE+FES-LCE were higher than in FES-LCE in all exercise intensities. These findings suggest that hybrid-FES training within the submaximal exercise intensities may lead to greater gains in cardiovascular fitness than arm exercise training alone.

Chapter Four

Exercise responses during outdoor versus virtual reality indoor Arm+FES-leg cycling in individuals with spinal cord injury

4.1 Abstract

Purpose: This study compared physiological and perceptual-psychological responses of 30-min submaximal exercise during outdoor hybrid cycling versus virtual reality (VR)-enhanced indoor hybrid cycling in persons with spinal cord injury (SCI).

Methods: Eight individuals with chronic thoracic-lesion SCI performed voluntary arm and FES-assisted leg cycling on a commercial hybrid recumbent tricycle. Exercise sessions were conducted outdoors and indoors incorporating VR technology whereby the outdoor environment was simulated on a large flat screen monitor in a darkened room. Electrical stimulation was applied bilaterally to the quadriceps, hamstrings and glutei muscle groups. Oxygen uptake (VO_2), heart rate, energy expenditures and Ratings of Perceived Exertion (RPE) were measured over a 30-min outdoor test course that was VR-simulated indoors. Arm and leg activity counts were derived from tri-axial accelerometers affixed to the wrist and ankle. Immediately after exercise, subjects were asked to complete the Exercise-induced Feeling Inventory, the Activation-Deactivation Adjective Checklist and the Quebec User Evaluation of Assistive Technology questionnaires to document their perceptual-psychological responses during each exercise mode.

Results: During outdoor cycling, mean 30-min VO_2 was 1255 ± 62 ml•min^{-1} compared to 1316 ± 39 ml•min^{-1} for indoor VR exercise. The outdoor cycling mean heart rate was 128 ± 4 b•min^{-1} compared to 125 ± 4 b•min^{-1} during VR exercise. ANOVA revealed that there was no significant differences ($p>0.05$) between indoor and outdoor cardiorespiratory or RPE responses. Arm and leg activity counts during VR-assisted hybrid FES cycling indoors were significantly higher than outdoor cycling; 42% greater for the arms and 23% higher for the legs ($p<0.05$). No differences were observed for

exercise effort or perceptual-psychological responses during VR-enhanced indoor cycling and outdoor cycling.

Conclusion: This study concluded that VR-enhanced hybrid indoor cycling evoked no different cardiorespiratory or perceptual-psychological responses than outdoor arm+leg cycling. Nevertheless, limb activity counts and power outputs were higher during the indoor cycling probably due to user-adjusted gearing, steering and cruising techniques during outdoor effort. Combining FES and VR technology may provide new opportunities for physical activity promotion or exercise rehabilitation in the SCI population, since these modes have similar exercise 'dose-potency' and self-perceived effort.

4.2 Introduction

4.2.1 Arm+FES-leg cycling in individuals with spinal cord injury

Persons with spinal cord injury (SCI) are at risk of developing many SCI-related complications and negative secondary sequelae. In addition, the enforced sedentary lifestyle as a result of wheelchair confinement, environmental barriers and on-going psychosocial issues may further complicate the consequences of SCI leading to poor physical fitness and health outcomes (Tremblay et al., 2010). There is good evidence that exercise is effective for improving physical fitness and health in the SCI population (Jacobs & Nash, 2004; Nash, 2005; Washburn & Figoni, 1998a). Technological advancements have allowed functional electrical stimulation (FES) to enable leg exercise for persons with SCI. FES-assisted exercise can be deployed as static muscle contractions, dynamic knee extensions, rhythmic cycling exercise or upright stepping (Hettinga & Andrews, 2008a; Nightingale, Raymond, Middleton, Crosbie, & Davis, 2007; Ragnarsson, 2008). Previous studies have demonstrated greater oxygen uptake, cardiorespiratory demands and enhanced venous return when FES leg cycling is combined with arm exercise (Davis et al., 1990; Hasnan et al., 2013; Raymond et al., 1999). This arm+FES-leg “hybrid” exercise results in increased activation of muscle mass, augmentation of sympathetic outflow, reduced venous pooling in the legs, higher cardiac outputs and elevated oxygen uptakes, thereby providing improved whole body exercise ’dose-potency’ (Hettinga & Andrews, 2008a; Verellen et al., 2007). In recent years, FES-integrated hybrid recumbent tricycles that can be used indoors and outdoors have become commercially available. Exercise training using these hybrid FES-cycles has resulted in improvements of physical fitness after only four weeks of training (Heesterbeek et al., 2005).

High intensity and high volume exercise programmes often provide superior health and fitness benefits, but might cause compliance issues in some users. Hettinga and Andrews suggested some strategies to simulate training compliance which includes virtual reality (VR) exercise (Hettinga & Andrews, 2008a). However, there is still limited evidence about the potential for FES-exercise combined with VR technology to produce aerobic fitness benefits.

4.2.2 Virtual reality technology in rehabilitation

VR technologies have begun to be used as rehabilitation strategies in recent years. The rationale is based on a number of unique attributes of this technology, such as enabling safe and ecologically valid environments, control of task-specific level of performance and the provision of enjoyable and motivating experiences to the user (Riva et al., 1999; Schultheis & Rizzo, 2001). In VR, the focus is shifted from the person's efforts in producing a movement or completing a task to that of interacting within a virtual environment. Virtual environments are usually experienced with the aid of special hardware and software for input and output. Visual information is often displayed using head-mounted displays, projection systems or large flat screen monitors. In addition to specialized hardware, compatible computer software is needed to link perceptual inputs with user performance (Weiss & Katz, 2004). One area of interest is VR-assisted exercise, whereby VR-enhanced exercises involving visual inputs with motion-tracking enables the individual to interact within the virtual environment and provide a sense of presence and positive involvement. Chuang and colleagues (Chuang et al., 2006) investigated the effect of a VR-enhanced exercise protocol after coronary artery bypass graft surgery, and observed that incorporating a VR environment into cardiac rehabilitation programs accelerated recovery of patients with cardiovascular impairment. In an earlier study, Chuang and colleagues (Chuang et al., 2003) found the maintenance of endurance, the increase in target intensity and total energy expenditure in exercise programmes could be assisted by introducing VR technology. In the SCI population, Chen and co-workers (Chen et al., 2009) investigated the effect of VR rehabilitation on the psychology of 30 patients. Their experimental group performed a researcher-designed rehabilitation therapy program using a VR-based exercise bike, while the control group underwent the same therapy without VR. The researchers observed that a VR-based rehabilitation programme could ease patients' tension and induce calm.

4.2.3 Exercise environment

Currently there is an increasing trend for people to undertake outdoor physical activity and exercise. Anecdotal evidence from persons with SCI suggests that nature experiences and outdoor pursuits are valued ingredients in a rehabilitation programme (Beringer, 2004). However there is a paucity of evidence directly comparing the outcomes during indoor versus outdoor exercise in terms of physiological or psychological responses after SCI. A literature review by Beringer (Beringer, 2004) revealed a gap of empirical research in this area for the SCI population.

This project sought to compare the acute exercise responses and the perceptual-psychological perceived experiences between outdoor hybrid-FES-cycling and indoor VR-enhanced hybrid FES-cycling in persons with SCI.

4.3 Methods

4.3.1 Participants

Eight male subjects (aged 49.9 ± 5.5 years, stature 1.75 ± 0.02 m, body mass 81.1 ± 5.8, time since injury 9.1 ± 1.5 years) with traumatic spinal cord injury T4-T12 ASIA A, B and C (with intact lumbosacral LMN and good hand function), volunteered to participate in this study. All subjects underwent full medical screening which included a physical and neurological examination, a 12-lead resting ECG, resting blood pressure and lower limb radiographs. The subjects were healthy, neurologically stable and had at least six weeks of previous experience with FES cycling exercise. This study was approved by the Human Research Ethics Committee of the University of Sydney (Ref N. 01-2010/12385) and all participants underwent written informed consent.

4.3.2 Design

All subjects performed indoor and outdoor cycling on a commercially available arm and FES-leg (hybrid) FES tricycle (Berkelbike, Berkelbike BV, Netherlands), which incorporated an in-built FES system to recruit leg musculature. The Berkelbike is a semi-recumbent tricycle with FES-evoked leg cycling and arm cranking modalities for over ground propulsion (Heesterbeek et al., 2005). Subjects regulated their muscle stimulation through the FES system independently to each muscle group via amplitude control, and they could also choose a user-preferred chain-rim gearing for different terrains. The maximum stimulation intensity was 150 mA at a frequency of 35Hz. The hybrid tricycle could be deployed for both indoor or outdoor arm+FES-assisted leg exercise. When used indoors it was mounted on a stationary cycle resistance trainer (Tacx i-Magic, Tacx BV, Netherlands) that was connected to a computer running commercial software for simulated cycling viewed on a large flat screen monitor.

Prior to the FES cycling, gel-backed self-adhesive surface electrodes were placed over the bellies of the quadriceps, hamstrings and glutei muscle groups. Electrode placement was kept consistent by measurements to key anatomical landmarks ensuring muscle group recruitment was similar between trials. Subject preparation and the experimental set-up were all performed by the author to maintain consistency. The electrodes were held securely in place by thigh stockings to prevent slippage. Following electrode placement, the subjects transferred onto the hybrid tricycle and had their feet and legs strapped to the pedals and held in position by customised carbon-fibre leg supports for lower-limb stability thereby minimizing leg movements in undesired directions.

4.3.2.1 Outdoor FES cycling

The cycling track consisted of paved concrete paths and tarred track around the Faculty of Health Sciences, University of Sydney campus grounds. The complete track was 1260.4 meters with elevation change of 19.4 m (+13.37m, -6.07m), requiring both left-hand and right-hand turns.

4.3.2.2 Virtual reality indoor cycling

Indoor cycling was performed on the same hybrid FES tricycle mounted onto a Tacx stationary cycle trainer. The hybrid FES tricycle and the cycle trainer were connected to a notebook PC and a 150cm flat screen full 1080p plasma television to enable virtual-reality (VR) enhanced cycling. Flat-screen technology was chosen, as it required no sensors, head mounted displays or other equipment to be attached to the subject. This enabled unrestricted movement that was deemed necessary for the large body motions elicited during arm and leg cycling. No individuals reported nausea or other symptoms of cybersickness sometimes associated with VR technologies (Sveistrup et al., 2004). The virtual environment software (Tacx i-Magic VR Trainer) was programmed to simulate the same outdoor cycling track so subjects cycled over the same virtual test course. The outdoor cycling track had been previously videotaped using a 1080p high-definition video camcorder and the track properties (distance and elevation) were recorded via a GPS unit (Garmin Edge 705, U.S.A). These data along with the video were professionally converted into virtual reality programme compatible with the Tacx i-Magic software.

4.3.3 Protocol

Following two sessions of familiarisation outdoors, each individual underwent two trials each of indoor and outdoor cycling. These were repeated at least one week apart at the same time of the day. Subjects were randomized between conditions of indoor versus outdoor cycling on each test day.

4.3.3.1 Outdoor trial

The subjects were instructed to cycle for 30 minutes (30-min) and complete as many circuits of the 1260m cycling track as they could within that duration. They were encouraged to cycle to their best effort within self-perceived safety limits and to increase their stimulation intensities to the legs within personal tolerance. The primary investigator (author) cycled behind the subject to provide encouragement and advice on terrain safety during turning.

4.3.3.2 Indoor (Virtual Reality) trial

As with the outdoor trial, the subjects were instructed to cycle for 30-min on the stationary tricycle in front of the television and to complete as many circuits of the simulated track as they could within that duration. The subjects were encouraged to cycle to their best effort within safety limits and increase their stimulation intensities, as they deemed necessary. Indoor VR testing was conducted in a quiet darkened room. The monitor was mounted 1.5m from the subjects' open eyes, with 0 deg elevation from eyes to screen centre. The primary investigator stood outside of subjects' field of vision to provide encouragement of best effort.

4.3.4 Measurements and techniques

4.3.4.1 Cycling Performance

During indoor cycling, speed ($m \cdot min^{-1}$), distance (m) and power output (W) were recorded from the software that controlled the hybrid tricycle (Tacx i-Magic). During outdoor cycling, the Garmin GPS system was used to record speed ($m \cdot min^{-1}$), and distance (m) cycled over the 30-min test duration. Unfortunately, power output during outdoor cycling could not be measured with the available measurement techniques.

4.3.4.2 Cardiorespiratory responses

Cardiorespiratory variables and heart rate (HR) were measured continuously breath-by-breath by using the Cosmed K4b^2 portable metabolic system (Cosmed, Italy). The K4b^2 has been accepted to accurately measure oxygen uptake (VO_2) and estimate energy expenditure over a wide range of metabolic rates in adults (McLaughlin, King, Howley, Bassett, & Ainsworth, 2001). The subjects breathed through a rubber face mask (Hans Rudolph Inc., Kansas City, USA), into the portable metabolic system. The system was calibrated before each test according to the manufacturer's instructions. This portable system and the battery pack were attached to the subject's trunk via a snug fitting harness (Abel, Platen, Rojas Vega, Schneider, & Struder, 2008). Breath-by-breath VO_2 was smoothed using a three-step ensemble-average, and then averaged every 15 seconds (Data management software, Cosmed, Rome, Italy).

An index of metabolic stress (Net O_2 cost; $mL \cdot kg^{-1} \cdot min^{-1}$) was calculated from speed, body weight and VO_2, while cardiorespiratory strain (Physical Cost Index, $b \cdot m^{-1}$) was calculated from heart rate and speed.

4.3.4.3 Mechanical efficiencies

Gross mechanical efficiency (ME_G; %) and net mechanical efficiency (ME_N; %) were calculated as a function of power output (described below) and oxygen uptake. These variables were calculated during indoor cycling only using the formulae:

ME_G (%) = (Power Output × 6.12/426.8)/((VO_2 / 1000) × (RER × 1.232+3.815)) ×100

ME_N = (Power Output × 6.12/426.8)/(((VO_2-VO_2rest) / 1000) × (RER×1.232+3.815)) ×100

where

[Power Output (W), 6.12 =kgm × W^{-1}, 426.8= kcal × kgm^{-1},VO_2 (mL•min^{-1}) and RER × 1.232+3.815 is Caloric Equivalent of non-protein RER by linear regression, but when RER>1.0 was taken to be RER =1.0]

4.3.4.4 Limb movements

Two Actigraph GT3x (ActiGraph, Pensacola, USA) tri-axial accelerometers were used for motion analysis of the cycling limbs. A study by Warms and Belza had previously established that actigraphy was suitable as a measurement of physical activity for people with SCI (Warms & Belza, 2004). A GT3x was strapped on the dorsal aspect of the left wrist and ankle of each subject. The activity monitor sampled movement data every second as the sum of the number of "counts" captured at a rate of 33 Hz along the x, y and z axes. The data was ensemble-averaged every 10 to reduce excess noise, and total activity counts over 30-min were collected. Activity counts represented by the GT3x, characterized a combination of limb movements and "vigour" (forces) as measured by the hardware in 0.01664 $g \cdot s^{-1} \cdot count^{-1}$ where each level is considered as one (1) count (Sasaki, John, & Freedson, 2011). By mounting the accelerometers on the wrists and ankles of the subjects during arm and leg (hybrid) cycling both indoors and outdoors, it was possible to collect data on how “active” the arms and legs were throughout the entire duration of the cycling.

4.3.4.5 Psychological measurements

Ratings of perceived exertion (RPE) were requested at 15 and 30 minutes using a Borg Category Ratio 10-point scale (BORG CR 10) during all trials. Grange and colleagues (Grange et al., 2002) had observed that perceived exertion using the Borg category–ratio 10 scale (Borg, 1998) was a useful measure of exercise intensity in individuals with SCI during 45-min wheelchair ergometry in a supervised clinical setting. During the familiarization session, each subject was given instructions on the use of the BORG CR 10. During the trial, subjects were requested their RPE score at 15-min and at 30-min. The answers were hand-signaled as they were breathing through facemasks.

At the end of each cycling trial, the subjects were asked about their cycling experience through face-to-face questionnaire interviews. The Exercise-induced Feeling Inventory (EIFI) developed by Gauvin and Rejeski was used to measure feelings evoked by the 30-min hybrid FES cycling exercise (Gauvin & Rejeski, 1993). The EIFI is a self-report which requires the user to answer on a 5-point scale anchored by 0 = do not feel and 4 = feel very strongly. The EIFI measures “positive engagement”, “revitalization”, “tranquility” and “physical exhaustion” by totaling three-item response scores in four subscales. Gauvin and Rejeski observed that the EIFI was very sensitive to changes in feeling states that occur with exercise, and that the measure was able to detect differences in the social context of different exercise interventions (Gauvin & Rejeski, 1993).

Subjects also completed the Activation-Deactivation Adjective Checklist (Thayer, 1986) (AD-ACL), which is a measure of activation or arousal state after the cooling down period post-exercise in all trials. The AD-ACL is a multidimensional test of various transitory arousal states consisting of 20 items with 4 subscales: energy, tiredness, tension and calmness. The items are rated on a 4-point Likert scale; higher scores reflect greater intensity of mood. In this study, the scores of subscales energy and tension were analysed since they are the best indications of energetic and tense arousal respectively.

4.3.4.6 User satisfaction

The Quebec User Evaluation of Satisfaction with Assistive Technology Questionnaire (QUEST 2.0) (Demers, Weiss-Lambrou, & Ska, 1996) was used to evaluate subjects experience and satisfaction with using the hybrid FES tricycle. The QUEST 2.0 was designed as an outcome measurement instrument to evaluate a person's satisfaction with a wide range of assistive technology. The QUEST 2.0 is a self-administered questionnaire consisting of 12 items rated on a 5-point satisfaction scale. Response ranges from 1 (not satisfied at all) and 5 (very satisfied). The 12 items are subscales of eight assistive device items and four service items. In this study only items within the assistive device items were included i.e. satisfaction with the dimensions, weight, ease of adjusting, safety and security, durability, usability and effectiveness of the assistive device.

4.3.4.7 Virtual reality experience

Finally, subjects' experience using VR assisted hybrid FES cycling was assessed using the Virtual Reality Symptom Questionnaire (VRSQ) (Ames, Wolffsohn, & McBrien, 2005). The VRSQ was developed for use in investigating symptoms that result from VR viewing. It consists of thirteen symptom questions: eight non-ocular (general discomfort, fatigue, boredom, drowsiness, headache, dizziness, difficulty concentrating and nausea) and five ocular (tired eyes, sore/aching eyes, eyestrain, blurred vision and difficulty focusing). The VRSQ was administered during the familiarization session so that subjects were familiar with the questionnaire during the test trials. The questionnaire was administered immediately following cessation of exercise before the symptoms dissipate as it was suggested by Ames and colleagues (Ames et al., 2005) that assessment of symptoms need to occur in the first 5 minute of post viewing.

4.3.5 Data analysis

Differences of outcome measures obtained during outdoor versus VR-assisted indoor hybrid FES cycling were analysed by two-way ANOVA. All statistical analysis was performed using the SPSS 21 statistical package. Data are presented as mean ± standard error (SE), and the level of statistical significance was set to the 95% confidence limit ($p<0.05$).

4.4 Results

Eight subjects completed all indoor and outdoor trials. Analysis of variance revealed that there were no differences between trials (trial 1 versus trial 2) or between conditions (outdoor exercise versus indoor VR-exercise) for most of the cardiorespiratory measurements ($p>0.05$). Where there were differences between exercise modes, but not between trials within modes, the data presented were pooled-data from both trials.

The average oxygen uptake during outdoor cycling was 1255 ± 62 $mL^{\cdot}min^{-1}$and during indoor VR-exercise was 1316 ± 39 $mL^{\cdot}min^{-1}$. The highest oxygen uptake observed during outdoor cycling was 1725 ± 77 mL·min^{-1} and during indoor exercise was 1615 ± 52 mL·min^{-1}. Average heart rate during outdoor cycling was 128 ± 4 b·min^{-1} and during indoor exercise was 125 ± 4 b·min^{-1}. The highest heart rate during outdoor cycling was 153 ± 5 b·min^{-1} and indoor 149 ± 6 b·min^{-1}. There were no significant differences between these oxygen uptakes or heart rates between modes ($p>0.05$).

The VR-assisted hybrid indoor FES cycling revealed a significantly higher activity counts for arms and legs, distance travelled in 30-min and speed compared to outdoor hybrid FES cycling ($p<0.05$). There were also significant differences in net oxygen (O_2) cost and physical cost index between modes. The cycle performance, metabolic stress (Net O_2 cost) and cardiovascular strain (Physical Cost Index) are presented in Table 4.1.

Table 4.1. Cycle performance, mechanical efficiencies, metabolic stress and cardiovascular strain during indoor-VR versus outdoor exercise

	Indoor-VR	Outdoor
Power output (W)*	21.6 ± 1.1	N/A
Distance in 30 min (m)*	6980 ± 236	3826 ± 123
Average velocity (m·min^{-1})	231.3 ± 7.3	105.2 ± 3.9
Gross mechanical efficiency (%)	4.56 ± 1.19	N/A
Net mechanical efficiency (%)	6.04 ± 1.34	N/A
Net O_2 Cost (ml•kg^{-1}•min^{-1})	0.058 ± 0.004	0.125 ± 0.013
Physical Cost Index (b•m^{-1})	0.26 ± 0.024	0.61 ± 0.054

Data are mean ± SE, * denotes $p < 0.05$. N/A denotes not measured.

As revealed in Table 4.1, a greater distance was cycled indoors compared to outdoors – almost twice (1.8 times) the distance over the 30 minutes of cycling. Hybrid tricycle speed was 2.2 times faster during indoor cycling compared to outdoor cycling. Since there were no significant differences of oxygen uptake between the two cycling modalities, the calculated net oxygen cost was significantly higher during outdoor cycling and the calculated physical cost index also significantly higher during outdoor cycling.

Arm, leg and arm+leg activity counts during VR-assisted hybrid FES cycling indoors were significantly greater than observed during outdoor cycling. During indoor cycling the total arm activity was 42% more and leg activity was 23% more than was observed during outdoor cycling (Figure 4.1).

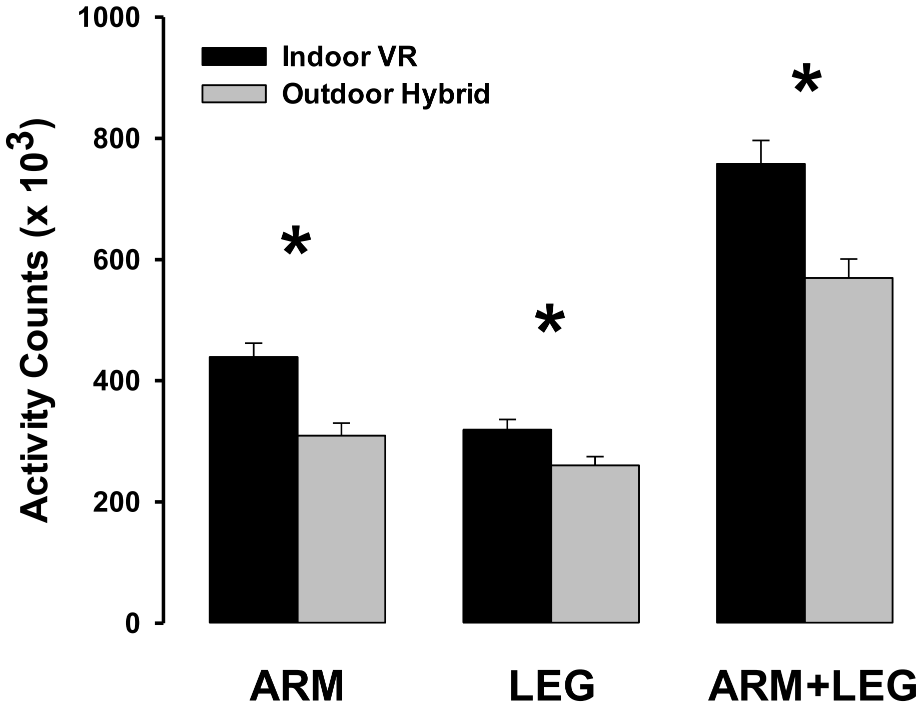

Figure 4.1. Arm and leg activity counts during indoor VR versus outdoor hybrid cycling. Arm and leg activity counts are number of counts ($\times$ 10^3) from Actigraph GT3x tri-axial accelerometers. * denotes $p < 0.05$ indoor versus outdoor. Data are mean ± SE

Despite the initial assumption that outdoor hybrid FES cycling might contribute to superior psychological outcomes than indoor exercise, two-way ANOVA showed no differences in the subscales of the EIFI (positive engagement, revitalization, tranquility and physical exhaustion) and the subscales AD-ACL (energy, tiredness, tension, calmness) between cycling modes. There were also no significant differences in ratings of perceived exertion (RPE) at fifteen minutes and thirty minutes of exercise during both modes. From the QUEST, it was observed that the subjects were satisfied with the hybrid FES tricycle, but there were no differences in satisfaction between modes. The VR-assisted FES cycling did not result in high ocular symptoms assessed from the VRSQ. The total scores for the ocular symptom ranged between 0 to 16 out of a possible score of 30.

4.5 Discussion

This study sought to compare the acute physiological and psychological responses of two exercise conditions i.e. outdoor hybrid FES cycling versus VR-assisted indoor cycling. It was the author's initial assumption that; (i) indoor VR hybrid-cycling might engender greater cardiorespiratory responses than outdoor cycling with greater distances covered at higher cycle velocities, (ii) outdoor hybrid cycling might evoke higher positive feelings and emotions that indoor exercise, and, (iii) arm and leg limb movements would be greater for indoor exercise. The findings of this study did not confirm all of the author's initial expectations, and revealed some interesting features about how SCI users approached the two exercise conditions by manipulating "cruising and steering" and "gearing" of the tricycle.

The participants were requested to self-select their preferred over ground or indoor speed, their choice of chain-rim gearing and adopt 'appropriate' steering strategies outdoors during the 30-min cycling task. The indoor cycling track was simulated from the outdoor course based on previously-recorded HD video and GPS data, wherein the stationary cycle trainer would simulate up-hills and down hills by increasing and decreasing resistance applied to the front wheel, respectively. Additionally, this study compared the limb activity counts as a proxy of arm and leg “movement intensity” over 30-min of cycling.

4.5.1 Cycling performance and limb movements

The expectation of a greater indoor VR-cycling performance over outdoor cycling was borne out in the current study. The cycling speed during indoor cycling was more than twice that of outdoor cycling, and thus covered a greater simulated distance indoors. This could be attributed to a number of casual factors. Indoors, the participants exhibited 42% higher arm movements and 23% greater leg movements as detected by the tri-axial accelerometers (Figure 4.1). What was clearly observed during the experiments was that during indoor cycling the subjects arm-cranked nearly continuously throughout the 30-min duration of the test course. In contrast, during outdoor cycling, the subjects incorporated cruising techniques while going down slopes and careful steering techniques during cornering. This “cruising and steering” effect lessened the number of arm activity counts and leg movements; when the arms were not cranking to cruise and steer the tricycle, the legs did neither (this is a manufacturer’s safety feature of the Berkelbike® tricycle). With less active limb movements developed over 30-min of outdoor cycling, the average velocity was slower (by 126 $m \cdot min^{-1}$) and the distance travelled was much less (by 55%) at approximately half of the estimated average power output. The author speculated that even though all participants were provided with familiarisation sessions, the nature of the undulating terrain of the test course and the nature of the tricycle (i.e. 3 wheels, with a single one to steer from the front) made them more cautious about possible tipping, and they adopted more careful cruising and steering strategies.

4.5.2 Cardiorespiratory responses

Notwithstanding the greater cycling performance indoors, there were few differences of cardiorespiratory responses between conditions. The average oxygen uptake during outdoor cycling (1255 ± 62 $mL \cdot min^{-1}$) and indoor (1316 ± 39 $mL \cdot min^{-1}$) cycling were within the expected range of moderate-intensity exercise, consistent with the observed heart rates (outdoor cycling 128 ± 4 $b \cdot min^{-1}$ and indoor cycling 125 ± 4 $b \cdot min^{-1}$, respectively). The highest heart rates observed during the most strenuous portions of the test course were 16-19% greater than the 30-min average, and the peak VO_2 was 23-37% higher than the average 30-min average oxygen uptake. The average and peak cardiorespiratory data were consistent with previously reported studies that employed submaximal and maximal FES arm and leg cycling exercise (Fornusek & Davis, 2008; Hasnan et al., 2013; Heesterbeek et al., 2005; Hettinga & Andrews, 2008a; Hooker et al., 1992a; Krauss et al., 1993b; Mutton et al., 1997b; Raymond et al., 1999; Raymond et al., 1997).

These findings, in part, reject the initial assumption that VR-indoor hybrid cycling would engender greater cardiorespiratory responses due to a higher cycling performance for that mode. The greater cycling performance for VR-indoor exercise was observed, but expected translation to higher cardiorespiratory responses was not. Therefore, it was suggested than in addition to the “cruising and steering” effects noted outdoors, their choice of chain-rim gearing and possible environmental effects (e.g. wind resistance) could have played a role to equalize the metabolic and heart rate demands between exercise conditions. The subjects were instructed to cycle to their best ability and were allowed to self-select their speed and gear ratio to ensure safety and comfort both indoors and outdoors. So they selected different gearing indoors and outdoors to maintain their metabolic responses within a range perceived as "safe" but "comfortable" (i.e. "moderate" exercise intensity) over 30-min. These findings clearly demonstrated that exercise outcomes in this subject population might not be influenced by the "reality" of exercise modality (i.e. outdoor exercise or VR-assisted indoor exercise), but by self-perceptions of effort that SCI users could control by "gearing" within a moderate-intensity metabolic range that could be sustained over 30-min.

The lack of difference in metabolic and heart rate demands between VR-assisted indoor exercise and outdoor over ground cycling has one positive implication. Either condition may be selected by the individual with SCI if the goal is physical activity for health promotion. For individuals desiring an "outside" experience or whether they may prefer indoor exercise, either is beneficial. For the clinician or therapist who might recommend hybrid cycling either for rehabilitation or fitness training, the selection of optimal condition becomes a matter of client-focused preferences.

4.5.3 FES cycling efficiency

The mechanical efficiencies (ME) observed in this study were low, but similar to findings of some previous studies for FES-leg cycling (Theisen et al., 2002). Previous studies have reported ME_G values as low as 4-6% for FES-evoked cycling (Dufell, 2009; Fornusek & Davis, 2008; Theisen et al., 2002). A low ME was not surprising as the mode of exercise was arm and FES-leg cycling, and it has been previously reported that metabolic efficiencies were lower during arm cranking compared with voluntary leg cycling due to the postural and body stabilization required during arm cranking exercise (Kang et al., 1997; Mayo, 2001). Hunt and colleagues (Hunt, Hosmann, Grob,

& Saengsuwan, 2012) recently reported that FES cycling was approximately half as efficient as volitional cycling and attributed this inefficiency to the crude timing of muscle activation, non-physiological muscle fibre recruitment and the disruption in sensory feedback and vasomotor control in paralyzed spinal cord injured subjects.

4.5.4 Energy cost

The energy cost of physical activity is usually determined by oxygen uptake, which reflects both internal and external work during submaximal exercise. In this study, there was no significant difference of average or highest oxygen uptakes between the two cycling conditions. It was interesting to find that the Net Oxygen Cost and Physical Cost Index were significantly higher during outdoor cycling compared to VR indoor exercise. This outcome could be attributed to the cycling inefficiencies during outdoor exercise previously discussed. Yet another contributing factor could be that the subjects were permitted to self-select speed and gearing i.e. free cycling. Scezi and colleagues (Szecsi, Krause, Krafczyk, Brandt, & Straube, 2007) have found that fixed-gear cycling or forced smooth FES cycling on an outdoor tricycle is superior to free cycling, whereby fixed-gear cycling results in more efficient production of energy and work production.

4.5.5 Perceptual-psychological responses

Anecdotally, it was observed that the subjects seemed more focused and engaged during VR-enhanced indoor cycling which significantly affected the number of cranks turned, resulting in higher arm and leg activity and subsequently greater speed, power output and the distance travelled. However, there were no differences between exercise conditions in the positive engagement subscale of the EIFI (Gauvin & Rejeski, 1993). Nor were there significant differences in the subscale of physical exhaustion of the

EIFI, or between the RPE at 15-min and 30-min of VR-enhanced indoor and outdoor cycling. The RPE at 15 min during outdoor cycling was 5.9 ± 0.4 and during indoor VR-enhanced cycling was 6.3 ± 0.4. These are consistent with the description of exercising hard. At the end of the exercise (i.e. at 30 min), the RPE was 8.1 ± 1.8 during both outdoor cycling and during VR-enhanced indoor cycling, consistent with the feeling of exercising very hard (Borg, 1998). It was interesting to note that these self-perceived ratings of exertion did not match up to the heart rate or oxygen uptake findings, which were generally in the moderate-intensity range for this population. Additionally, even when exercising at a high self-perceived intensity (hard to very hard), the subjects only scored between 6 to 10 points on the 15-point physical exhaustion EIFI subscale (Gauvin & Rejeski, 1993). This study also assessed their arousal state following exercise through the AD-ACL, specifically the subscales energy and tension, and observed no significant differences in post-exercise arousal states between outdoor and VR-enhanced indoor cycling. Chen and co-workers (Chen et al., 2009) used AD-ACL to measure the mood states of SCI subjects who underwent endurance cycling with and without VR and found less tension and increased calmness in the experimental group which underwent VR therapy. As with the findings in this study, they found no differences in the RPE and average heart rate. However they found their subjects who underwent VR therapy could perform for a longer duration, indicating enjoyment and motivation. In the study, the duration of exercise was set to 30-min for both conditions. Only three out of the total eight subjects reported mild visual symptoms with scores between 4.5 to 8 out of possible 30 on the VRSQ.

In the psychological domain, the results of this investigation were not consistent with some previous studies. Pretty and colleagues (Pretty, Peacock, Sellens, & Griffin, 2005) observed that "green" or outdoor exercise could improve mental well-being and physiological health. Ceci and Hassmen (Ceci & Hassmen, 1991) reported greater physiological effort, verified by heart rate and blood lactate when performing exercise outdoors. Notably, these studies were conducted using able-bodied populations and modalities of exercise dissimilar to the current investigation.

4.6 Conclusion

This study concluded that VR-enhanced hybrid indoor cycling produced no different cardiorespiratory responses than outdoor arm+leg cycling. Nevertheless limb movement counts and power output were higher during the indoor cycling probably due to user-adjusted gearing, steering and cruising techniques that were adopted during outdoor exercise. Combining FES technology and virtual reality technology may provide new opportunities for physical activity promotion or exercise rehabilitation in the SCI population.

Chapter Five

A six-week high-intensity virtual-reality exercise programme in individuals with spinal cord injury

5.1 Abstract

Purpose: This study aimed to investigate the effects of high-intensity interval training employing "hybrid" exercise (arm and FES-leg cycling) on aerobic fitness, lipid profiles, glucose tolerance and psychosocial perceptions in persons with chronic spinal cord injury (SCI).

Methods: A quasi-experimental pre-post design was employed for this study. Twelve individuals with chronic thoracic-lesion SCI were recruited. The study intervention was high-intensity (80-90% predicted HRmax) interval cycling using a hybrid FES semi-recumbent tricycle (Berkelbike®) mounted on a stationary cycle trainer Tacx i-Magic VR trainer). The training regimen was either 32 minutes, thrice-weekly for 6 weeks or 48 minutes, twice-weekly for 6 weeks. The hybrid tricycle was connected to a VR simulator, a flat panel LCD monitor via the Tacx i-Magic VR trainer. Computer-controlled electrical stimulation to the lower limbs was applied bilaterally to the quadriceps, hamstrings and glutei muscle groups. The training cadence was self-selected to meet the target training heart rate. The subjects' peak cardiorespiratory responses were assessed on the hybrid tricycle before and following completion of the 6-week training programme. Lipid profiles and oral glucose tolerance were also measured pre- and post-training. Thigh girths measurements were recorded. Ratings of Perceived Exertion (RPE), Exercise-induced Feeling Inventory (EIFI) and Profile of Mood States (POMS) were conducted at baseline and at the end of the final training session.

Results: At the end of the 6-week high-intensity arm+leg interval training program, subjects increased their peak aerobic fitness from 1215 ± 284 $ml \cdot min^{-1}$ to 1404 ± 315 $ml \cdot min^{-1}$ ($p<0.05$). Their body mass-adjusted VO_2 peak also increased from 18.8 ± 3.1

$mL \cdot kg^{-1} \cdot min^{-1}$ to from 21.8 ± 4.0 $mL \cdot kg^{-1} \cdot min^{-1}$ ($p<0.05$). Arm+ leg peak power output during "hybrid" exercise was significantly raised from 50.0 ± 11.3 W to 66.7 ± 16.2 W. Resting heart rate was reduced from 71 ± 17 $b \cdot min^{-1}$ to 68 ± 11 $b \cdot min^{-1}$ ($p<0.05$) but there was no change in peak heart rate. High-density lipoprotein levels improved but other parameters of the lipid profile did not after six weeks training. Although there were decreases in post-training fasting and two-hour gluose levels, the change was not significant. Total thigh volume, derived from thigh girth measurements, revealed a significant increase from 5,866 ± 1848 ml to 6,228 ± 2107 ml. The RPE and the depression, vigor, anger, tension and fatigue subscales of the POMS changed favourably ($p<0.05$). Post-exercise feeling states (positive engagement, revitalization and tranquility) also improved ($p<0.05$).

Conclusion: These results demonstrated that a short six-week high-intensity interval training programme using "hybrid" exercise (arm and FES-leg cycling) is able to improve aerobic fitness, muscle mass, mood and post-exercise feeling states in persons with chronic SCI. The lack of change in their lipid profiles and oral glucose tolerance suggested that six weeks of twice- or thrice-weekly training, even at a high intensity, may be too short to modify these indices of cardiovascular risk in the SCI population.

5.2 Introduction

Survival rates following spinal cord injury (SCI) have improved since the 1970s. These improvements however are seen in the first two years post trauma and not beyond that period (Strauss, Devivo, Paculdo, & Shavelle, 2006). Such improvements arise from better medical care including improved management at the injury scene, augmented emergency care, more efficient transportation to specialised units, and increases in skilled medical, surgical and nursing care in acute care, post-acute care and during rehabilitation. Despite their increased life expectancy since World War II, life expectancy in people with SCI remains lower than the normal population, estimated to be 70 to 90% of normal lifespan (Devivo et al., 1999b; Imai, Kadowaki, & Aizawa, 2004; Soden et al., 2000; Yeo et al., 1998). People with SCI still die at younger ages due to medical complications and secondary conditions.

Garshick and colleagues, in their prospective assessment of mortality from 1994-2000, reported that the risk factors for death are diabetes, heart disease, reduced pulmonary function and smoking-related complications (Garshick et al., 2005). It is clear that higher morbidity in chronic SCI is related to potentially treatable factors. The recognition and treatment of cardiovascular disease, diabetes mellitus and lung disease along with smoking cessation may reduce both morbidity and early mortality in the chronic SCI population.

With longer post-injury survival times, numerous literature have described morbidity from cardiovascular disease, particularly coronary artery disease in people with SCI is higher relative to the ambulatory population and tend to occur earlier (DeVivo, Shewchuk, Stover, Black, & Go, 1992; Garshick et al., 2005; Myers et al., 2007; Phillips et al., 1998). Higher coronary artery disease risk was found in SCI patients with a higher level (tetraplegia) and the completeness of SCI. The prevalence is highest in complete tetraplegia and lowest amongst incomplete paraplegia group. It has also been reported that the prevalence of asymptomatic cardiovascular disease in SCI is between 60-70% (Bauman et al., 1993; Lee, Lu, Lee, Lin, & Ding, 2006). The increased risk of cardiovascular disease is attributed to the fact that risk factors such as abnormal lipid profile (increased total cholesterol, increased LDL, reduced LDL), obesity and diabetes have been shown to be comparatively high among individuals with SCI (Bauman, Adkins, et al., 1999; Demirel et al., 2001; Lee et al., 2005; Myers et al., 2007; Phillips et al., 1998). Additional factors include enforced sedentary lifestyle and reduced physical function due to wheelchair use (Buchholz et al., 2003). It is known that physical inactivity is a major independent risk factor for cardiovascular disease and premature mortality (Warburton et al., 2007; Warburton et al., 2006). Tanhoffer and colleagues have reported low total daily expenditure even in active SCI individuals and inverse relationship is noted between neurological level and total daily expenditure. The authors suggest that leisure time physical activities performed by wheelchair-bound individuals were not effective, and therefore, a more specific approach for prescribing exercise is needed (Tanhoffer, 2011; Tanhoffer, Tanhoffer, Raymond, Hills, & Davis, 2012).

Exercise opportunities for people with SCI are limited by physiological, physical and technical factors (Krauss et al., 1993b). Decreased functional mass, impaired autonomic control of myocardial function and decreased venous return limits training responses (Wheeler et al., 2002). Upper body exercise, such as arm crank ergometer (ACE) and wheelchair propulsion, are commonly prescribed but not as beneficial as lower limb exercise due to the smaller muscle mass (Glaser, 1989). Furthermore it elicits greater cardiorespiratory stresses when compared with similar workloads during leg exercise

(Davis et al., 1990). Earlier studies using functional electrical stimulation cycling exercise have shown improvement in physical conditioning and cardiorespiratory endurance (Davis et al., 1990; Figoni et al., 1991; Pollack et al., 1989; Raymond et al., 1999). However FES leg cycling exercise alone has often resulted in significantly lower submaximal oxygen uptakes compared with arm exercise (Barstow et al., 2000; Hasnan et al., 2013; Raymond et al., 1999). There is good evidence that combining arm exercise and FES leg cycling exercise also known as hybrid FES exercise results in greater oxygen uptake and cardiovascular demands thereby enhancing training effects (Davis et al., 1990; Hasnan et al., 2013; Hooker et al., 1992a; Raymond et al., 1999; Wheeler et al., 2002).

Stefanizzi and Overend concluded in their review that hybrid exercise training appears to hold promise for improvement of cardiovascular fitness in people with SCI (Stefanizzi & Overend, 1998). There is limited data however on training protocols, dose-response and training intensity in order to achieve favourable training effects. Hesteerbeek and colleagues reported that exercise training using FES integrated hybrid recumbent tricycles resulted in improvement of physical fitness after only four weeks (Heesterbeek et al., 2005). Although there has been other hybrid FES exercise training studies measuring outcomes in physical fitness, to date none had investigated the metabolic and psychosocial changes following training (Brurok, Helgerud, Karlsen, Leivseth, & Hoff, 2011; Krauss et al., 1993b; Mutton et al., 1997b).

There is increasing evidence that high-intensity interval training (HIIT) can serve as an alternative to traditional endurance-based training, providing effective physiological adaptations in healthy and clinical populations. HIIT refers to exercise that is characterized by brief, intermittent bursts of vigorous activity, interspersed by periods of rest or low-intensity exercise (Gibala, Little, Macdonald, & Hawley, 2012; Hwang, Wu, & Chou, 2011). HIIT has been shown to improve cardiorespiratory fitness in a range of populations including those with coronary artery disease, congestive heart failure, middle age adults with metabolic syndrome and obese individuals. It has also been shown that the increase in cardiorespiratory fitness after HIIT was superior to moderate-intensity training (Tjonna et al., 2008; Warburton et al., 2005; Wisloff et al., 2007). There is also preliminary evidence from smaller studies that short-term HIIT improved estimated insulin sensitivity in previously sedentary, overweight individuals (Hood, Little, Tarnopolsky, Myslik, & Gibala, 2011; Whyte, Gill, & Cathcart, 2010) and reduction in postprandial glucose excursions in patients with Type 2 DM (Little et al., 2011). The evidence concerning HIIT in the SCI population is sparse. Previous studies have shown that increasing maximum current improved power output and cardiorespiratory response (Glaser, 1989, 1994; Janssen & Pringle, 2008). Janssen and colleagues investigated the effect of an interval training programme involving FES cycling over six weeks whereby the subjects were given bouts of higher electrical stimulation intensity, higher than the "standard" 140-150 mA to 300 mA (Janssen & Pringle, 2008). Janssen and Pringle found that the high-intensity interval program could elicit marked improvements in power output, peak metabolic and cardiorespiratory response and muscle strength in subjects who underwent a total of 18 training sessions of 25 to 30 minute cumulative exercise which included high-intensity bouts of five to ten minutes over six weeks (Janssen & Pringle, 2008). De Groot and colleagues compared the outcome of an 8-week interval arm training protocol between high-intensity (70-80% heart rate reserve (HRR)) and low-intensity (40-50% HRR) training group in six subjects (de Groot et al., 2003). Results from the study indicated improvements in physical capacity and lipid profile following high-intensity training. Brurok and colleagues found that aerobic high-intensity hybrid interval training at 85-

95% of peak Watt was feasible for his participants of six men with ASIA A SCI who showed significant increase in peak stroke volume and peak oxygen uptake (Brurok et al., 2011). There are no known studies that have investigated changes of lipid profile and oral glucose tolerance following "hybrid" HIIT FES training in SCI. Another benefit of HIIT revealed by a more recent study suggests that HIIT is perceived to be more enjoyable than moderate-intensity continuous exercise (Bartlett et al., 2011).

The purpose of this study was to investigate the effects of a 6-week high-intensity interval training (HIIT) programme using hybrid exercise (arm and FES-leg cycling) on peak oxygen consumption, muscle mass, lipid profiles and glucose tolerance in persons with chronic SCI. We additionally, sought to examine the psychological outcomes in terms of feeling states and mood profile following FES training.

This study proposed five primary hypotheses regarding the effectiveness of HIIT:

1. Maximal oxygen uptake in persons with chronic SCI following 6-week HIIT comprising indoor VR-enhanced hybrid FES-cycling would be higher than baseline.
2. There would be improvement in lipid profiles following 6-week HIIT.
3. There would be improvement in glucose tolerance following a 6-week HIIT programme.
4. Six-week HIIT of indoor VR-enhanced exercise would result in greater thigh girths and volume in persons with chronic SCI.
5. The subjects would demonstrate improvements in mood and cycling experience after the 6-week HIIT of indoor VR-enhanced hybrid FES-cycling.

5.3 Methods

5.3.1 Participants

Twelve subjects (aged 39.3 ± 10.1 y, stature 1.67 ± 0.65 m, body mass 65.1 ± 12.6 kg, BMI 23.5 ± 4.5, time since injury 8.9 ± 4.9 y) were recruited for this study. Ten males and two females with chronic SCI (ASIA A, B and C) between T1 and T12 with intact lumbosacral LMN and good hand function, volunteered. All subjects had undergone full medical screening to identify contraindications to FES, which included a physical and neurological examination including lower limb radiographs prior to the study. All subjects were healthy and neurologically stable. This study was approved by the Medical Ethics Committee, University of Malaya Medical Center (Ref No. MEC 889.12), and all participants underwent written informed consent. Subject recruitment was done at the Spinal Rehabilitation Clinic, Department of Rehabilitation Medicine, University of Malaya Medical Centre, Kuala Lumpur, Malaysia.

Subjects were assessed clinically and a portable FES system, the Stiwell med4 stimulator (Otto Bock HealthCare GmbH, Duderstadt, Germany) was used to determine if the muscle groups involved were responsive to neuromuscular stimulation. Subject preparation and the experimental set-up were all performed by the primary investigator. The testing and training were all done at the Human Physiology Lab, Faculty of Medicine, University of Malaya, Kuala Lumpur, Malaysia.

All subjects were novice FES users and during the exercise intervention were asked to continue their normal activities and diet. Any individuals who were undergoing physiotherapy sessions were asked to stop their physiotherapy sessions during the training programme.

5.3.2 Instrumentation

All subjects performed six weeks of indoor HIIT comprising VR-enhanced arm and FES-leg ("hybrid") cycling on a commercially available tricycle (Berkelbike Pro, Berkelbike BV, 's-Hertogenbosch, The Netherlands). The Berkelbike® is a combination of a recumbent bike and a hand bike (Heesterbeek et al., 2005). The hybrid tricycle was designed as an alternative for indoor and outdoor combined arm and FES-assisted leg exercise. When used indoors it was mounted on a stationary cycle resistance trainer (Tacx i-Magic, Tacx BV, Wassenaar, the Netherlands) for stationary cycling.

The FES unit on the hybrid tricycle consists of a small box connected to an incremental angle encoder, brake sensor and a neuromuscular stimulator. Electrical pulses stimulate the muscles through the gel-backed electrodes, which were placed over the bellies of three lower limb muscle groups - quadriceps, hamstrings and glutei. The tricycle was propelled by the stimulated leg muscle contractions and voluntary arm cranking. The maximum stimulation intensity was 150 mA at a frequency of 35Hz and pulse duration of 1 ms. The timing of the stimulation of the muscles was controlled by the neuromuscular stimulator and was based on the cadence selected by the user.

Prior to the FES cycling on the hybrid tricycle, gel-backed self-adhesive surface electrodes were placed over the bellies of the quadriceps, hamstrings and glutei muscle groups. Electrode placement was kept consistent by measurements to key anatomical landmarks to ensure muscle fibre recruitment was similar during training sessions and between trials. The electrodes were held securely in place by thigh stockings to prevent slippage. Following electrode placement, the subjects transferred onto the hybrid tricycle and had their feet and legs strapped and held in position by carbon-fibre leg supports for lower-limb stability to minimize leg movements in undesired directions during cycling.

For the current study, the cycle trainer was connected to a computer programme via a notebook computer and an 82 cm LCD television to enable virtual reality (VR) enhanced cycling in front of a large screen monitor. The monitor was mounted 1.5m from the subjects' open eyes, with 0-deg elevation from eyes to screen centre. Flat-screen technology was chosen, since it required no sensors, head mounted displays or other equipment to be attached to the subject. This enabled unrestricted movement, which was deemed necessary for the large body motions elicited during arm and leg cycling. There have also been no issues with nausea or other symptoms of cyber sickness often associated with VR programmes involving flat-screen technology. The virtual reality cycling experience was created using the Tacx i-Magic VR Trainer software.

5.3.3 Exercise training

5.3.3.1 Familiarisation phase

All subjects underwent four sessions of the VR-assisted hybrid cycling to provide familiarisation and experience with FES cycling and virtual reality training.

5.3.3.2 The training protocol

The subjects determined whether they could attend twice-weekly or thrice-weekly training based on their transport availability, employment and other commitments. Each subject maintained his or her frequency of choice over the six weeks of training. For the three times per week training group, the subjects were instructed to do 32-min of cycling exercise incorporating four intervals of high-intensity training (80-90% of predicted HRmax) interspersed with four intervals of low-intensity training (40% of predicted HRmax). For the two times per week training group, the subjects were instructed to do 48-min of exercise incorporating six intervals of high-intensity training (80-90% of predicted HRmax) interspersed with six intervals of low-intensity training (40% of predicted HRmax). The training regime is presented in Figure 5.1.

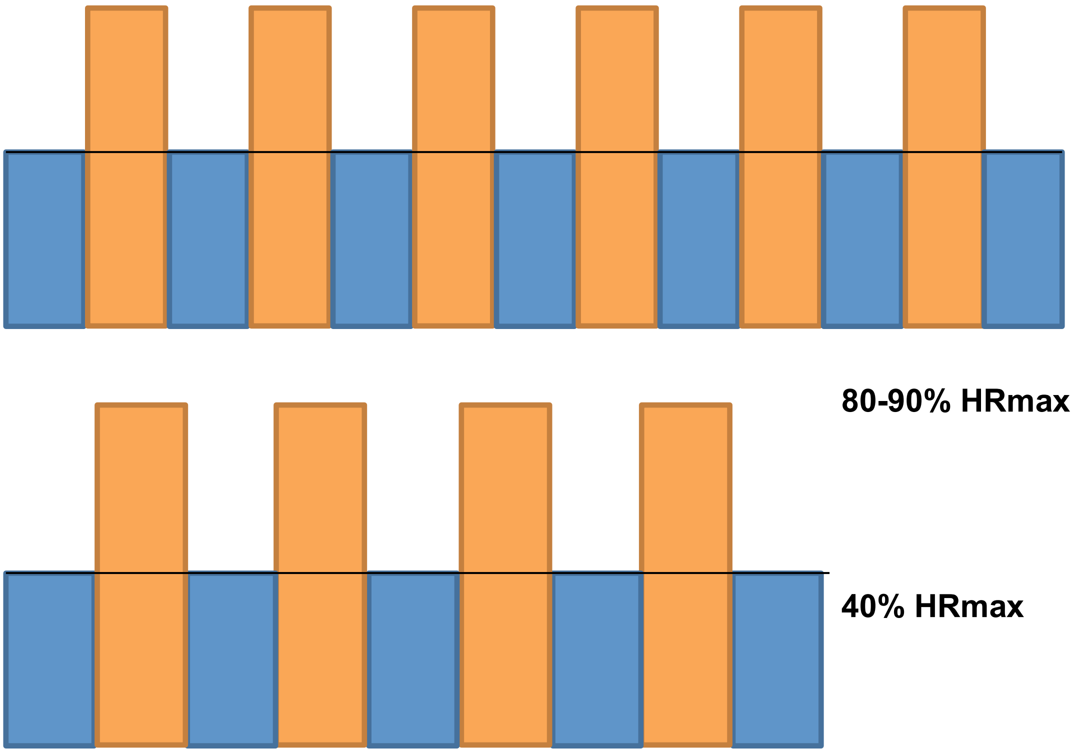

Figure 5.1. Training Regime. Top panel is three times per week training. Bottom panel is two times per week training. Bar widths denote intervals of 4-minutes at high-intensity (orange) and low-intensity (blue) training. Bar heights denote training intensity (blue = 40% HRmax and orange = 80% HRmax) Abbreviations: HRmax = maximum heart rate.

For both training regimes, all subjects completed 96 minutes of HIIT per week. During the high-intensity training, the subjects were instructed to do concurrent arm cranking and FES-leg cycling and during the low-intensity training; only FES-leg cycling was performed. All training incorporated VR technology whereby the subjects trained to a pre-selected VR programme. The subjects were encouraged to cycle to their best effort within safety limits and increase/ramp up their stimulation intensities based on their comfort and tolerance level whilst maintaining their training intensity.

5.3.4 Measurements and techniques

5.3.4.1 Physiological measurements

The subjects' peak cardiorespiratory responses and peak power outputs were assessed before and following completion of the six-week training programme. Peak aerobic fitness was assessed following the arm and leg loading protocol of Heesterbeek and colleagues (Heesterbeek et al., 2005). The graded hybrid test consisted of a warming up phase at 0W for 3-min followed by an increase in workload of 10W every minute. Subjects were instructed to perform voluntary arm cranking and FES-leg cycling simultaneously and to maintain pedaling cadence at 50 rev·min^{-1}. The electrical stimulation was increased manually in four increments (minimum contraction, 33%, 66% and 100% of maximum amplitude of 150mA) at equivalent heart rates of resting HR, 33%, 66% and 100% of heart rate reserve. The goal of this protocol was to exhaust the arm and leg muscles simultaneously by the test conclusion. The endpoint of the test was determined when cadence fell below 35 rev·min^{-1} and when power output dropped below 70% of the imposed power.

5.3.4.2 Oxygen uptake and heart rate

Heart rate and cardiorespiratory variables were measured continuously breath-by-breath using open-circuit spirometry with a metabolic gas analysis system at rest and during the maximal effort assessments. The metabolic gas analysis system (Quark CPET, Cosmed, Rome, Italy) was calibrated before each test according to the manufacturer's instructions. The subjects breathed through a rubber facemask (Hans Rudolph Inc., Kansas City, USA) into the metabolic gas analysis system. Breath by breath oxygen uptake (VO_2), carbon dioxide production (VCO_2), expired ventilation (V_E) and respiratory exchange ratio (RER) were smoothed using a three-step average filter (Data management software, Cosmed, Rome, Italy). Subsequently, all measures were averaged over 15-s periods during the third to fourth minute of rest and during the last minute of maximal exercise to derive the resting VO_2, and the VO_{2peak} during maximal effort.

5.3.4.3 Power output

The power output (PO) from the hybrid FES tricycle was recorded from the Tacx i-Magic software and was a summation of both the arm and leg power output. Power outputs during the maximal tests were recorded from power output obtained during the last minute of maximal exercise testing.

5.3.4.4 Thigh volume

Thigh volume measurements were performed on both thighs before and after completion of the six weeks training programme. Five thigh girth measurements were done 5 cm apart above the superior border of the patella. The thigh volumes were then derived from the formula according to Jones and Pearson (Jones & Pearson, 1969).

5.3.4.5 Blood lipids

Fasting blood lipid profiles including total cholesterol, triglyceride, high-density lipoprotein (HDL) and low-density lipoprotein (LDL) were obtained before and after the 6-week training period.

5.3.4.6 Oral glucose tolerance

One baseline fasting blood sample was obtained from all subjects. After collection of the baseline sample, subjects were asked to drink 75g of glucose in an orange flavoured drink over a 5-min period. Following that, blood samples were drawn again at 60 and 120 minutes.

All tests were performed before training commenced and after the 6-week training period. Subjects were asked to fast overnight for 12 hours and blood samples were drawn by the primary investigator. All samples were analyzed at the clinical chemistry laboratory, Division of Laboratory Medicine, Department of Pathology, University of Malaya Medical Centre, Kuala Lumpur, Malaysia.

5.3.4.7 Psychological and perception measurements

5.3.4.7.1 Rating of perceived exertion (RPE)

Subjects were requested to give an RPE score by responding to the question, "How hard did you exercise?" at the end of the exercise session at the end of the first exercise session in the first week and the last session in the sixth week using the Borg Category Ratio 10 (Borg CR10) Scale (Borg, 1998). Grange and colleagues observed that perceived exertion using the Borg CR10 scale was a useful measure of exercise intensity during a 45-min exercise performed on a wheelchair ergometer in a supervised clinical setting (Grange et al., 2002). During the familiarization session, each subject was given instructions on the use of the BORG CR 10.

The subjects' feeling states post-exercise and mood states were asked through face-to-face questionnaire interviews using the Exercise-induced Feeling Inventory and the Profile of Mood States at the end of the first exercise session in the first week and the last session in the sixth week.

5.3.4.7.2 Feeling States

The Exercise-induced Feeling Inventory (EIFI), developed by Gauvin and Rejeski, was used to measure feelings following the hybrid FES cycling exercise. The EIFI is a self-report questionnaire, which requires the user to answer on a 5-point scale anchored by 0

= do not feel and 4 = feel very strongly. The EIFI measures “positive engagement”, “revitalization”, “tranquility” and “physical exhaustion” by totaling three-item response scores in four subscales. For example, the score for “positive engagement” subscale is the sum of scores for “enthusiastic”, “happy” and “upbeat”. For “physical exhaustion” subscale, it is the sum of scores for “fatigued”, “tired” and “worn-out”. Each subscale has a total score of 12. Gauvin and Rejeski observed that the EIFI was very sensitive to changes in feeling states that occur with exercise, and that the measure was able to detect differences in the social context of different exercise interventions (Gauvin & Rejeski, 1993). All subjects completed the 1-minute self-report questionnaire immediately after cooling down.

5.3.4.7.3 Mood

The Profile of Mood States (POMS) inventory, developed by McNair and colleagues was primarily used as a measure of mood states in psychiatric outpatients (McNair, Lon, & Droppelman, 1971). It is a measure of subjective well-being and was developed to assess transient and fluctuating distinct mood states. The original form of the measure consisted of 65 adjectives within six factor-based scales that were rated on a 5-point scale from “not at all” to “extremely”. The POMS has been used extensively for the assessment of mood in the sport and exercise environments. Horvat and co-workers had used the POMS to compare the psychological characteristics of male and female able-bodied and wheelchair athletes which included spinal cord injured paraplegic and tetraplegic subjects (Horvat, French, & Henschen, 1986). Shacham developed the POMS-SF, a shorter 37-item form of the POMS that retained the six subscales based on responses of cancer patients (Shacham, 1983). The six subscales are “depression” (8 items), “vigour” (6 items), “anger” (7 items), “tension” (6 items), “confusion” (5 items) and “fatigue” (5 items). The POMS-SF is a self-report, which requires the user to answer on a 5-point Likert scale, from 0 (not at all) to 4 (extremely), responding to the question “How have you been feeling during the past 24 hours”.

Additionally, the subjects were asked about their satisfaction with the FES hybrid tricycle through face-to-face questionnaire interviews using the Quebec User Evaluation of Satisfaction with Assistive Technology Questionnaire (Demers et al., 1996). Symptoms related to the use of VR were assessed using the Virtual Reality Symptom Questionnaire following the last training session in the sixth week (Ames et al., 2005).

5.3.4.7.4 User satisfaction

The Quebec User Evaluation of Satisfaction with Assistive Technology Questionnaire (QUEST 2.0) was used to evaluate subjects experience and satisfaction with using the hybrid FES tricycle. The QUEST 2.0 was designed as an outcome measurement instrument to evaluate a person’s satisfaction with a wide range of assistive technology (AT). The QUEST 2.0 is a self-administered questionnaire consisting of 12 items rated on a 5-point satisfaction scale. Response ranges from 1 (not satisfied at all) and 5 (very satisfied). The 12 items are subscales of eight assistive device items and four service items (Demers et al., 1996). In this study only items within the assistive device were included i.e. satisfaction with the dimensions, weight, ease of adjusting, safety and security, durability, usability and effectiveness of the assistive device.

5.3.4.7.5 Virtual reality experience

Subjects’ experience using VR-assisted hybrid FES cycling was assessed using the Virtual Reality Symptom Questionnaire (VRSQ). The VRSQ was developed for use in investigating symptoms that result from VR viewing. It consists of thirteen symptom questions: eight non-ocular (general discomfort, fatigue, boredom, drowsiness, headache, dizziness, difficulty concentrating and nausea) and five ocular (tired eyes, sore/aching eyes, eyestrain, blurred vision and difficulty focusing). The 13 symptoms are rated on a 6-point scale. Response ranges from 1 (none) to 6 (severe). The VRSQ was tried out during the familiarization session so that subjects were familiar with the questionnaire when it was administered. The questionnaire was administered immediately following cessation of exercise before the symptoms dissipate as it was suggested by Ames et al that assessment of symptoms have to occur in the first 5 minutes of post VR experience (Ames et al., 2005).

5.3.5 Data analysis

Statistical analysis was performed using the SPSS 21 statistical package. A paired-samples t-test was conducted to compare the aerobic fitness, lipid profiles, glucose tolerance and psychosocial perception in persons with chronic SCI before and after a six-week high-intensity interval "hybrid" exercise (arm and FES-leg cycling) programme. Data are presented as mean ± standard deviation (SD), and the level of statistical significance was set to the 95% confidence limit ($p<0.05$).

5.4 Results

5.4.1 Training Outcomes

All twelve subjects completed the six-week training programme. Five subjects underwent twice-weekly training of 48-min cycling exercise incorporating six intervals of 4-min high-intensity training (80-90% of predicted HRmax) interspersed with six cycles of 4-min low-intensity training (40% of predicted HRmax). Seven subjects underwent thrice-weekly training of 32-min cycling exercise incorporating intervals of four cycles of 4-min of high-intensity training (80-90% of predicted HRmax) interspersed with four cycles of 4-min low-intensity training (40% of predicted HRmax). For both training regimes, all subjects completed 96 minutes of HIIT per week. Exercise adherence was excellent in this study, all subjects did not miss any session but adherence to exercise schedule was 88% (between 67-100%). Rescheduling of sessions were for illness and transportation issues.

5.4.2 Physiological and performance

5.4.2.1 Graded hybrid exercise testing

Peak physiologic responses for VO_2, V_E, HR, O_2 pulse and PO during graded hybrid exercise testing before and after the six-week training for the twelve subjects are displayed in Table 5.1. There was a 16% increase in aerobic fitness and 33% increase in peak power output after six weeks of training. Resting heart rate showed a reduction from 71±17 $b\cdot min^{-1}$ pre-training to 68±11 $b\cdot min^{-1}$ post-training and this change was statistically significant ($p<0.05$). The O_2 pulse showed a 15% increase and V_E showed 11% increase following the training programme.

Table 5.1. Peak Physiologic Responses During Graded Hybrid Exercise Testing before and after FES Hybrid High-intensity Interval Training (HIIT). (N=12, * denotes p<0.05 pre- to post-training). Data are mean ± SD.

	Pre – HIIT	Post – HIIT
Heart rate ($b\cdot min^{-1}$)	156 ± 13	157 ± 15
VO_2 ($mL\cdot kg^{-1}\cdot min^{-1}$)	18.8 ± 3.1	21.8 ± 4.0*
V_E ($L\cdot min^{-1}$)	57.2 ± 14.1	63.4 ± 15.0*
O_2 pulse ($mL\cdot b^{-1}$)	7.80 ± 1.70	9.00 ± 2.05

Abbreviations: VO_2 = oxygen uptake; V_E = pulmonary ventilation; O_2 = oxygen

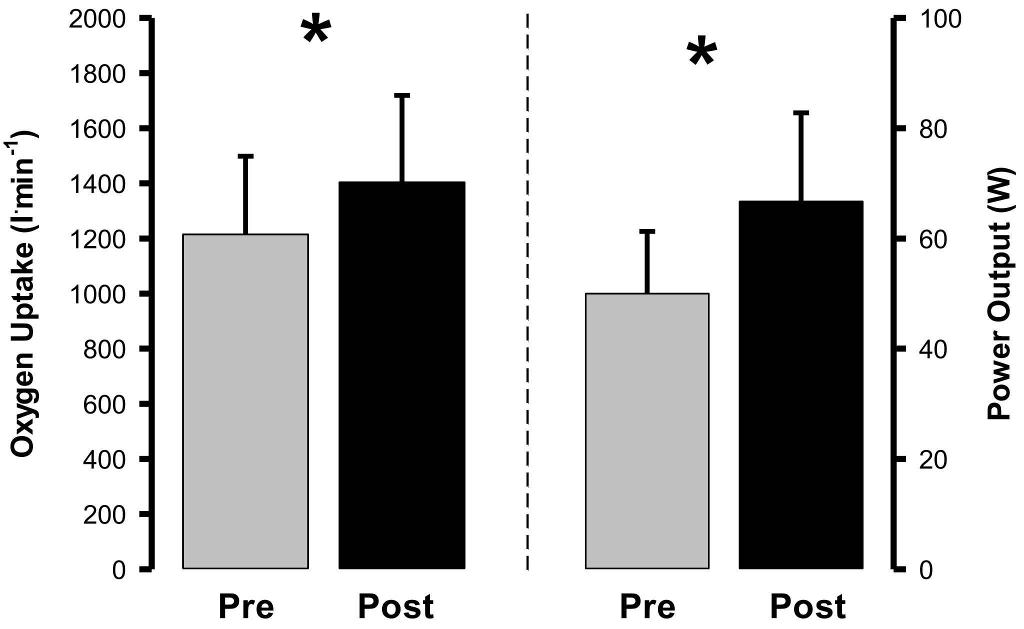

Figure 5.2. Changes in aerobic fitness and peak power output after HIIT. * denotes $p<0.05$. Data are mean ± S.D. Abbreviation: HIIT = High-intensity Interval Training

5.4.2.2 Thigh girths and volumes

Mean total thigh volume (ml) of all subjects increased significantly from baseline, showing a 6.2% increase in thigh volume, from 2950 ± 884 ml pre-training to 3116 ± 1001 ml post-training. The right thigh and left thigh showed increases of 6.7% and 5.6% volume change respectively following training. The distribution of increases in thigh girths following training was similar for both thighs with the mid thigh areas between 15 cm and 25 cm above the suprapatellar line showing greater increases of thigh girths with resulting volume change of 6.1% and 5.4% for the right and left thighs respectively.

5.4.3 Blood lipids and oral glucose tolerance

The pre-training and post-training mean values of lipid profiles and oral glucose tolerance test (OGTT) are shown in Table 5.2.

Out of the twelve subjects, five subjects had pre-training total cholesterol values of more than 5.17 $mmol{\cdot}L^{-1}$ putting them at increased risk of coronary artery disease. Five subjects demonstrated low HDL levels (<1.03 $mmol{\cdot}L^{-1}$). (Expert Panel on Detection, 2001). Out of the five subjects with high pre-training total cholesterol levels, only one subject showed a reduction in total cholesterol level post-training, however, three out of the five subjects showed increases in HDL levels post-training. There were no significant changes in the group lipid profile values except for a strong trend for HDL increase post-training ($p=0.051$). Subsequent non-parametric analysis of variance (Friedman's test) revealed that ten out of twelve subjects increased their HDL ($p<0.05$), although there were no other changes in the blood biochemistry measures were altered.

None of the subjects in this study had fasting glucose levels that fell into the DM category pre-training, however two subjects had showed impaired glucose tolerance with glucose level of more than 7.8 $mmol{\cdot}L^{-1}$ two hours after a 75-g glucose load indicating increased risk of diabetes (American Diabetes, 2010; Patel & Macerollo, 2010). These two subjects with impaired glucose tolerance showed decreased OGTT two-hour glucose level post-training. Of the twelve subjects, seven demonstrated decreases in the post-training values of fasting and 2-hour post-prandial glucose levels but the change was not statistically significant.

Table 5.2. Total cholesterol, triglyceride, HDL, LDL and blood glucose response before and after FES Hybrid High-intensity Interval Training (HIIT). (N=12 except for 1-hr PP N=11) * denotes p<0.05 pre- to post-training. Data are mean ± SD.

	Pre – HIIT	Post – HIIT
Total Cholesterol ($mmol\bullet l^{-1}$)	4.99 ± 0.90	5.23± 0.99
Triglyceride ($mmol\bullet l^{-1}$)	1.39 ± 0.65	1.28± 0.67
HDL ($mmol\bullet l^{-1}$)	1.06 ± 0.18	1.16 ± 0.15*
LDL ($mmol\bullet l^{-1}$)	3.32 ± 0.76	3.49 ± 0.93
OGTT fasting ($mmol\bullet l^{-1}$)	4.73± 0.52	4.50 ± 0.51
OGTT one-hour ($mmol\bullet l^{-1}$)	7.93 ± 2.11	7.90 ± 2.05
OGTT two-hour ($mmol\bullet l^{-1}$)	6.08 ± 1.88	5.71 ± 1.67

Abbreviations: HIIT=high-intensity interval training; HDL=high-density lipoproteins; LDL=low-density lipoproteins; OGTT=oral glucose tolerance test

5.4.4 Psychological and perceptual outcomes

The six-week high-intensity interval "hybrid" FES training resulted in significant improvements in feeling states and mood as portrayed in Figure 5.3.

5.4.4.1 Rating of Perceived Exertion (RPE)

Subjects reported a mean score of 6.0 ± 2.2 at baseline on the BORG CR10 RPE Scale compared to 3.2 ± 1.8 at the end of the six-week training period ($p<0.05$).

5.4.4.2 Feeling States

Feeling states improved at the end of the training period in all the subscales of EIFI, showing a 44% improvement in feeling of positive engagement, 76% increase in feeling of revitalization, 73% increase in feeling of tranquility and 30% decrease in physical exhaustion. Each subscale has a total score of 12. All with the exception of physical exhaustion subscale changed significantly as shown in Figure 5.3.

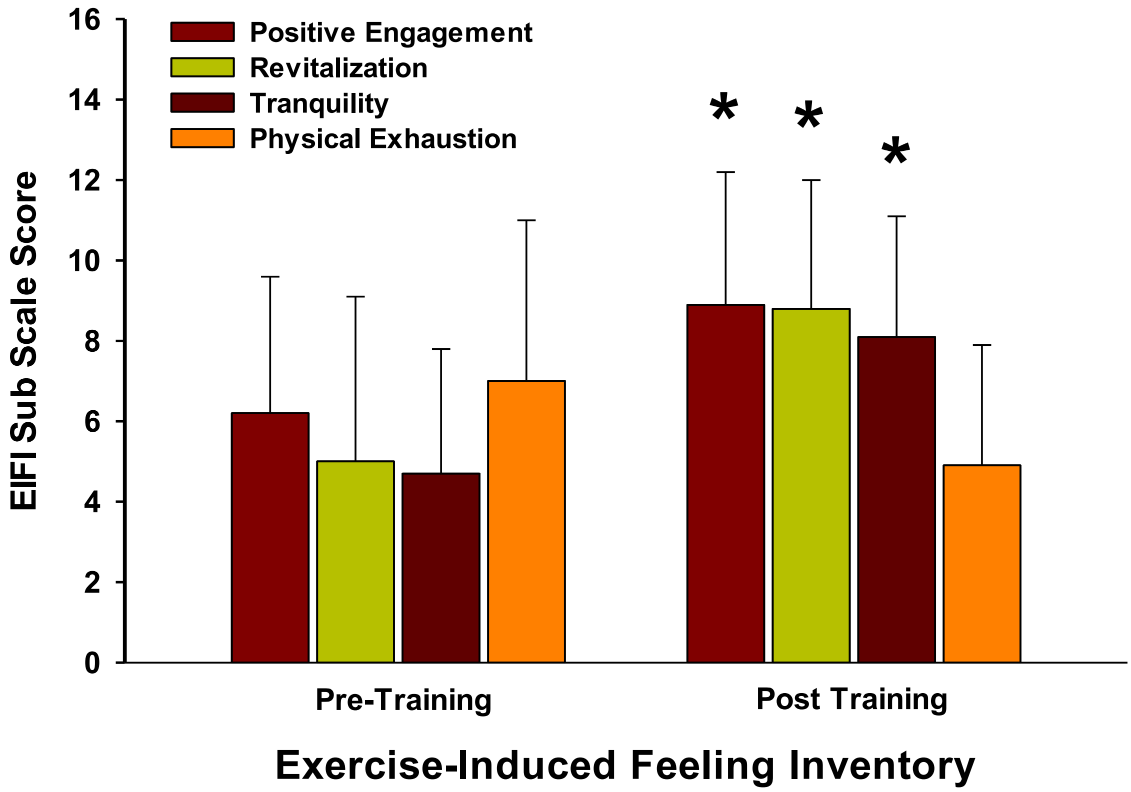

Figure 5.3. Changes in exercise-induced feelings after HIIT. * denotes $p<0.05$. Data are mean ± S.D.

5.4.4.3 Mood

The six-week training programme also showed statistically significant improvement in four of the subscales of the POMS-SF as shown in Table 5.3. The mean ± SD scores of all the subscales are as detailed in Table 5.3.

5.4.4.4 User satisfaction and virtual reality experience

The mean score for the 8 items on QUEST 2.0 was 28.4 ± 3.9 out of a possible total of 40 points. Only minimal body and visual symptoms were reported by the subjects with a mean score of less than one point (out of a possible 48/30 points) for each domain.

Table 5.3. POMS-SF subscales before and after FES Hybrid High-intensity Interval Training (HIIT). (N=12), * denotes p<0.05 pre- to post-training. Data are mean ± SD.

	Pre – HIIT	Post – HIIT
Depression	6.25 ± 9.04	1.33± 2.06
Vigor	9.00 ± 6.81	14.08± 4.81*
Anger	5.92 ± 8.57	1.08 ± 2.11*
Tension	6.67 ± 7.57	1.50 ± 1.73*
Confusion	3.75± 4.54	1.17 ± 2.13
Fatigue	6.00 ± 6.92	2.33 ± 2.46*

Abbreviations: HIIT = high-intensity interval training

5.5 Discussion

The Stockholm Spinal Cord Injury Study reported that almost one-third of persons with paraplegia were eligible for cardiovascular disease risk intervention in their studied population (Wahman, Nash, Lewis, Seiger, & Levi, 2011). The number in need of intervention was dramatically increased when overweight/obesity or BMI ≥ 22 as a cardiovascular disease risk was considered. In the current study, the mean BMI was 23.5 ± 4.5 suggesting that these individuals were at risk of cardiovascular disease and would be eligible for cardiovascular disease risk intervention. Unfortunately, waist circumference, which may be a more valid indicator for overweight /obesity in this population was not assessed (Buchholz & Bugaresti, 2005).

The primary findings of this study were (i) a 6-week HIIT programme of indoor VR-enhanced hybrid cycling improved aerobic fitness, lowered resting heart rate and augmented muscle mass after training (ii) a 6-week HIIT regime of indoor VR-enhanced hybrid cycling also improved mood and post-exercise feeling states (iii) a 6-

week HIIT programme of indoor VR-enhanced hybrid cycling improved HDL level, and (iv) a 6-week HIIT programme of indoor VR-enhanced hybrid cycling did not change oral glucose tolerance in this group.

5.5.1 Peak cardiorespiratory responses

The improved VO_{2peak} indicated the dose-potency of 2-3 times per week, 6-week HIIT in persons with SCI. This significant improvement in peak oxygen uptake (1.22 to 1.40 $L \cdot min^{-1}$) could be attributed to the fact that the subjects were novice FES users, and these data are consistent with previous research involving hybrid FES-cycling (Heesterbeek et al., 2005; Krauss et al., 1993b; Mutton et al., 1997b; Thijssen et al., 2005; Wheeler et al., 2002). The pre- and post- VO_{2peak} values were lower than what was found in Brurok and colleagues who also employed high intensity interval training (1.96 to 2.43 $L \cdot min^{-1}$) and observed 24% increase in their 8-week study (Brurok et al., 2011). Based on Janssen and colleagues' normative values for physical capacity parameters in individuals with tetraplegia and paraplegia, it is clear that the subjects in this study initially had a "poor" fitness level at the start of the programme and improved to "fair" fitness level after six weeks of HIIT (Janssen, Dallmeijer, Veeger, & van der Woude, 2002). The 15% increase in aerobic fitness in the current study was comparable to Krausse and colleagues' 14% increase of aerobic fitness after six weeks of FES training followed by six weeks of FES+ACE training (Krauss et al., 1993b). Other studies have demonstrated improvement of aerobic fitness in the range of 6-11%, although often after training at lower intensities of effort (Mutton et al., 1997b; Thijssen et al., 2005; Wheeler et al., 2002). As with the VO_{2peak}, the peak power output was significantly higher at post-training, by 33% increase. It is worth noting that the graded exercise tests in all previous studies, except for Heesterbeek and colleagues', comprised arms-only testing (Heesterbeek et al., 2005).

Peak oxygen pulse increased by 15% following training without a change in peak heart rate. It is commonly understood that oxygen pulse is a surrogate for stroke volume and arteriovenous oxygen difference. Thus the significant increase observed in the current study might reflect both “central” cardiovascular and “peripheral” metabolic adaptations following HIIT. Previous studies have measured O_2 pulse (Mutton et al., 1997b; Wheeler et al., 2002) but some have observed larger increases as much as 35% following a FES rowing training of six months duration (Taylor, Picard, & Widrick, 2011).

5.5.2 Thigh girths and volumes

The significant 6% increase in thigh volumes could be directly attributed to increased muscle mass or muscle hypertrophy as a result of leg exercise during the 6-week hybrid training programme as the subjects did not have any other lower limb training during the study period. Heesterbeek and colleagues also recorded a significant increase of 6% in thigh volume (Heesterbeek et al., 2005). Other studies that showed improvements of muscle mass following FES training were studies by Hjeltnes and colleagues who reported 2% increase in whole body lean mass following eight weeks of training (Hjeltnes et al., 1997), Mohr and co-workers who reported a 12% increase following a year of FES training (Mohr et al., 1997), Skold et al. who reported a 10% increase after six months of FES cycling (Skold et al., 2002) and Griffin and colleagues who reported a 4% increase in lean muscle mass following ten weeks of FES training (Griffin et al., 2009). A common limitation to comparing these studies to the current investigation is that muscle mass has been assessed in different ways. A limitation to the study was that we did not measure skin fold thickness to control for non-muscle hypertrophy-related volume changes. Increase in muscle mass is one of the important factors for the contribution of active aerobic metabolism, improving whole body glucose metabolism and reducing cardiovascular risk factors in people with SCI (Bhambhani, Tuchak, Burnham, Jeon, & Maikala, 2000; Hjeltnes et al., 1997). Griffin and colleagues stressed that even after prolonged inactivity, the muscles of individuals with SCI are still capable of adapting to a stimulus exercise overload (Griffin et al., 2009). In this current study, the subjects were allowed to self-select their pedaling cadence to match the target heart rate. It was observed that the cycling cadence was consistently above 50 $rev \cdot min^{-1}$ during high intensity intervals. Fornusek and colleagues reported that lower pedaling cadences at 10 $rev \cdot min^{-1}$ evoke greater muscle hypertrophy in electrically stimulated muscle compared with higher cadences (Fornusek, Davis, & Russold, 2013). The higher pedaling cadence used by the subjects in this study could be the cause of the modest increase in thigh girths in this study.

5.5.3 Blood biochemistry

In this study, there was no significant change in the lipid profiles values except for a HDL post-training ($p=0.051$). Of the twelve participants, ten increased their HDL levels, a significant finding using Friedman's non-parametric ANOVA ($p=0.039$). Out of the twelve subjects, pre-training lipid profile showed five subjects had total cholesterol values of more than 5.17 $mmol \cdot L^{-1}$ putting them at increased risk of coronary artery disease based on the Framingham Risk Equation values (Expert Panel on Detection, 2001). Three out of the five subjects with high total cholesterol levels also demonstrated high LDL levels (>3.33 $mmol \cdot L^{-1}$). In appears that six weeks of a HIIT programme was not able to reduce the total cholesterol and LDL levels to below increased risk levels. Five out of twelve subjects demonstrated low HDL levels (<1.03 $mmol \cdot L^{-1}$) and it is interesting to observe that despite not showing improvements in reducing the total cholesterol and LDL levels with training, three out of the five subjects showed increases in HDL levels post-training. The findings of improvement in

HDL levels in ten out of twelve subjects and in the three out of five subjects with low HDL levels pre-training in this current study may indicate that HIIT programme is somewhat effective for SCI individuals in particular, individuals with demonstrated cardiovascular risk.

Previous reviews have identified that exercise can improve lipoprotein levels in diabetics and overweight able-bodied individuals (Shaw, Gennat, O'Rourke, & Del Mar, 2006; Thomas, Elliott, & Naughton, 2006). An SCI-specific CVD prediction model is unavailable therefore previous studies have used models validated on the general population such as the Framingham Risk Equation and the Systematic Coronary Risk Evaluation (Graham et al., 2007; Wahman, Nash, Lewis, Seiger, & Levi, 2010; Wahman et al., 2011). El-Sayed and Younesian (2005) assessed the outcomes of lipid profiles in five SCI subjects who underwent 12 weeks of arm cranking exercise and found favourable effects on HDL but not total cholesterol and triglyceride levels (El-Sayed & Younesian, 2005). Griffin and colleagues did not find any improvement in plasma cholesterol levels or triglycerides and even found unexplainable significant reduction in HDL level following 10 weeks of FES training (Griffin et al., 2009).

In this study, two subjects had impaired glucose tolerance as demonstrated in the OGTT two-hour glucose level (>7.8 $mmol{\cdot}L^{-1}$). Although both subjects showed reduction in the OGTT two-hour glucose level post-training, only one subject had reduction of glucose level to below 7.8 $mmol{\cdot}L^{-1}$. Although there were decreases in the post-training values of fasting and two-hour glucose levels, the change was not statistically significant. There is increasing evidence that the postprandial state is an important contributing factor in the development of atherosclerosis. The OGTT, although highly non-physiological, has been used largely as a model of the post-prandial state, and epidemiological studies have shown that impaired OGTT is associated with an increased risk of cardiovascular disease, because the glycaemia level after two hours of the glucose challenge is a direct and independent risk factor (Ceriello, 2004). Griffin and colleagues found significant improvement in glucose tolerance and insulin response following ten weeks of FES training (Griffin et al., 2009). Similar findings have been found by Hjeltnes and colleagues and Jeon and colleagues following eight weeks of FES training (Hjeltnes et al., 1997; Jeon et al., 2002). The findings of this study clearly show that despite the improvement in cardiorespiratory variables and stimulated muscles, a six week FES training programme may be too short to improve glucose tolerance and modify the cardiovascular risk in individuals with SCI.

5.5.4 Psychoperceptual outcomes

5.5.4.1 Perceived exertion

Even though individuals with SCI demonstrate a unique exercise response, it has been shown that the RPE is reliable and effective in controlling moderate and vigorous intensity exercise (Goosey-Tolfrey et al., 2010; Grange et al., 2002). The subjects were requested to cycle at 80-90% predicted HRmax (high intensity training) intervals, which were carefully monitored throughout the training. RPE recorded at the end of the first training session was 6.0 ± 2.2 and at the end of the last training session was 3.2 ± 1.8. This finding shows that the training was perceived to be easier over time despite maintaining exercise at a high intensity. This findings support the earlier findings of reduced resting heart rate following the six weeks programme indicating a training effect and exercise tolerance.

5.5.4.2 Feeling states

The acute psychological benefits of aerobic exercise are well established in the able-bodied population and the spinal cord injured population (Hicks et al., 2003). Chen and colleagues also reported positive psychological outcomes following VR exercise programme in people with SCI (Chen et al., 2009). The current study showed significant improvements in the post-exercise states following six weeks of HIIT in the subscales of positive engagement, revitalization and tranquility. The subscale of physical exhaustion showed improvement in mean scores, however did not achieve significant change. It is interesting that in a previously sedentary subject population, positive feeling states post-exercise was reported despite having had to undergo high-intensity interval training which was physically and physiologically demanding. This concurs with Hick who concluded that individuals with SCI can significantly enhance their sense of subjective well-being by engaging in a structured exercise programme (Hicks et al., 2003).

5.5.4.3 Mood

The subjects in this study also showed a significant improvement in their mood measured by the POMS-SF. They felt improved vigour and less anger, tension and fatigue following the 6-week training programme. It is also worth noting that the subscale of depression almost achieved significance at p=0.051. There seems to be limited literature on mood and exercise in SCI. Annesi and colleagues found that mood significantly improved following a 6-month moderate intensity aerobic exercise programme in 137 obese women and the changes in mood contribute to the variance in exercise attendance (Annesi, Unruh, Marti, Gorjala, & Tennant, 2011). Several other studies also showed improvement with mood following exercise training in clinical populations such as breast cancer, traumatic brain injury and multiple sclerosis (Driver

& Ede, 2009; White & Dressendorfer, 2004; Yang, Tsai, Huang, & Lin, 2011). Hicks and Ginis reported improvement in mood with BWSTT even with acute bouts of training (Hicks et al., 2005; Hicks & Ginis, 2008).

The favourable outcomes of mood and feeling states in this study population are reflected in the excellent adherence to the training programme. The 100% exercise adherence (percent of prescribed sessions attended) and 88% adherence to exercise schedule (percent of keeping to exercise schedule) were very high compared to previous studies. A study of exercise adherence to two 8-week home-based FES cycling by individuals with SCI by Dolbow and colleagues reported up to 72% exercise adherence rate (Dolbow et al., 2012). Hicks and colleagues reported 82.5% exercise adherence rate in a SCI group who underwent nine months arm exercise programme (Hicks et al., 2003).

The overall findings of this study proved our hypotheses that a 6-week HIIT of indoor VR-enhanced hybrid-FES-cycling improve aerobic fitness in persons with chronic SCI; that a 6-week HIIT of indoor VR-enhanced hybrid-FES-cycling results in increased thigh volume in persons with chronic SCI and that a 6-week HIIT of indoor VR-enhanced hybrid-FES-cycling improvement in mood and post-exercise feeling states. The 6-week HIIT programme improved HDL levels but not other parameters of the lipid profile. However, the hypotheses that there will be improvement in glucose tolerance in persons with chronic SCI following a 6-week HIIT of indoor VR-enhanced hybrid-FES-cycling is rejected.

5.6 Conclusion

These results suggest that a high-intensity interval training employing "hybrid" exercise (arm and FES-leg cycling) of six weeks duration is able to improve aerobic fitness, muscle mass, post-exercise feeling states and mood in persons with SCI. The lack of change in the lipid profile and non-significant change in the oral glucose tolerance test suggest that six weeks of twice- or thrice-weekly training even at high-intensity may be too short to modify the cardiovascular risk in the SCI population.

Chapter Six

Discussion

6.1 Introduction

Knowledge and understanding of the pathophysiology of spinal cord and spinal cord injuries in the medical world have enabled more people with SCI to survive their spinal cord injuries in the past six decades since World War II. SCI survivors have benefitted from the medical advancement of emergency trauma care, acute medical care and spinal cord injury rehabilitation, living longer with many being productive members of the community. Health outcomes have also improved dramatically. Research into best practices in medicine and rehabilitation continue alongside research towards finding the cure for spinal cord injuries. Unfortunately, with increased life expectancy, people with SCI are also now at risk of developing secondary health conditions associated with living with chronic SCI and inactivity. Even with increased life expectancy, people with chronic SCI have a higher mortality rate than the general population (Frankel et al., 1998). When excluding deaths during the first year after injury, all-cause cardiovascular disease is the leading source of mortality in people with chronic SCI (DeVivo, Krause, & Lammertse, 1999a). Risk factors for CVD such as abnormal lipid profile, diabetes and obesity are higher in people with SCI. It is well established that physical fitness has a positive effect on lipid profiles. Being wheelchair bound, people with SCI have a diminished level of activity leading to low physical capacity and fitness (De Groot, Dallmeijer, Post, Angenot, & van der Woude, 2008).

The experiments presented in this thesis compared the acute physiological responses of FES-assisted exercise during four different modalities specifically including FES hybrid cycling in people with SCI. Subsequently, the acute physiological and psychological responses to FES hybrid cycling was further assessed during outdoor and VR-enhanced indoor cycling. The final experiment examined training outcomes after short-term hybrid FES cycling on fitness, lipid and glucose metabolism and psychological benefits.

In this chapter, an overview of the flow and interactions of the experiments will be discussed, followed by discussion on the clinical implications of the findings for people with SCI. The limitations of the studies and future research directions are discussed at the end of this chapter before the final conclusions of this thesis are presented.

6.1.1 Exercise for health promotion for people with SCI

There are numerous and irrefutable evidence of the effectiveness of regular exercise as a health promoting activity in the primary and secondary prevention of several chronic diseases and premature death (Fernhall et al., 2008; Jacobs & Nash, 2004; Kehn & Kroll, 2009; Lavis et al., 2007; Nash, 2005; Rimmer, 1999; Warburton et al., 2006).

6.1.2 What is the best exercise modality for health promotion for people with SCI?

Arm exercise modes have been used traditionally for fitness training of wheelchair users including people with SCI. The arm crank ergometer represents a universally available mode of arm exercise training as well as exercise testing for non-ambulatory individuals. Glaser had suggested that ACE alone might be less effective than lower limb exercise for health and fitness promotion for people with SCI. The relatively small muscle mass, deficient cardiovascular reflex responses and inactivity of the venous muscle pump cause early onset of fatigue during arm activity thus resulting in difficulty in developing and maintaining aerobic fitness (Glaser, 1989). Hopman and colleagues had reported that a three or six months of ACE training period has no measureable positive effect on the fitness level of people with tetraplegia (Hopman, Dallmeijer, Snoek, & van der Woude, 1996). The same group of investigators also had shown lack of elevation in cardiac output and stroke volume during submaximal and maximal exercise during ACE in able-bodied and SCI population (Eijsbouts, Hopman, & Skinner, 1997; Glaser, 1989).

Arm exercise also produces mechanical strain in the upper extremities and can further complicate problems associated with early shoulder pain and injuries as well as overuse syndromes in SCI wheelchair users (Figoni, 2009; Powers et al., 1994). In people with SCI, the upper limbs are often overused especially with activities that require strength such as wheelchair propulsion and wheelchair transfers, and activities of daily living that require a wide range of motion of the shoulder joint. The prevalence of shoulder pain in people with SCI ranges between 35% and 51% (Facione et al., 2011).

With this knowledge of physiological and mechanical limitations of arm exercise in people with SCI, it is imperative that a search for an optimal exercise option for people with SCI is made in order to enable fitness training and maintenance.

FES leg exercise, since its recommendation as an exercise mode instead of primarily a return to walk exercise prescription, has been extensively investigated. Use of FES-LCE in acute SCI individuals has shown attenuation of loss muscle mass and power output, increases blood flow and increases muscle fatigue resistance (Demchak et al., 2005; Sabatier et al., 2006). FES-LCE exercise promotes central hemodynamic responses that are superior to those observed during upright ACE (Hooker et al., 1992b). Previous studies have also shown that persons with SCI can perform short-duration and prolonged FES leg cycling without undue physiologic stress or complications (Hooker et al., 1990; Hooker et al., 1992b; Raymond et al., 1999).

Previous FES studies have also indicated improved exercise performance in people with SCI. Indeed, studies have also shown FES to ameliorate some of the degenerative changes associated with chronic SCI. FES therefore shows great promise and potential to be the choice exercise intervention for people with SCI. However, previous studies have also shown that FES leg exercise alone even though promoting increases in peak aerobic capacity in SCI individuals, have often resulted in significantly lower submaximal oxygen uptakes compared to ACE.

The first experiment performed in this series compared acute exercise responses between the different exercise modalities. The study demonstrated lower oxygen uptakes and heart rate during FES-LCE compared to ACE during maximal and low to moderate to high intensity submaximal exercise conditions. When combined, ACE and FES-LCE whether in adapted form (two independent equipment for simultaneous but asynchronous arm and leg movements) or purpose-built (a commercial FES hybrid bike enabling synchronous arm and leg movements) had shown elevated maximal and submaximal oxygen uptakes compared to FES-LCE only and ACE only modes. Similarly, the combined exercise modes i.e. hybrid FES exercise showed 10% higher cardiac output than ACE alone, and 50% higher cardiac output than FES-LCE alone. Findings from this experiment and previous studies clearly indicate that hybrid FES exercise elicits greater whole-body oxygen uptake and central haemodynamic responses, supporting the view that hybrid FES exercise promotes better aerobic fitness potential.

The subsequent experiments reported in this thesis showed how hybrid FES exercise can be deployed and the physiological, psychological and metabolic outcomes of hybrid FES exercise.

6.1.3 Strategies for exercise participation for people with SCI

Problem with exercise compliance exists in the able-bodied population and the SCI population. In the SCI population, there is a multitude of barriers preventing participation and maintaining interest in participation in physical activity and exercise presenting in functional, psychological and architectural domains. Some of the barriers cited by SCI individuals include “exercise will not improve my condition”, “exercise is boring and monotonous”, and “it’s just not worth the time it takes to exercise” (Roberton, Bucks, Skinner, Allison, & Dunlop, 2011). Identification of these barriers can facilitate the participation of these individuals improving their wellness and long-term health (Roberton et al., 2011; Scelza et al., 2005). Clearly, a more concerted effort is warranted in promoting the benefits of exercise and identifying exercise options that are attractive, attainable and sustainable in the SCI population.

Hettinga and Andrews in their review of fitness implications for health and exercise suggested some strategies to stimulate training compliance, which includes VR exercise (Hettinga & Andrews, 2008a). Chuang and colleagues found that the maintenance of endurance, the increase in target intensity and total energy expenditure in cardiopulmonary exercise programmes could be assisted by incorporating VR technology (Chuang et al., 2003; Chuang et al., 2006). Several authors have also reported enhancement of enjoyment and energy, feeling of calmness and reduced tiredness and tension in VR-assisted exercise programmes participants (Chen et al., 2009; Kizony et al., 2005; Plante et al., 2003; Smith et al., 1998). With VR technology, people with SCI (and clinicians) are able to get feedback of training performance, modify training targets and evaluate outcomes more objectively.

The second experiment in this thesis compared the acute cardiorespiratory responses during hybrid FES cycling between outdoor environment and a simulated environment indoors using VR. Outdoor cycling was chosen to enable better comparison of the simulated environment. Furthermore, there is an increasing trend for people to undertake outdoor physical activity and exercise. Anecdotal evidence from people with SCI suggests that nature experiences and outdoor pursuits are valued ingredients in rehabilitation programmes particularly for those who were outdoor enthusiasts pre-injury and/or who sustained their injury during outdoor pursuits. Model SCI centres in North America offer outdoor activities as components of SCI rehabilitation (Beringer, 2004).

In the second study, even though there were technical differences during indoor and outdoor cycling with regards to the different strategies and techniques employed during hybrid FES cycling in the different environment, cardiorespiratory responses during the 30-minute moderate-intensity hybrid FES cycling did not show any significant differences. This is an important acknowledgement that similar physiological benefits can be achieved through both indoor and outdoor exercises. It is interesting that there was also no statistical difference in perceptual-psychological responses. It is important to note that the subjects in the second study were regular FES cycling practitioners in Sydney, Australia and have engaged in outdoor hybrid FES cycling before. These findings imply that combining an “effective whole-body exercise” method and VR technology may provide new alternatives and opportunities for promotion of exercise participation in people with SCI since these modes gave similar dose potency and self-perceived effort.

The third study in this thesis found improved physiological and psychological outcomes in novice FES users following a six-week VR-assisted hybrid FES exercise training programme. The third study was conducted in a laboratory setting in Kuala Lumpur, Malaysia. All the subjects except for one have not had prior exposure to FES-assisted exercise. The one who had FES experience, only had a single exposure to FES-LCE in Australia three years before. All the subjects reported positive experience with the VR-assisted hybrid FES training programme as detailed in Chapter 5. Despite being exercise and FES novices, the subjects were able to complete high-intensity interval exercise sessions with excellent compliance and adherence to schedule. There were no subject drop out and minimal rescheduling of training sessions.

6.1.4 Benefits of exercise for people with SCI

The research subjects who participated in the experiments were given explanation on the benefits of exercise to people with SCI and the whole-body exercise benefit with arm and leg exercise. Some of the participants were quite well-informed having had prior exercise experience.

The first study found higher oxygen uptakes during maximal hybrid FES cycling, higher oxygen uptakes, and greater cardiovascular demands during submaximal exercise strongly indicating that greater gains of aerobic fitness are achievable through hybrid FES cycling.

In the second study, the subjects were required to complete 30-minute moderate-intensity hybrid FES cycling in both indoor and outdoor environment and the subjects were able to complete the tasks. The ACSM recommend that people with SCI exercise three to five times weekly for 20 to 60 minutes at moderate-vigorous exercise intensities (*ACSM's Guidelines for Exercise Testing and Prescription*, 2006; Garber et al., 2011). It is clear that people with SCI are able to meet this exercise recommendation based on the experiments performed in this thesis.

The cardiorespiratory and cardiovascular benefits are evident, and so are the psychological benefits. The third study revealed statistically significant positive mood and post-exercise feeling states outcomes following exercise training. The outcomes of positive psychological benefit is an important finding which suggest that the exercise modalities employed in this series of experiments are acceptable, enjoyable and contribute to the exercise compliance, motivation and adherence in people with SCI.

The most important benefit of exercise in people with SCI and in the context of this thesis is the possible reduction of cardiometabolic risk factors in the prevention of cardiovascular disease with high-intensity hybrid FES cycling. Wahman and colleagues screened 134 people with paraplegia of at least one year duration in Stockholm, Sweden for cardiovascular disease risk using the Systematic Coronary Risk Evaluation (SCORE) and the Framingham Risk Equation (FRE) and found that almost one-third of persons screened were eligible for cardiovascular disease risk intervention (Wahman et al., 2011). The authors concluded that the unacceptably high levels of risk observed in the study indicated the need for routine clinical assessment of CVD hazards in people with SCI and that evidence-based multifactorial health promotion programmes must be developed and implemented. The risk factors in the screening included lipid profiles and there is evidence that more favourable lipid profiles were seen in people with a higher physical capacity (Dallmeijer et al., 1999; De Groot et al., 2008). The third experiment showed no change in LDL and triglycerides levels but non-parametric ANOVA testing revealed significant increase of HDL ($p<0.05$) following the 6-week high-intensity interval hybrid FES cycling training. The HDL is believed to be an inhibitor of artherogenesis and have cardiovascular protective effects (National Cholesterol Education Program Expert Panel on Detection & Treatment of High Blood Cholesterol in, 2002). Even though the overall finding in the third study suggests that six weeks exercise training was not sufficient to modify the cardiometabolic risk in this group of SCI subjects, the findings indicate that the training intervention was somewhat effective for the SCI individuals with demonstrated cardiovascular risk at baseline.

Glucose intolerance occurs more frequently in people with SCI than in able-bodied population (Bauman & Spungen, 1994; Duckworth et al., 1980). Impaired glucose tolerance usually is associated with insulin resistance (Bauman et al., 2012; Bauman & Spungen, 2000). The mechanism leading to impaired glucose tolerance in people with SCI has not been thoroughly studied but it is thought that it is highly linked to muscle paralysis. The predominant peripheral action of insulin is upon muscles and animal studies have indicated that denervated muscles have been shown to cause insulin resistance (Bauman & Spungen, 2000; Buse & Buse, 1959). Because diabetes and pre-diabetes are artherogenic risk factors for cardiovascular disease, glucose metabolism was also studied concurrently with lipid metabolism in the third experiment in this thesis. In the third study, three subjects had impaired glucose tolerance and of the three, only one subject had reduction in the 2-hour post-prandial glucose level to below acceptable level. There were decreases in the post-training fasting and 2-hour post-prandial glucose values; again there was no significant change. Unlike lipid metabolism which had shown inconsistencies in the effects of exercise in its metabolism, previous studies of carbohydrate metabolism had shown significant improvements in glucose tolerance and insulin response in FES leg cycling studies (Griffin et al., 2009; Hjeltnes et al., 1998; Jeon et al., 2010; Jeon et al., 2002). Despite the hybrid high-intensity interval training employed in the exercise protocol in the third experiment, there was no change in glucose tolerance. Based on previous positive outcomes with longer duration of exercise programme, it was concluded that a 6-week exercise programme was too short to induce any change to carbohydrate metabolism. Modification of exercise protocol, longer exercise duration or increased length of programme should all be considered in future studies.

6.1.5 Exercise and technology for health promotion people with SCI

The experiments in this thesis showed a continuum of work that first compared and discussed the available exercise modalities and their physiological outcomes, and identifying an optimal exercise mode for people with SCI. This was followed by evaluation of the exercise mode in different environments and introducing another rehabilitation assistive technology into the evaluation i.e. the VR technology. Finally, an outcome study of a training programme of combined FES technology and VR technology was carried out incorporating the recommended hybrid FES cycling which provided “whole-body fitness benefit” and high-intensity interval training which in the recent years viewed as being an alternative to traditional endurance-based training to provide effective physiological adaptations in healthy and clinical populations. This author believes that this series of experiments although not in total had provided some insight into the complexities of exercise in people with SCI, exercise modalities and use of assistive technologies in exercise and rehabilitation, and the benefits of exercise for people with SCI.

6.2 Clinical implications

Several clinical implications can be drawn from the literature review and studies performed in this thesis, in relation to exercise and technology-assisted exercise for health promotion in people with SCI.

First, exercise for people with SCI should not be viewed as an option but a prescription and lifelong lifestyle adoption. The importance of exercise for health maintenance, promotion and prevention of cardiometabolic risks following SCI including options and strategies for exercise must be incorporated into patient education programmes during the various phases of SCI rehabilitation and follow-up.

The second implication that may be drawn from this thesis is that it is important for rehabilitation professionals to broaden their services to include health promotion interventions in addition to their primary roles of managing impairment and disability. Health and wellness for the population with disability including SCI depends on the advocacy of the professionals who are most knowledgeable about their patients' needs (DeLisa, 2005). Therefore rehabilitation professionals should be advocates of exercise for the clinical populations in particular those with chronic disability such as SCI.

Third, the use of FES-LCE on its own, even though promotes central haemodynamic responses, does not result in high peak and submaximal oxygen uptakes. The cardiorespiratory responses are not sufficient to produce a training effect. Therefore, as demonstrated in Chapter 3, the addition of ACE to FES-LCE provided a boost to the aerobic metabolism during peak and submaximal exercise suggesting a greater potential to provide "whole-body" training benefit and fitness in people with SCI.

The fourth implication concerns the use of technology for exercise and rehabilitation. The results from the studies in this thesis strongly indicate positive physiological and psychological benefits with the use of FES-assisted exercise and VR-assisted exercise. Together with the need to broaden scope of services to include health promotion for people with SCI, rehabilitation professionals should keep abreast with advancement of assistive technology and techniques in exercise and rehabilitation.

Finally, from the literature and outcomes from the training study i.e. Chapter 5, modification of cardiometabolic risk in terms of changes in lipid and carbohydrate metabolism as a result of FES training is non-conclusive. Even with high-intensity interval training, a 6-week training programme was too short to modify the cardiometabolic risk factors. A longer training duration and meeting the ACSM training frequency standards as recommended by ACSM is warranted. A change in FES stimulation protocol to allow longer and/or more intense stimulation through the use of low cadence protocol or higher intensities may be considered to induce greater muscle metabolism. A mixed mode of training, which includes resistance exercise, may provide the missing element in the training protocol.

Chapter Seven

Conclusions

7.1 Objectives and hypotheses

The overall purpose of this thesis was to assess cardiorespiratory responses and training effects during acute and chronic hybrid FES cycling exercise in individuals with SCI. One objective was to compare the acute cardiorespiratory and metabolic exercise responses and the indices of cardiac performance during submaximal and maximal exercises in four exercise modes. Another objective was to compare the acute physiological and psychological responses between outdoor hybrid FES cycling and indoor virtual reality-FES cycling. The third and final objective was to investigate the outcome of a training programme consisting FES and VR technology on aerobic fitness, lipid profiles, glucose tolerance and psychological perception.

To satisfy the objectives, the following hypotheses were proposed:

h1: *Submaximal steady-state and peak cardiorespiratory responses during hybrid FES cycling exercise would be higher than those elicited during ACE alone or FES-LCE alone.*

This hypothesis was **accepted.** Combined arm and leg exercise clearly demonstrated significantly higher peak and submaximal oxygen uptake and heart rate compared to FES-LCE alone. Steady-state hybrid FES cycling evoked 99-148% higher oxygen uptake, 31-36% higher cardiac output and 23-56% higher heart rate than FES-LCE alone as demonstrated in Chapter 3.

h2: *There would be no differences of cardiorespiratory and perceptual-psychological responses during steady-state submaximal exercise between* *indoor VR-enhanced "hybrid" exercise versus outdoor overground "hybrid" exercise.*

This hypothesis was **accepted**. There was no difference between indoor and outdoor hybrid FES cycling cardiorespiratory and perceptual-psychological responses as shown in Chapter 4.

h3: *Six weeks of indoor 'hybrid' high-intensity interval training would produce greater aerobic fitness and other beneficial physiological and psychological adaptations compared to pre-training.*

This hypothesis was **accepted**. The training produced greater aerobic fitness (16% increase), improved mood and post-exercise feeling states post-training. Biochemical adaptations of lipid and carbohydrate metabolism did not occur within the limited duration of this study.

7.2 Limitations

7.2.1 Study 3 was a continuum from Studies 1 and 2. However due to institutional requirement requiring logistical change, the demographics of research participants in Study 3 who were SCI participants sampled in Kuala Lumpur, Malaysia were different from the research participants in Studies 1 and 2 who were sampled in Sydney, Australia.

7.2.2 Non-invasive assessment techniques were used to measure several of the cardiovascular and haemodynamic variables. In addition, some variables were derived from indirect measurements.

7.2.3 Small sample sizes may have limited the statistical power of the results reported in this thesis. However, small sample sizes have always been a challenge for the majority of research involving the people with SCI.

7.2.4 The subjects recruited for Study 3 had not undergone any substantial FES cycling exercise training or even any exercise prior to their participation, which resulted in a large range of exercise ability and perception between subjects.

7.2.5 The questionnaires used for the perceptual-psychological assessments of exercise experience have not been validated in a Malaysian population

7.2.6 At various points in this manuscript and interalia Chapter 3, it was noted that some modes of exercise had higher cardiorespiratory demands than others, the reader is cautioned to note that a higher or lower acute cardiorespiratory demand may not necessarily transfer to a training outcome

7.3 Future research and directions

7.3.1 A randomized-controlled trial design is to be employed in future research.

7.3.2 A similar research as those developed within this thesis should be conducted, employing higher number of participants.

7.3.3 Replication of indoor VR versus outdoor hybrid FES cycling should be done in an SCI sample in Kuala Lumpur, Malaysia and compared with the Australian population.

7.3.4 Exploratory study on dose-response in FES cycling and its relationship with level of lesions, completeness of injury and other factors

7.3.5 Assessment of lifestyle physical activity should be included in future studies involving exercise.

7.3.6 Future studies on lipid profile should include obesity profiling, measurement of abdominal circumference, measurement of visceral fat radiologically, measurement of C-reactive protein and cardiac risk assessment.

7.3.7 Future studies on carbohydrate metabolism should include measurements of plasma insulin.

7.3.8 Diet and food diary should be included in future studies involving measurements of post-exercise lipid profile and carbohydrate metabolism.

7.3.9 Future studies requiring limb volume measurement should employ optoelectronic automated methods.

7.4 Conclusions

In accordance with the primary and secondary objectives, the following overall conclusions were drawn:

7.4.1 Hybrid FES cycling should be prescribed for people with SCI for long-term health maintenance and prevention of secondary health conditions.

7.4.2 Virtual reality provides an alternative for enhancement of exercise experience and adherence.

7.4.3 Structured exercise training results in improved aerobic fitness, mood and feeling states.

7.4.4 Indoor and outdoor exercise training produce no different training benefits.

7.4.5 Exercise training has the potential to modify cardiometabolic risk in people with SCI.

7.4.6 ACE alone is not the best exercise training option for people with SCI.

7.4.7 FES-LCE does not provide whole-body fitness benefit in people with SCI.

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Appendices

Appendix 1- Ethics approval

The University of Sydney

Human Research Ethics Committee
Web: http://www.usyd.edu.au/ethics/human

ABN 15 211 513 464

Marietta Coutinho
Deputy Manager
Human Research Ethics Administration

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Mailing Address:
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The University of Sydney
NSW 2006 AUSTRALIA

Ref: PB/PE

27 October 2009

Associate Professor Glen Davis
Clinical Exercise and Rehabilitation Unit
Discipline of Exercise and Sport Sciences
Cumberland Campus - C42
The University of Sydney
Email: g.davis@usyd.edu.au

Dear Professor Davis

I am pleased to inform you that the Human Research Ethics Committee (HREC) at its meeting held on 15 September 2009 approved your protocol entitled **"Acute Responses to Arm and Leg Exercise in Spinal Cord Injury (SCI)".**

Details of the approval are as follows:

Ref No.:	***09-2009/12147***
Approval Period:	***September 2009 to September 2010***
Authorised Personnel:	***Associate Professor Glen Davis***
	Associate Professor James Middleton
	Dr Che Fornusek
	Dr Nazirah Hasnan

The HREC is a fully constituted Ethics Committee in accordance with the *National Statement on Ethical Conduct in Research Involving Humans-March 2007* under *Section 5.1.29*

The approval of this project is **conditional** upon your continuing compliance with the *National Statement on Ethical Conduct in Research Involving Humans*. We draw to your attention the requirement that a report on this research must be submitted every 12 months from the date of the approval or on completion of the project, whichever occurs first. Failure to submit reports will result in withdrawal of consent for the project to proceed.

Chief Investigator / Supervisor's responsibilities to ensure that:

(1) All serious and unexpected adverse events should be reported to the HREC as soon as possible.

(2) All unforeseen events that might affect continued ethical acceptability of the project should be reported to the HREC as soon as possible.

(3) The HREC must be notified as soon as possible of any changes to the protocol. All changes must be approved by the HREC before continuation of the research project. These include:-
- If any of the investigators change or leave the University.
- Any changes to the Participant Information Statement and/or Consent Form.

(4) All research participants are to be provided with a Participant Information Statement and Consent Form, unless otherwise agreed by the Committee. The Participant Information Statement and Consent Form are to be on University of Sydney letterhead and include the full title of the research project and telephone contacts for the researchers, unless otherwise agreed by the Committee and the following statement must appear on the bottom of the Participant Information Statement. *Any person with concerns or complaints about the conduct of a research study can contact the Deputy Manager, University of Sydney, on (02) 8627 8176 (Telephone); (02) 8627 8177 (Facsimile) or human.ethics@usyd.edu.au (Email).*

(5) Copies of all signed Consent Forms must be retained and made available to the HREC on request.

(6) It is your responsibility to provide a copy of this letter to any internal/external granting agencies if requested.

(7) The HREC approval is valid for four (4) years from the Approval Period stated in this letter. Investigators are requested to submit a progress report annually.

(8) A report and a copy of any published material should be provided at the completion of the Project.

Yours sincerely

Associate Professor Philip Beale
Chairman
Human Research Ethics Committee

Copy: Dr Nazirah Hasnan nhas7882@uni.sydney.edu.au

Encl. Approved Participant Information Statement
Approved Participant Consent Form
Approved Advertising Flyer

The University of Sydney

Human Research Ethics Committee
Web: http://www.usyd.edu.au/ethics/human

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Ref: IM/AS

20 January 2010

Associate Professor Glen Davis
Rehabilitation Research Centre
Cumberland Campus – C42
The University of Sydney
Email: g.davis@usyd.edu.au

Dear Associate Professor Davis

Thank you for your correspondence dated 10 December 2009 addressing comments made to you by the Human Research Ethics Committee (HREC). After considering the additional information, the Executive Committee at its meeting held on **14 January 2010** approved your protocol entitled ***Comparison of physiological responses and perceptual experiences between outdoor arm and FES-leg exercise and indoor Virtual Reality (VR)-enhanced exercise after spinal cord injury.***

Details of the approval are as follows:

Ref No.:	***01-2010/12385***
Approval Period:	***January 2010 – January 2011***
Authorised Personnel:	***Associate Professor Glen Davis***
	Dr James Middleton
	Dr Che Fornusek
	Nazirah Hasnan

The HREC is a fully constituted Ethics Committee in accordance with the *National Statement on Ethical Conduct in Research Involving Humans-March 2007* under *Section 5.1.29*

The approval of this project is **conditional** upon your continuing compliance with the *National Statement on Ethical Conduct in Research Involving Humans*. We draw to your attention the requirement that a report on this research must be submitted every 12 months from the date of the approval or on completion of the project, whichever occurs first. Failure to submit reports will result in withdrawal of consent for the project to proceed.

Chief Investigator / Supervisor's responsibilities to ensure that:

(1) All serious and unexpected adverse events should be reported to the HREC as soon as possible.

(2) All unforeseen events that might affect continued ethical acceptability of the project should be reported to the HREC as soon as possible.

(3) The HREC must be notified as soon as possible of any changes to the protocol. All changes must be approved by the HREC before continuation of the research project. These include:-
- If any of the investigators change or leave the University.
- Any changes to the Participant Information Statement and/or Consent Form.

(4) All research participants are to be provided with a Participant Information Statement and Consent Form, unless otherwise agreed by the Committee. The Participant Information Statement and Consent Form are to be on University of Sydney letterhead and include the full title of the research project and telephone contacts for the researchers, unless otherwise agreed by the Committee and the following statement must appear on the bottom of the Participant Information Statement. *Any person with concerns or complaints about the conduct of a research study can contact the Manager, Ethics Administration, University of Sydney, on (02) 8627 8176 (Telephone); (02) 8627 8177 (Facsimile) or human.ethics@usyd.edu.au (Email).*

(5) Copies of all signed Consent Forms must be retained and made available to the HREC on request.

(6) It is your responsibility to provide a copy of this letter to any internal/external granting agencies if requested.

(7) The HREC approval is valid for four (4) years from the Approval Period stated in this letter. Investigators are requested to submit a progress report annually.

(8) A report and a copy of any published material should be provided at the completion of the Project.

Yours sincerely

Associate Professor Ian Maxwell
Chairman
Human Research Ethics Committee

cc: *Nazirah Hasnan, nhas7882@uni.sydney.edu.au*

Approved Documents
The Exercise-induced Feeling Inventory (Gauvin L & Rejeski WJ, 1993)
The Activation-Deactivation Adjective Check (Thayer RE, 1986)
The Virtual Reality Symptom Questionnaire (Ames SL, Wolffsohn JS et al, 2005)

Encl. Approved Participant Information Statement
Approved Participant Consent Form
Approved Advertisement

UNIVERSITI MALAYA

PUSAT PERUBATAN UM

MEDICAL ETHICS COMMITTEE
UNIVERSITY MALAYA MEDICAL CENTRE
ADDRESS: LEMBAH PANTAI, 59100 KUALA LUMPUR, MALAYSIA
TELEPHONE: 03-79493209 FAXIMILE: 03-79494638

NAME OF ETHICS COMMITTEE/IRB: Medical Ethics Committee, University Malaya Medical Centre **ADDRESS:** LEMBAH PANTAI 59100 KUALA LUMPUR	**ETHICS COMMITTEE/IRB REFERENCE NUMBER:** 889.12
PROTOCOL NO: **TITLE:** Outcomes of a short-term fes-cycling exercise programme in a spinal cord injured population in Malaysia	
PRINCIPAL INVESTIGATOR: Dr. Nazirah Hasnan **TELEPHONE:** **KOMTEL:**	**SPONSOR:**

The following item [✓] have been received and reviewed in connection with the above study to be conducted by the above investigator.

[✓] Borang Permohonan Penyelidikan — Ver date:
[✓] Study Protocol — Ver date:
[✓] Investigator's Brochure — Ver date:
[✓] Patient Information Sheet
[✓] Consent Form
[ ] Questionnaire
[✓] Investigator(s) CV's (Dr. Nazirah Hasnan)

and have been [✓]

[✓] Approved
[ ] Conditionally approved (identify item and specify modification below or in accompanying letter)
[ ] Rejected (identify item and specify reasons below or in accompanying letter)

Comments:

Investigator are required to:

1) *follow instructions, guidelines and requirements of the Medical Ethics Committee.*
2) *report any protocol deviations/violations to Medical Ethics Committee.*
3) *provide annual and closure report to the Medical Ethics Committee.*
4) *comply with International Conference on Harmonization – Guidelines for Good Clinical Practice (ICH-GCP) and Declaration of Helsinki.*
5) *note that Medical Ethics Committee may audit the approved study.*

Date of approval: 23rd NOVEMBER 2011

c.c Head
Department of Rehabilitation Medicine

Deputy Dean (Research)
Faculty of Medicine

Secretary
Medical Ethics Committee
University Malaya Medical Centre

PROF. DATUK LOOI LAI MENG
Chairman
Medical Ethics Committee

Appendix 2 – Consent forms

The University of Sydney

Clinical Exercise and Rehabilitation Unit
Exercise, Health, & Performance FRG
Faculty of Health Sciences

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Clinical Exercise and Rehabilitation Unit
Exercise Health and Performance FRG

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Web: www.usyd.edu.au

PARTICIPANT CONSENT FORM

I, ...[PRINT NAME], give consent to my participation in the research project:

TITLE: ACUTE RESPONSES TO ARM AND LEG EXERCISE IN SPINAL CORD INJURY(SCI)

In giving my consent I acknowledge that:

1. The procedures required for the project and the time involved (including any inconvenience, risk discomfort or side effect, and of their implications) have been explained to me, and any questions I have about the project have been answered to my satisfaction.

2. I have read the Participant Information Statement and have been given the opportunity to discuss
the information and my involvement in the project with the researcher/s.

3. I understand that I can withdraw from the study at any time, without affecting my relationship with
the researcher(s) or the University of Sydney now or in the future.

4. I understand that my involvement is strictly confidential and no information about me will be used in any way that reveals my identity.

5. I understand that being in this study is completely voluntary – I am not under any obligation to consent.

Signed: ....

Name: ....

Date: ....

The University of Sydney

Clinical Exercise and Rehabilitation Unit
Exercise, Health, & Performance FRG
Faculty of Health Sciences

Assoc Prof Glen Davis
Director,
Clinical Exercise and Rehabilitation Unit
Exercise Health and Performance FRG

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Web: www.usyd.edu.au

PARTICIPANT CONSENT FORM

I, ...[PRINT NAME], give consent to my participation in the research project:

TITLE: COMPARISON OF PHYSIOLOGICAL AND PSYCHOLOGICAL RESPONSES BETWEEN OUTDOOR FES-CYCLING AND INDOOR VIRTUAL REALITY-ENHANCED FES-CYCLING IN SPINAL CORD INJURY

In giving my consent I acknowledge that:

1. The procedures required for the project and the time involved (including any inconvenience, risk discomfort or side effect(s), and of their implications) have been explained to me, and any questions I have about the project have been answered to my satisfaction.

2. I have read the Participant Information Statement and have been given the opportunity to discuss the information and my involvement in the project with the researcher(s).

3. I understand that I can withdraw from the study at any time, without affecting my relationship with the researcher(s) or the University of Sydney now or in the future.

4. I understand that my involvement is strictly confidential and no information about me will be used in any way that reveals my identity.

5. I understand that being in this study is completely voluntary – I am not under any obligation to consent.

Signed: ....

Name: ....

Date: ....

UNIVERSITY MALAYA MEDICAL CENTRE

CONSENT BY PATIENT FOR CLINICAL RESEARCH

I, ...
Identity Card No...
(Name of Patient)
of ....
(Address)
hereby agree to take part in the clinical research (clinical study/questionnaire study/drug trial) specified below:

Title of Study: OUTCOMES OF A SHORT-TERM FES-CYCLING EXERCISE PROGRAMME IN A SPINAL CORD INJURED POPULATION IN MALAYSIA

the nature and purpose of which has been explained to me by
DR. NAZIRAH HASNAN, (Senior Lecturer & Rehabilitation Physician)
(Name & Designation of Doctor)

and interpreted by ....
(Name & Designation of Interpreter)

to the best of his/her ability in .... language/dialect.

I have been told about the nature of the clinical research in terms of methodology, possible adverse effects and complications (as per patient information sheet). After knowing and understanding all the possible advantages and disadvantages of this clinical research, I voluntarily consent of my own free will to participate in the clinical research specified above.

I understand that I can withdraw from this clinical research at any time without assigning any reason whatsoever and in such a situation shall not be denied the benefits of usual treatment by the attending doctors.

Date: ....   Signature or Thumbprint ....
(Patient)

IN THE PRESENCE OF

Name ....)
)
Identity Card No. ....)   Signature

(Witness for Signature of Patient)
Designation ....)

I confirm that I have explained to the patient the nature and purpose of the above-mentioned clinical research.

Date ....   Signature ....
(Attending Doctor)

CONSENT BY PATIENT FOR CLINICAL RESEARCH

R.N.
Name
Sex
Age
Unit

UNIVERSITY MALAYA MEDICAL CENTRE

KEIZINAN OLEH PESAKIT UNTUK PENYELIDIKAN KLINIKAL

Saya,..
No. Kad Pengenalan ....
(Nama Pesakit)

beralamat...
(Alamat)

dengan ini bersetuju menyertai dalam penyelidikan klinikal (pengajian klinikal/pengajian soal-selidik/percubaan ubat-ubatan) disebut berikut:

TajukPenyelidikan: OUTCOMES OF A SHORT-TERM FES-CYCLING EXERCISE PROGRAMME IN A SPINAL CORD INJURED POPULATION IN MALAYSIA

yang mana sifat dan tujuannya telah diterangkan kepada saya oleh DR. NAZIRAH HASNAN (Pensyarah Kanan dan Pakar Perubatan Pemulihan)

mengikut terjemahan ....
(Nama & Jawatan Penterjemah)

.... yang telah menterjemahkan kepada saya dengan sepenuh kemampuan dan kebolehannya di dalam Bahasa / loghat...

Saya telah diberitahu bahawa dasar penyelidikan klinikal dalam keadaan methodologi, risiko dan komplikasi (mengikut kertas maklumat pesakit). Selepas mengetahui dan memahami semua kemungkinan kebaikan dan keburukan penyelidikan klinikal ini, saya merelakan/mengizinkan sendiri menyertai penyelidikan klinikal tersebut di atas.

Saya faham bahawa saya boleh menarik diri dari penyelidikan klinikal ini pada bila-bila masa tanpa memberi sebarang alasan dalam situasi ini dan tidak akan dikecualikan dari kemudahan rawatan dari doktor yang merawat.

Tarikh: .... Tandatangan/Cap Jari ....
(Pesakit)

DI HADAPAN

Nama ....)
)
No. K/P...) Tandatangan
....
) *(Saksi untuk Tandatangan Pesakit)*
Jawatan ....)

Saya sahkan bahawa saya telah menerangkan kepada pesakit sifat dan tujuan penyelidikan klinikal tersebut di atas.

Tarikh: .... Tandatangan ....
(Doktor yang merawat)

KEIZINAN OLEH PESAKIT UNTUK PENYELIDIKAN KLINIKAL

No. Pend.
Nama
Jantina
Umur
Unit

Appendix 3 – Flyers

The University of Sydney

Clinical Exercise and Rehabilitation Unit
Exercise, Health, & Performance FRG
Faculty of Health Sciences

HYBRID CYCLING EXERCISE FOR SPINAL CORD INJURY

You are invited to participate in a research study involving functional electrical stimulation (FES)-assisted exercise.

We are investigating aerobic exercise responses in four exercise modalities for **spinal cord injured individuals**. We need volunteers aged 18-65 who are willing to come for eight 3-hourly visits to our lab.

You will need to do arm cycling exercise (ACE), FES-leg cycling exercise (LCE), combined ACE & FES-LCE and the hybrid FES-cycle bike for no more than 10 minutes per exercise.

If you are interested, please contact:
Dr. Nazirah Hasnan (93519628)
Dr. Che Fornusek (93519200)
Assoc Prof Glen Davis (93519466)

A detailed patient information sheet is available for your reference

The University of Sydney

Clinical Exercise and Rehabilitation Unit
Exercise, Health, & Performance FRG
Faculty of Health Sciences

VIRTUAL REALITY-FES EXERCISE FOR SPINAL CORD INJURY

You are invited to participate in a research study involving virtual reality (VR) and functional electrical stimulation (FES) cycling.

We are investigating aerobic exercise responses and the cycling experience of people with spinal cord injury. We need volunteers aged 18-65 who are willing to come for nine 2-hourly visits to our lab.

You will need to do 30 minutes of indoor VR-enhanced cycling on a stationary FES-bike and outdoor cycling around the Faculty of Health Sciences campus on separate visits.

If you are interested, please contact:
Dr. Nazirah Hasnan (93519628)
Dr. Che Fornusek (93519200)
Assoc Prof Glen Davis (93519466)

The University of Sydney
Clinical Exercise and Rehabilitation Unit
Exercise, Health, & Performance FRG
Faculty of Health Sciences

UNIVERSITY OF MALAYA
The Leader in Research & Innovation
Department of Rehabilitation Medicine
Faculty of Medicine &
University of Malaya Medical Centre

OUTCOMES OF A SHORT-TERM FES-CYCLING EXERCISE PROGRAMME IN A SPINAL CORD INJURED POPULATION IN MALAYSIA

INTERESTED IN BECOMING MORE FIT? INTERESTED IN IMPROVING YOUR HEALTH?

You are invited to participate in a collaborative research study between University of Sydney and University of Malaya. The research involves functional electrical stimulation (FES) cycling on a hybrid (arm & leg) FES bike.

We are investigating aerobic exercise responses, lipid and glucose metabolisms; and exercise experience of people with spinal cord injury. We need volunteers aged 18-65 who are willing to come for an indoor FES cycling exercise programme 2-3 visits per week over 6 weeks. Each visit will take a maximum of 2 hours of your time. You will be required to cycle for 36-52 minutes each visit. A fitness test and blood investigations will be done before and after the exercise programme.

You qualify as a subject if you:

- have spinal cord injury, ASIA A,B,C with lesions from T1 to T12
- SCI at least 1 year ago
- have no medical conditions preventing exercise
- respond to FES
- do not have history of lower limb fracture
- do not have severe lower limb contractures, excessive spasms, osteoporosis
- have good hand functions
- able to commit to a continuous 6 weeks exercise programme

A thorough physical examination will be done prior to your enrolment into the study

If you are interested or for further details, please contact:

Dr. Nazirah Hasnan (012-3286844, nazirah@um.edu.my)
Prof Ruby Husain (ruby@ummc.edu.my)
Prof Glen Davis (g.davis@usyd.edu.au)

A detailed patient information sheet is available for your reference

Appendix 4 – Questionnaires

rating	description
0	NOTHING AT ALL
0.5	VERY, VERY LIGHT
1	VERY LIGHT
2	FAIRLY LIGHT
3	MODERATE
4	SOMEWHAT HARD
5	HARD
6	
7	VERY HARD
8	
9	
10	VERY VERY HARD (MAXIMAL)

The Exercise-Induced Feeling Inventory (EFI)

0 = Do Not Feel (DNF)
1 = Feel Slightly
2 = Feel Moderately
3 = Feel strongly
4 = Feel Very Strongly (FVS)

	Item	Score						
1.	Refreshed	DNF 0	1	2	3	4 FVS		
2.	Calm	DNF 0	1	2	3	4 FVS		
3.	Fatigued	DNF 0	1	2	3	4 FVS		
4.	Enthusiastic	DNF 0	1	2	3	4 FVS		
5.	Relaxed	DNF 0	1	2	3	4 FVS		
6.	Energetic	DNF 0	1	2	3	4 FVS		
7.	Happy	DNF 0	1	2	3	4 FVS		
8.	Tired	DNF 0	1	2	3	4 FVS		
9.	Revived	DNF 0	1	2	3	4 FVS		
10.	Peaceful	DNF 0	1	2	3	4 FVS		
11.	Worn-out	DNF 0	1	2	3	4 FVS		
12.	Upbeat	DNF 0	1	2	3	4 FVS		

The EFI consists of 4 distinct subscales. Subscale scores are obtained by summing or averaging the numerical values chosen for the adjectives within a particular subscale. The four subscales include:
(1) Positive engagement (Items 4,7 & 12)
(2) Revitalization (Items 1,6 & 9)
(3) Tranquility (Items 2, 5 & 10)
(4) Physical Exhaustion (Items 3, 8 & 11)

The Activation-Deactivation Adjective Check List (AD ACL)

Thayer, R.E., 1986. Activation-Deactivation Adjective Check List: Current overview and structural analysis. *Psychological Reports* **58**, pp. 607–614

Each of the words describes feelings or mood. Please use the rating scale next to each word to describe your feelings at this moment. Circle the appropriate answer.

1.	active	vv	v	?	no
2.	placid	vv	v	?	no
3.	sleepy	vv	v	?	no
4.	jittery	vv	v	?	no
5.	energetic	vv	v	?	no
6.	intense	vv	v	?	no
7.	calm	vv	v	?	no
8.	tired	vv	v	?	no
9.	vigorous	vv	v	?	no
10.	at-rest	vv	v	?	no
11.	drowsy	vv	v	?	no
12.	fearful	vv	v	?	no
13.	lively	vv	v	?	no
14.	still	vv	v	?	no
15.	wide-awake	vv	v	?	no
16.	clutched-up	vv	v	?	no
17.	quiet	vv	v	?	no
18.	full-of-pep	vv	v	?	no
19.	tense	vv	v	?	no
20.	wakeful	vv	v	?	no

vv	v	?	no	Definitely feel
vv	**v**	?	no	Feel slightly
vv	v	**?**	no	Cannot decide
vv	v	?	**no**	Definitely do not feel

Example:

relaxed **vv** v ? no	If you circle the **double check (vv)** it means that you *definitely* feel relaxed *at the moment*
relaxed vv **v** ? no	If you circle the **single check (v)** it means that you feel slightly relaxed *at the moment.*
relaxed vv v **?** no	If you circled the **question mark (?)** it means that the word does not apply or you cannot decide if you feel relaxed *at the moment.*
relaxed vv v ? **no**	If you circled the **no** it means that you are *definitely not relaxed at the moment*

QUEST 2.0 (5 point numerical scale)				
1	2	3	4	5
Not satisfied at all	Not very satisfied	More or less satisfied	Quite satisfied	Very satisfied

How satisfied are you with:

Dimensions of the BerkelBike (size, height, length, width)	1	2	3	4	5
Weight of the BerkelBike	1	2	3	4	5
Ease of adjusting the BerkelBike	1	2	3	4	5
Safety of the BerkelBike (Does it feel safe and secure)	1	2	3	4	5
Ease of use (Is it easy to use?)	1	2	3	4	5
Comfort of the BerkelBike (Does it feel comfortable?)	1	2	3	4	5
Effectiveness of the BerkelBike (Does it give you a good exercise/workout?)	1	2	3	4	5

QUEST 2.0 (The Quebec User Evaluation of Satisfaction with Assistive Technology) consists of 12 questions related to satisfaction with an assistive technology device and satisfaction with assistive technology service provision (Demers, Weiss-Lambrou, & Ska, 2002).

Dimensions
Weight
Adjustments
Safety
Durability
Easy to use
Comfort
Effectiveness
Service delivery
Repairs/servicing
Professional service
Follow-up services

THE VIRTUAL REALITY SYMPTOM QUESTIONNAIRE (VRSQ)

SUBJECT:

DATE:

TEST:

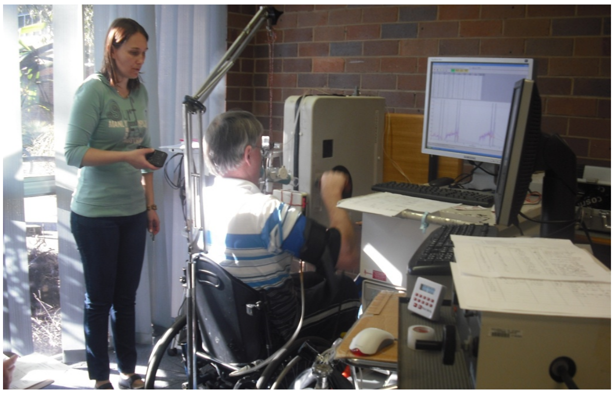
CORRECTION: CL SPECS NONE

GENERAL BODY SYMPTOMS							
	None	Slight		Moderate		Severe	
General discomfort	0	1	2	3	4	5	6
Fatigue	0	1	2	3	4	5	6
Boredom	0	1	2	3	4	5	6
Drowsiness	0	1	2	3	4	5	6
Headache	0	1	2	3	4	5	6
Dizziness	0	1	2	3	4	5	6
Difficulty concentrating	0	1	2	3	4	5	6
Nausea	0	1	2	3	4	5	6

EYE RELATED SYMPTOMS							
	None	Slight		Moderate		Severe	
Tired eyes	0	1	2	3	4	5	6
Sore / aching eyes	0	1	2	3	4	5	6
Eye strain	0	1	2	3	4	5	6
Blurred vision	0	1	2	3	4	5	6
Difficulty focussing	0	1	2	3	4	5	6

Other symptoms / feelings	

Appendix 5 – Photos of equipment, exercise training and testing



ARM CRANK ERGOMETRY (ACE) - EXERCISE TESTING

FUNCTIONAL ELECTRICAL STIMULATION – LEG CYCLE ERGOMETRY (FES-LCE)

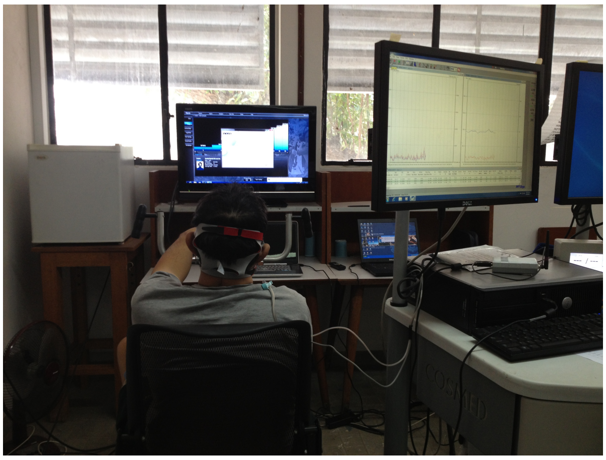
ACE+LCE

HYBRID FES LCE

OUTDOOR HYBRID FES CYCLING

VIRTUAL REALITY INDOOR HYBRID FES CYCLING

INDOOR HYBRID HIGH-INTENSITY INTERVAL TRAINING



GRADED HYBRID FES TESTING