SPINA BIFIDA, OBESITY, AND HEALTH: A CASE STUDY

A Thesis

by

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Spring 2010

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DEDICATION

This is dedicated to the stubborn, hardworking Fukushima women and their poor men (four of which had no choice of being a Fukushima, by being born into the family and the two silly men who were married in). Without our family visits marinated in margaritas, I wouldn’t have survived my master’s! A special thanks to my husband; I am so thankful for your support and love throughout this process...This was all just practice to better prepare you for my doctoral work!

But, mostly, I dedicate this to Grandma Nellie who passed on the stubborn, hardworking genes.
ACKNOWLEDGEMENTS

I owe a great deal of gratitude to my thesis chair and mentor, Dr. Azevedo, for all of his time, patience, ideas and guidance through the research and writing process. I am very fortunate to have had the opportunity to work with him. I learned so much about the research process and working in a lab! I truly enjoyed it.

I would also like to thank the other members of my committee, Dr. Rebecca Lytle and Thomas Fahey. I truly appreciate all of their time, support, feedback and expert editing skills.

Finally, my research would not have been possible without the help of Nurse Sandy Gorter, PACS coordinator, Anne Taylor, X-ray technician, Tanja Anderson, and fellow student, Bill Byrne.
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ABSTRACT

SPINA BIFIDA, OBESITY, AND HEALTH: A CASE STUDY

by

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Master of Arts in Kinesiology

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Spring 2010

This investigation described the physiological characteristics of two trained subjects with spina bifida (TSB). The subjects were of normal weight and met the ACSM guidelines for participating in physical exercise. The data were compared with existing data untrained subjects with spina bifida (UTSB).

Peak power output (PO\textsubscript{peak}) and peak oxygen uptake (VO\textsubscript{2peak}) were assessed using arm ergometry. Body composition was assessed using dual x-ray absorptiometry. Glucose tolerance was determined using an oral glucose tolerance test (OGTT) after an overnight fast.

VO\textsubscript{2peak} was 33\% greater in male TSB compared to UTSB and female TSB. VO\textsubscript{2peak} was 43\% higher compared to UTSB. PO\textsubscript{peak} was 70 watts in the male TSB compared to 62 watts in the UTSB, a difference of 12\%. Female TSB PO\textsubscript{peak} was 19\% greater than UTSB (60 vs. 48.9 watts). Body fat percentage was 26.6\% and 36\% in male TSB and UTSB, respectively. Body fat percentage was 29 and 46\% in female TSB and
UTSB. Fasting blood glucose in TSB was 89.5 mg/dl which is comparable to UTSB. After consuming a 75 gram glucose load, blood glucose was 127, 124, 111, and 62 mg/dl at 30, 60, 90, and 120 min in TSB.

The results of the present study must be interpreted with caution it was a case study of two individuals. However, we can infer from these data that people who are physically active and within a normal weight respond positively to exercising as indicated by the higher VO2peak and maximum power output and more robust body composition (i.e., lower percent fat and high fat-free weight. This study supported the role of physical activity in promoting health in people with spina bifida.
CHAPTER I

INTRODUCTION

Obesity has become a world-wide epidemic. The World Health Organization’s (WHO) latest figures from 2005 estimate that globally there are 1.6 billion overweight adults and approximately 400 million obese adults (aged 15 years or older). Globally, at least 20 million children under the age of five are overweight. These figures will increase to 2.3 billion overweight adults and 700 million obese adults by 2015.

The combination of people living with spina bifida and spinal cord injuries represents a significant portion of the population. Spina bifida is the most common birth defect, occurring in approximately every 1-2 per 1,000 live births in the United States (Center for Disease Control and Prevention, 2003). In the United States, an estimated 70,000 people have the condition (Spina Bifida Association, 2008). Current estimates of people living with a spinal cord injury in the United States are approximately 255,703 with approximately 12,000 new injuries occurring each year (Spinal Cord Injury Information Network, 2007).

In the past, the life expectancy for SCI patients was significantly lower than the rest of the population due to many diseases to which the SCI patients were especially susceptible. Due to medical advances, the risks of infectious diseases are no longer a primary concern in SCI patients (Cooper, et al., 1993). However, life expectancy for people with spinal cord dysfunction remains shorter due to cardiovascular and respiratory
disease, even though many are asymptomatic (Wells & Hooker, 1990; Bauman, Khan, Grimm, & Spungen, 1999).

According to the Spina Bifida Association of America (2008), beyond the age of six, approximately 50% of people with spina bifida (SB) are overweight and by adolescence and adulthood 50% are obese. Obesity in spina bifida is important to address because children and adults with spina bifida who are overweight or obese will have limited mobility, causing problems involving independence in activities of daily living (ADL’s), skin lesions, social and emotional issues, and an increased risk of chronic diseases.

The purpose of the present study was to examine the relationship between aerobic fitness and adiposity in trained subjects with spina bifida who use a wheelchair as their primary means of mobility compared with untrained subjects from a previous study. Measures of health outcomes in subjects with spina bifida that met the ACSM’s guidelines for being physically active at least one hour per day were observed. The majority of the literature in the review focused on people with acquired spinal cord lesions because few studies examined obesity in people with spina bifida. For the purposes of this review, the author assumed that the results of the studies examining the spinal cord injured population also pertained to the spina bifida population. The terms spina bifida and myelomeningocele may be used interchangeably.

This study is significant because healthy, active individuals with spina bifida were observed. It was hypothesized that subjects with spina bifida who are active will have similar measures of health as those who are able-bodied, which translates to a decreased risk for many chronic diseases that are associated with physical inactivity.
In this study, the differences in aerobic fitness (VO₂peak), peak power output (PO_peak), body composition and glucose tolerance via an oral glucose tolerance test (OGTT) as measures of health were compared to previously published research of untrained spina bifida patients. It was hypothesized that the trained subjects with spina bifida would have higher VO₂peak and PO_peak values, lower body fat percentage, and normal glucose disposal than untrained subjects with spina bifida observed in previous research.

Statement of the Problem

The purpose of the present study was to describe aerobic fitness and adiposity in active, normal weight subjects with spina bifida who use a wheelchair as their primary means of mobility compared with sedentary spina bifida subjects, from a previous study (Dopler-Nelson, et al., 2007; Widman, Abresch, Styne, & McDonald, 2007).

Operational Definitions

The following operational definitions were used in this study:

1. Trained subjects in this study met the guidelines for being physically active according to the American College of Sports Medicine.
2. Untrained subjects were sedentary subjects.
3. Peak oxygen uptake (VO₂peak) was the highest level of oxygen consumption achieved during the final stages of graded exercise testing.
4. Spinal cord injury (SCI) referred to acquired lesions of the spinal column that are resulted in loss of motor and sensory function.
5. Spinal cord dysfunction referred to lesions of the spinal column that were either acquired or congenital and resulted in loss of motor and sensory function.

Limitations

This was a case study; therefore results cannot be extrapolated to the population of people with spina bifida. The mean age of the subjects in the study involved in the comparison was younger than the two case subjects studied in this research. Physical activity and height were self-reported. Often, self-reported physical activity is over-estimated (Klesges et al., 1990). There are limited numbers of studies examining physical activity, health and people with spina bifida.

Delimitations

The research participants in this study were an active, 20 year old male and 30 year old female with spina bifida. Both subjects are physically active at least one hour a day, five to seven times a week. Therefore, the results from this study were delimited to two active subjects with spina bifida, exercising on an arm crank ergometer in a controlled laboratory setting.

Assumptions

The following assumptions were made during this investigation:

1. Self-reported levels of physical activity were accurate
2. All subjects abstained from eating and drinking 12 hours prior to exercise testing
3. All subjects abstained from vigorous exercising 24 hours prior to exercise testing.
4. All subjects worked to exhaustion during exercise testing.
5. All subjects were motivated to try their best during exercise testing.
6. All subjects abstained for eating and drinking 12 hours prior to the oral glucose tolerance test (OGTT).
CHAPTER II

A REVIEW OF THE LITERATURE

The purposes of this review of literature was to present (a) a description of spina bifida, (b) the problem of overweight and obesity in the able-bodied population and how it is measured, (c) the problem of overweight and obesity in people with spinal cord dysfunction, and (d) the health consequences of overweight and obesity in both populations. It is important to have an understanding of these areas to prevent and treat overweight and obesity in people with spinal cord dysfunction.

Overview of Spina Bifida

Neural tube defects are the most common birth defects worldwide (Jallo & Becske, 2005). It is an anomaly of the central nervous system, where the neural tube fails to close in the primary phase of neurulation or during postneurulation (Padmanabhan, 2006). Spina bifida is a neural tube birth defect which is the most compatible with life (Padmanabhan, 2006).

Primary phase neural tube defects are categorized as open in which the entire central nervous system is affected. Due to the opening along the spinal column, neural tissues are exposed and cerebral spinal fluid leaks. The open-type neural tube defects are associated with hydrocephalus and Arnold-Chiari-II Malformation (Jallo & Becske, 2005).
A closed neural tube defect is localized, confined to the spine and does not affect the brain (Jallo & Becske, 2005). It is thought to occur during secondary neurulation, but there is not enough evidence to prove this (Jallo & Becske, 2005).

The three types of spina bifida are *occulta*, *meningocele*, and *myelomeningocele*, (Patten, 1953). The neural arches are unfused in *spina bifida occulta*. The spinal cord may not be involved, and there may not be any visible malformation of the vertebral column or neurological conditions (Patten, 1953). Because asymptomatic, it is the mildest form of spina bifida and many people with spina bifida occulta may not know they have it.

With *meningocele*, the meninges are involved in the formation of a saccular enlargement without the spinal cord being displaced or distorted (Patten, 1953).

*Myelomeningocele* is the most severe and most common type of spina bifida where the spinal cord is distorted and/or displaced within the meningeal sac (Patten, 1953). Surgery is usually performed between 24 and 48 hours after birth to cover the exposed spinal cord, nerves, and tissue (Northup & Volcik, 2000).

There are many problems associated with *meningocele* and *myelomeningocele*. As a result, children usually require many surgeries and extensive medical care throughout life. The main clinical complications include paralysis of the lower extremities, bladder and bowel incontinence, tethering of the spinal cord, hydrocephalus, and Arnold Chiari-II Malformation (Jallo & Becske, 2005).

The spinal cord is exposed to amniotic fluid throughout gestation in the fetus with a spina bifida lesion that remains open in the amniotic cavity (Millicorsky & Lazar, 1995). Leg movement has been observed until the third trimester, with less movement
after, resulting in paralysis later in the pregnancy. Fetal leg movements could have been mistaken for movements of other parts of the body (Millicorsky & Lazar, 1995). Researchers believe that the exposed tissues of the spinal cord are chemically attacked by the amniotic fluid. They have shown that the exposed tissues of the fetus appear abnormal and are covered with a vascularized spongy layer. This theory of paralysis in open spina bifida due to exposure to amniotic fluid is aptly named the “amniotic fluid damage hypothesis” (Millivorsky & Lazar, 1995, pp. 300-301). We need more research to test this hypothesis.

Another explanation of the paralysis of the lower extremities is called the “two-hit hypothesis.” It states that the primary factor of paralysis in spina bifida with an open lesion is due to the malformation of the spinal cord development. The secondary event, or the “second hit,” is the necrosis and erosion of the spinal cord due to exposure to the amniotic fluid throughout gestational age (Pinto-Correia et al., 2002).

Depending on the severity and location of paralysis, some individuals with spina bifida may be able to walk independently or may need to use a walker, cane, ankle foot orthoses, or wheelchair for mobility.

Overweight and Obesity

Obesity has become a worldwide epidemic. The World Health Organization (WHO) estimates that there are 1.6 billion overweight adults and approximately 400 million obese adults globally (WHO, 2003a). It has devastating effects on health, quality of life, and represents a significant economic burden (Racette, Deusinger & Duesinger,
In the U.S. alone, obesity causes approximately 300,000 deaths a year and has indirect and direct costs of $117 billion per year (Stein & Colditz, 2004).

Obesity is a comorbidity—“with the increase of body weight comes the increased risk for some of the most prevalent diseases of modern society” (Booth, Gordon, Carlson, & Hamilton, 2000, p. 776). Overweight and obesity greatly increase the risk of morbidity and mortality from type 2 diabetes, hypertension, dyslipidemia, coronary heart disease, gallbladder disease, stroke, osteoarthritis, sleep apnea, breast, and prostate, endometrial, and colon cancer (Expert Panel, 1998).

Overweight and Obesity in People with Spina Bifida and Spinal Cord Injuries

Approximately 20% of U.S. citizens are disabled and people with physical disabilities have a 1.2 to 3.9 fold increase risk of obesity (Liou, Pi-Sunyer, & Lauferere, 2005). Healthy People 2010 ranked obesity as one of the top 10 leading health indicators and aimed at reducing obesity among people with disabilities by half to 15% (Liou et al., 2005).

Many studies reported a higher incidence of overweight and obesity in youth and adults with spina bifida compared to typically developed youth and adults (Littlewood, Trocki, Shepherd, R., Shepherd, K., & Davies, 2003; Liusuwan, Widman, Abresch, Styne, & McDonald, 2007; Rimmer, Rowland, & Yamaki, 2007). An increased incidence of obesity was observed in people with spina bifida as early as 1973 (Hayes-Allen & Tring, 1973). Obesity is often overlooked or neglected compared with other acute conditions such as urinary tract infections and joint problems in people with spinal cord dysfunction. A variety of secondary conditions may exacerbate primary conditions
in people with spinal cord dysfunction who are overweight or obese. These include decubitus ulcers, depression, chronic pain, mobility problems, social isolation, and a number of diseases and metabolic disorders, which have high morbidity and mortality (Liou et al., 2005; Liusuwan et al., 2007; Rimmer, Rowland, & Yamaki, 2007).

Measurements of Overweight and Obesity in People with Spina Bifida and Spinal Cord Injuries

After a spinal cord injury, there are dramatic decreases in bone density, lean muscle tissue, total body water, an altered balance of intra- and extracellular water, and increase in fat mass, bringing up questions about the validity of using body composition methods in the spinal cord injured population. Specific regression equations have yet to be developed in field assessments of body composition in reference to multi-compartment models for the spinal cord injured population (Jacobs & Beekhuizen, 2005).

Research has shown that using body mass index (BMI) for the spinal cord injured population can greatly underestimate body fat (Jacobs & Beekhuizen, 2005). BMI measures weight in kilograms (kg) relative to height in meters squared (m²) (WHO, 2003a). BMI is used to categorize the weight as underweight, normal, overweight, or obese. Normal weight is considered a BMI of 18.5-24.9 kg/m², overweight is defined as a BMI of over 25 kg/m², and obesity is defined as having a BMI of 30 kg/m² or greater (Expert Panel, 1998). Obesity has three subdivisions: class I (30-34.9 kg/m²), class II (35-39.9 kg/m²), and class III-morbid obesity (greater or equal to 40 kg/m², Expert Panel, 1998). Evidence has shown that BMI is not suitable for predicting overweight and obesity in certain populations because it fails to differentiate between bone density, fat mass, and
fat free mass (Jones, Legge, & Goulding, 2003). It was found that even though BMI values were normal, SCI may actually have body fat levels greater than 30% as determined by Dual energy x-ray absorptiometry (DXA), falling within the obese range (Jones, et al., 2003). DXA is considered to be the gold standard for measuring body composition (Brooks, Fahey, & Baldwin, 2005). It assesses total bone mineral density, as well as estimates regional quantities of bone, fat, and lean mass (American College of Sports Medicine, 2000). There is a substantial amount of adiposity in spinal cord injured subjects that is not detected using BMI (Jones et al., 2003). BMI underestimates body fat in the spinal cord injured population because it does not differentiate between bone density, lean mass, and fat mass.

It has also been shown that skin-fold thickness is an inappropriate method to assess body composition in SCI individuals (Maggioni et al., 2003). The skin fold method significantly underestimated fat mass compared to the DXA scans (19.6±4.2 vs. 31.1±8.2, respectively).

By the age of four, children with myelomeningocele show a decrease in lean mass and an increase in adipose tissue (Littlewood et al., 2003). Fat percentage, fat weight, percent lean body mass, and height were related to the total skinfolds in children with myelomeningocele. It was also found that the percent of body fat was significantly correlated with the individual skin fold sites of the thorax and abdomen. Further, potassium content and creatinine excretion were good measurements of total muscle mass (Grogan & Eckvall, 1999). Thus, skin fold thickness is an acceptable method to assess body fat in the spina bifida population. However the findings of Grogan & Eckvall (1999) that the skinfold method was a reliable measure for this group do not agree with
the results of Maggioni, et al. (2003). This could be due to the use of two different subject populations. Grogan and Eckvall examined children with spina bifida, while Maggioni et al. (2003) examined adult spinal cord injured subjects. Each study used different skin fold sites. More research should be conducted to test the accuracy of skin fold techniques and develop reliable and useful regression equations.

Body composition often determines ambulatory capacity. Non-ambulatory people with spina bifida tend to have more body fat than those who are ambulatory (27.6±8.4% vs.23.1±6.2%). Most (58%) spina bifida subjects over the age of six had a greater percentage of body fat compared to able-bodied control subjects (Mita, et al., 1993). However, these data should be evaluated with caution because of a limited sample size (15) and questionable methods.

Typically, people with spina bifida have a shorter stature than people without spina bifida (Rotenstein, Adams, & Regal, 1995). Although little research has examined spina bifida and BMI accuracy, there has been research examining the difference between different ethnic groups. Duerenberg & Duerenberg-Yap (2001) proposed that the inaccuracy in BMI-based prediction formulae for many Asian populations are due to a difference in relative leg lengths. Asian subjects may present healthy BMI values for body fat percents that are considered overweight or obese, compared to the Caucasian population (Duerenberg & Duerenberg-Yap, 2001).

Complications in People with Spina Bifida and Spinal Cord Injuries

People with spinal cord injuries are experiencing age-associated conditions prematurely and at a higher prevalence (Spungen et al., 2003). These diseases include
carbohydrate intolerance, insulin resistance, lipid abnormalities, and heart disease. The age-related diseases are compounded by changes in body composition. Decreased muscle mass, increased fat mass, and reduced bone mineral density can be attributed to spinal cord dysfunction, whether congenital or acquired (Spungen, et al., 2003). In spinal cord injuries, lean body mass deteriorates significantly in the first six months post injury (Spungen, et al., 2003).

Almost all (96%) spinal cord injured war veterans are overweight or obese (Gupta, White, & Sandford, 2005). SCI patients have about 5kg more fat mass (or 50% greater) than controls.

**Metabolic Rate**

Resting metabolic rate (RMR) is one component of energy expenditure. It is the energy requirement for an awake, resting individual and accounts for approximately 70% of daily energy expenditure. It typically declines with age and with a decrease in lean body mass (Brooks, Fahey, & Baldwin, 2005). Physical activity is probably the most important factor determining energy expenditure. It helps maintain or increase lean body mass, RMR, thermic response to food, and increase metabolic rate after physical activity (Brooks et al., 2005).

The relationship between fat-free mass and energy expenditure is important. The increased risk for metabolic complications and cardiovascular disease becomes more complex with a decrease in energy expenditure (Monroe et al., 1998). Twins with SCI had a significantly lower body weight, BMI, as well as FFM and total body potassium. Basal energy and resting energy expenditures were significantly lower in the SCI twin compared to the non-disabled twin, however there was no difference between the SCI
twin and the non-disabled twin when energy expenditure was scaled per kilogram of body weight. Energy expenditure is lower due to the loss of lean body tissue after chronic SCI (Bauman, Spungen, Wang, & Peirson, 2004). However, the decrement in 24 hour energy expenditure cannot be explained be loss of muscle mass alone. Most SCI patients engage in far less physical activity than their able-bodied counterparts (Monroe et al., 1998).

Finally, the thermic effect of food was found to be much lower in the spinal cord injured group than in able-bodied controls. Metabolizing food can account for five to ten percent of an individual’s daily energy expenditure, but these effects are much less for individuals who are obese than in persons with more fat free mass Brooks et al. (2005). Whether the decreased thermic effect of food was due to the actual spinal cord injury or an increase of fat mass or loss of lean muscle is unknown. Further, the spinal cord injury group consisted of nine paraplegics and one independent tetraplegic, all of which were highly mobile and used manual chairs. If the spinal cord injured subjects were not as mobile, one could hypothesize that there would be even greater reductions in daily activity levels.

Monroe et. al (1998) noted that the long term effects of spinal cord injury on total daily energy expenditure is unknown and may be helpful in studying accurately the daily energy expenditure needs of the spinal cord injured population. Knowing the energy expenditure will be helpful to determine a recommended energy intake to prevent and treat overweight and obesity in the spinal cord injured and spina bifida population.
Health Consequences of Overweight and Obesity

Cardiovascular Disease

The relationship between obesity and cardiovascular disease (CVD) is well established. In a long-term, large cohort study, it was found that obesity is a significant independent risk factor for CVD (Hubert, Feinleib, McNamara, & Castelli, 1983). Weight gain after young adulthood increased the risk of cardiovascular disease (Hubert et al., 1983).

WHO (2003b) has estimated that in 2005, 17.5 million deaths globally were caused by some form of CVD. Approximately 7.2 million of the deaths are caused by ischemic heart disease; 5.5 million are caused by cerebrovascular disease; and 3.9 million are due to hypertension and other heart conditions (WHO, 2003b). Cardiovascular disease has been the number one killer in the US every year since 1900, except one (1918). It claims more lives than the next seven prevalent causes of death combined (Booth et al., 2000). Alarmingly, CVD is no longer a disease of developing countries: some eighty percent of all deaths were in developing, low to middle-income countries and by 2015 will have killed 20 million people world-wide (WHO, 2003b). Mortality rate is very high when CVD is present with obesity. A high BMI (>29 kg/m²) increases risk for hypertension, even after other factors (such as smoking and family history) had been accounted for (Hu et al., 2004; Huang et al., 1998; Manson et al., 1995).

People with spina bifida and spinal cord injuries have a greater number of risk factors to develop CVD (Dopler-Nelson et al., 2007). Cardiovascular disease is the number one killer in the spinal cord injured population, and compared to the able bodied
population, is reported to have an increase mortality rate at a younger age due to CVD (Bauman, Kahn, Grimm, & Spungen, 1999). As seen in the able-bodied population, many studies have illustrated that lifestyle, physical activity, lipid management, and dietary restrictions can affect risk factors for CVD. This clustering of risk factors includes hyperlipidemia, hypertension, diabetes mellitus, and hyperinsulinemia (Bauman et al., 1999).

Impaired fasting glucose, diabetes mellitus, hyperuricemia, high total cholesterol (TC), low density lipoprotein (LDL), low high density lipoprotein (HDL), and high TC/HDL, LDL/HDL ratios were found to be statistically more common in the spinal cord injured group. From these results, the researchers concluded that the spinal cord injured population has an increased risk for cardiac heart disease than the able bodied population (Demirel, S.E., Demirel, G., Tukek, Erk, & Yilmaz, 2001).

Lipid profiles are a risk factor for CVD. Lipid profiles do not appear to be different between non-obese control and non-obese MMC children (Rendeli et al., 2004). However, Rendeli and colleagues (2004) found TC and LDL were higher with increasing age in girls with spina bifida. Non-ambulating MMC girls had higher TC serum levels compared to all other girls. There were also differences in very low density lipo-protein (VLDL) levels in non-ambulating MMC girls compared to MMC girls ambulating with walking aids and without aids (Rendeli et al., 2004). It is not known whether the difference in the MMC non-ambulatory group is due to inactivity, hormone changes, or some other factor. These results were observed in the absence of obesity. These results demonstrated the importance of monitoring lipid changes throughout the lifespan of
someone with spinal cord dysfunction to help predict the risk of CVD (Rendeli et al., 2004)

**Type 2 Diabetes and Metabolic Syndrome**

Obesity is a strong risk factor for type 2 diabetes (Lindmark et al., 2005). Type 2 diabetes has become a major worldwide concern and is in progress of reaching epidemic proportions (WHO, 2006). The latest estimates from 2000, show that 171 million people worldwide have diabetes and by the year 2030, 366 million will have developed diabetes, the majority having type 2 diabetes (WHO, 2006). Diabetes is the leading cause of blindness, kidney failure, and non-traumatic lower limb amputations (WHO, 2006). WHO (2006) reported that fifty to eighty percent of deaths in people with diabetes are due to cardiovascular disease. Most cases of type 2 diabetes can be attributed to obesity (Zimmet & Shaw, 2001).

In long-term, large cohort studies, overweight adults were three times more likely to develop diabetes (Field et al., 2001) and the highest mortality rates among the overweight were due to diabetes. In obese (BMI of $\geq 30 \text{ kg/m}^2$) men, the rate of death was five times higher compared to lean male subjects and for obese women the rate was eight times higher (Lew & Garfinkel, 1979).

It has been demonstrated that obese children who become obese adults had a very high risk of developing metabolic syndrome and that childhood obesity alone increases the risk for metabolic syndrome in adulthood. In adolescents with spinal cord dysfunction, the prevalence of metabolic syndrome is high (Dopler-Nelson et al., 2007). Independent of childhood obesity, the risk of developing metabolic syndrome was very low in non-obese subjects overall (Vanhala, M., Vanhala, P., Kumpusalo, Halonen, &
Takala, 1998). Childhood obesity that continues into adulthood may be more harmful than adult-onset obesity. Continuous obesity from childhood through adulthood may serve as a “generator” for prolonged insulin resistance, which leads to a clustering of metabolic abnormalities (Vanhala, Vanhala, Kumpusalo, Halonen, & Takala, 1998). These findings coupled with the results from Dopler-Nelson, et al. (2007) that adolescents with spina bifida have a higher incidence of metabolic syndrome, suggest that there is potentially a life-long, low health level and poor quality of life for the majority of the spina bifida population. An obese child, who decreases relative weight and becomes a non-obese adult, may be protected from the metabolic syndrome (Vanhala et al., 1998).

Physical activity is a determinant of insulin action. People with SCI are at a greater risk of type 2 diabetes due to the immobilization of the majority of skeletal muscle (Phillips et al., 2004). Bauman & Spungen (1994) found that 22% of 100 individuals with SCI had diabetes mellitus vs. only 6% in the able-bodied control group. Insulin sensitivity was negatively correlated with body fat. In paraplegics the strongest determinant of insulin sensitivity was cardiopulmonary fitness (Bauman & Spungen, 1994). Exercise intervention can induce beneficial adaptations in muscle and increase glucose uptake. The improved glycemic control observed from an exercise intervention may present long-term benefits for reducing the incidence of type 2 diabetes in the spinal cord injured population (Jeon et al., 2002; Phillips et al., 2004)
Role of Skeletal Muscle and GLUT4

The mechanisms behind the function of skeletal muscle and its role in the development of type 2 diabetes are important. Skeletal muscle make up approximately one-half of the body’s mass (Brooks, S., 2003). Quantitatively, it is responsible for virtually all of post-prandial glucose disposal (DeFronzo, Bonadonna, & Ferannini, 1992). Further, working (contracting) skeletal muscle is responsible for the majority of whole body glucose disposal during exercise (Kjaer, Kiens, Hargreaves, & Richter, 1991). Both insulin and contraction stimulate glucose uptake in skeletal muscle independently via translocation of the glucose transport protein GLUT-4 (Brook, Fahey, & Baldwin, 2005). Skeletal muscle GLUT-4 content is important for glucose regulation, therefore whole-body glucose homeostasis (Block, Menick, Robinson, & Buse, 1991; Friedman, Sherman, Reed, Elton, & Dohm, 1990; Tsao, Burcelin, Katz, Huang, & Charron, 1996). Insulin resistance leads to impaired glucose uptake by skeletal muscle. As a compensatory mechanism the pancreas then releases more insulin to normalize blood glucose (glycemia). Over time as insulin resistance worsens and/or pancreatic compensation fails, type 2 diabetes develops (DeFronzo, Bonadonna, & Ferannini, 1992).

GLUT-4 expression is controlled by nervous stimulation and contractile activity of muscle. It has been shown in denervated muscle that GLUT4 content decreases rapidly thus impairing the ability of skeletal muscle to take-up and clear glucose from the blood. Therefore, in denervated muscle, lack of GLUT-4 may contribute to impaired glucose tolerance and insulin resistance which is often observed in people with spinal cord dysfunction (Duckworth et al., 1980).
Type 2 Diabetes and Muscle Fiber Type

There is a suggestive relationship between skeletal muscle fiber composition, adiposity, in vitro glucose transport rate in humans, and mitochondrial defects in skeletal muscle (Hampton, 2004; Hickey et al., 1995; Lowell & Shulman, 2005; Tanner et al., 2001). Skeletal muscle is made up of a variety of fiber types. Type I fibers are slow twitch and have higher levels of oxidative enzymes, type IIa are fast twitch, and oxidative, and type IIb are fast twitch and glycolytic. It is known from many studies that overweight and obese subjects, insulin-resistant subjects, as well as de-conditioned subjects have lower prevalence of type 1 muscle fibers. Type 1 muscle fibers are oxidative; they contain more mitochondria than type 2 muscle fibers.

Hickey et al. (1995) found that muscle from obese patients had a significantly lower proportion of type I fibers with a concomitant higher proportion of type IIb fibers compared to non-obese subjects. BMI was significantly and inversely correlated to type I fibers, independent of age. BMI was inversely related to in vitro glucose transport and type I fiber population in the rectus abdominus muscle. Thus, in vitro skeletal muscle glucose transport is directly related to skeletal muscle type I fiber content.

Mitochondria and Insulin Resistance

Lowell & Shulman (2005) report that accumulation intracellular triglycerides as well as by products from incomplete fatty acid oxidation may cause insulin resistance by directly inhibiting insulin-stimulated glucose transport activity. They suggested that the accumulation of fatty acids in the liver and or muscle, and any defect in these organs ability to metabolize fatty acids, might result in insulin resistance (Lowell & Shulman, 2005). Supporting this idea, when skeletal muscle cells (myocytes) or liver cells
(hepatocytes) are overloaded with fatty acids, pathways are not able to dispose of the large amount of fatty acids, and this results is in incomplete oxidation of fatty acids and insulin resistance (Koves et al., 2008; Schenk, Saberi, & Olefsky, 2008).

To summarize, the emerging theory is that mitochondrial deficiency may be a common underlying cause of insulin resistance. Mitochondrial function is required for normal glucose-stimulated insulin secretion from pancreatic beta cells. A more subtle defect in mitochondria may play a large role in the pathogenesis of insulin resistance and type 2 diabetes (Hampton, 2004; Lowell & Shulman, 2005). Again, research has shown that skeletal muscle is responsible for the majority of insulin-mediated glucose disposal in humans. Activating skeletal muscle through regular physical activity will increase GLUT4 (Friedman, Sherman, Reed, Elton, & Dohm, 1990), ameliorate the mitochondrial deficiency with regard to the ability to oxidize fatty acids (Cortright et al., 2006), and increase type I fibers resulting in increasing insulin-mediated glucose disposal (Mengeney, Neufer, & Dohm, 1993).

Conclusion

Obesity has become a problem worldwide in the able-bodied population. The problem is just as significant in the spinal cord injured and spina bifida population. The rates of overweight and obesity and the associated complications are increased for people with spinal cord dysfunction. Healthy People 2010 identified people with disabilities as a priority to focus on to promote health, prevent secondary problems, and eliminate disparities between people with and without disabilities in the U.S. population (U.S. Department of Health and Human Services, 2000).
The prevention and treatment of overweight and obesity has yet to be thoroughly investigated in people with spinal cord dysfunction. Preventing and prescribing treatment in this population is difficult because of a lack of cohort studies focusing on the people with physical disabilities, health, overweight and obesity.
CHAPTER III

METHODOLOGY

The Institutional Review board at California State University, Chico approved this study. All subjects signed informed consent forms before the study commenced. Subject’s rights and the procedure were explained before and during the testing. Testing was in accordance to the approved protocol.

Subjects

Two subjects with myelomeningocele volunteered to participate in this investigation. Both subjects primarily used a wheelchair as a means of mobility, and surpassed the recommended ACSM guidelines for physical exercise, exercising for at least one hour to 2 hours a day, 5 days per week. Both subjects were within a normal, healthy weight range. Neither subject had any adverse health conditions that prevented them from completing the exercise portion of the testing. Subject characteristics are shown in Table 1.

Subjects were recruited from the Ability First Youth Sports Camp (Chico, CA). Informed consent was obtained from both subjects in accordance with the established human subjects’ protocol at California State University, Chico (Appendix A).

Subjects were compared to subjects from an existing study using the same, or as close to the same as possible testing protocols. The comparison study used a group of spina bifida and spinal cord injured subjects (lesion levels in the thoracic level or below) that were overweight or obese.
Table 1

Subject Characteristics

<table>
<thead>
<tr>
<th>Subject</th>
<th>Sex</th>
<th>Age (yrs)</th>
<th>Weight (kg)</th>
<th>BMI</th>
<th>Body Fat (%)</th>
<th>Lean Body Mass (g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>20.6</td>
<td>48.08</td>
<td>18.8</td>
<td>26.6</td>
<td>36.35</td>
</tr>
<tr>
<td>2</td>
<td>Female</td>
<td>30.3</td>
<td>38.10</td>
<td>18.2</td>
<td>29.0</td>
<td>26.76</td>
</tr>
</tbody>
</table>

Medical and Exercise History

A medical and health history form was filled out by each subject prior to testing. Subjects were screened for current medical problems that would prevent them from participating in exercise, type 2 diabetes, overweight, obesity, or pregnancy. Exercise history was evaluated to determine if the subjects complied with the current ACSM guidelines for physical exercise of at least one hour a day, 5 days a week (Appendix B).

Anthropometric Measurements

Weight was measured to the nearest kilogram on a balance beam column scale. Height was self-reported. Body composition was obtained with a dual energy x-ray absorptiometry (DXA, GE Prodigy Lunar Pro, and Belgium).

Aerobic Fitness

Peak oxygen uptake (VO$_{2peak}$) and peak heart rate (HR$_{peak}$) were assessed during a graded exercise test to volitional fatigue using an arm crank ergometer (Monark 881E, Sweden) and a standard ramp protocol. The ergometer was adjusted so that when
the subject sat, the arm crank axis was at shoulder level at a distance that allowed a slight bend in the elbow. Subjects were seated for 3 minutes to obtain resting values for HR and VO₂ (HR_{rest} and VO₂_{rest}). This was followed by 3 minutes of unloaded cranking.

After this initial 3 minutes, the subjects cranked at a cadence of 70 rpm and the power output increased 10 watts every minute. Subjects were verbally encouraged to continue as long as they could. The procedure continued until the subject could no longer able to maintain the required 70 rpm cadence or until they reached fatigue. At this point, the subject continued with unloaded cranking to warm down.

HR was recorded throughout the testing using a HR monitor. Subjects sat in their own wheelchairs during the testing with chairs externally stabilized. Oxygen consumption was assessed using the open-circuit indirect calorimetry method using a TrueMax 2400 (ParvoMedics, Sandy, UT) metabolic cart. Oxygen consumption (VO₂), carbon dioxide production (VCO₂), ventilation (Vₑ) were measured and respiratory exchange ratio (RER = VCO₂/VO₂) was calculated. Maximum power output (PO_{max}) was also recorded.

Oral Glucose Tolerance Test (OGTT)

Subjects reported to the lab at approximately 8am after an overnight fast. A nurse inserted an intravenous catheter into the non-dominant antecubital vein. A zero time (baseline) blood sample was drawn. Then, each subject was given 1.75 g per kg body weight up to 75 g total glucose in 256 ml (trunol dextrose glucose solution, NERL Diagnostics, E. Providence, RI). Subjects were instructed to drink the solution within five minutes. One ml of blood was drawn every 30 minutes for 2 hours (baseline, 30, 60, 90,
120 minutes) for a total of five draws. The catheter was flushed with 0.9% sterile saline between each blood draw to prevent clotting. A final blood glucose level was checked with a portable glucose meter to assure glucose was within an acceptable (safe) range before subjects left the lab.

Glucose Assays

Approximately one ml of blood was immediately put into a pre-weighed Vacutainer tubes containing two ml of chilled 8% perchloric acid (HClO₄) and were weighed to determine blood weight. All blood samples were stored at -80°C until analysis. Blood glucose samples were analysed using the Hexokinase-linked assay procedure (Bonder & Mead, 1974, Sigma, Saint Louis, MO, USA).

The blood samples were thawed. An empty 96-well microtiter plate was read on the microplate reader (Spectramax 340, Molecular Devices, Sunnyvale, CA) to determine if there were any scratches or dust that would interfere with reading. Ten µl of the blanks, standards and samples were added to their respective wells of a microtiter plate in triplicate. The standard concentrations included a 0, 0.25, 0.5, and 1.0µg/µl. Each subject had wells corresponding to their baseline blood draw, 30 min, 60 min, 90 min and 120 min draws. The microplate information was then input into the spectrophotometer Softmax software corresponding to the appropriate wells. Once the samples were distributed into each well, a cover was placed over the entire plate and it was placed on the vortex for 5 seconds on a setting of 3. It was then incubated at 37°C in the spectrophotometer for 6 minutes. The O.D. was read at a wavelength of 340 nm (Figure 3).
Statistical Methods

Because this was a case study, only percents were calculated.
CHAPTER IV

RESULTS AND DISCUSSION

Results of aerobic capacity, power output (PO), and heart rate (HR) are presented in Table 2 for the trained subject group. When comparing TSB and UTSB, the mean of the UTSB was used.

Table 2

*Trained Subject Performance Data*

<table>
<thead>
<tr>
<th>Subject</th>
<th>VO$_{2peak}$ (L/min)</th>
<th>VO$_{2peak}$ (ml/kg)</th>
<th>VO$_{2peak}$ (ml/kg FFM)</th>
<th>VCO$_{2peak}$ (L/min)</th>
<th>RER$_{peak}$ (VCO$_2$/VO$_2$)</th>
<th>PO$_{peak}$ (Watts)</th>
<th>HR$_{rest}$</th>
<th>HR$_{peak}$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1.32</td>
<td>30.8</td>
<td>37.1</td>
<td>1.64</td>
<td>1.24</td>
<td>70</td>
<td>82</td>
<td>199</td>
</tr>
<tr>
<td>2</td>
<td>0.95</td>
<td>24.9</td>
<td>27.7</td>
<td>1.16</td>
<td>1.22</td>
<td>60</td>
<td>93</td>
<td>179</td>
</tr>
</tbody>
</table>

**Peak Exercise Response**

VO$_2$ peak was 33% greater in male TSB compared to UTSB (30.8 vs. 20.6 ml/kg/min in TSB and UTSB, respectively). Female TSB VO$_2$ peak was 43% higher in TSB compared to UTSB (24.9 and 14.2 ml/kg/min in TSB and UTSB, respectively). PO$_{peak}$ was 70 watts in the male TSB compared to 62 watts in the UTSB, which represents a 12% increase. Female TSB, PO$_{peak}$ was 19% greater than UTSB (60 and 48.9 watts, respectively).
The male TSB and the male CTRL had comparable VO₂peak. The female TSB had a 15.7% greater VO₂peak compared to the female CTRL. The PO for the TSB vs. the CTRL was 14% lower, respectively. The female TSB had an 18% greater PO vs. the female CTRL.

Comparing sex, the male TSB had a 20% higher VO₂peak than the female. The UTSB males had a 9% higher VO₂peak compared to the UTSB females. Peak PO was 17% greater for the male TSB vs. the female. In the UTSB, males had a 20% higher PO than the females.

**Body Composition**

Body fat percentage was 26.6% and 36% in male TSB and UTSB, respectively for almost a ten percent difference in body fat. Body fat percentage was 29 and 46% in female TSB and UTSB, respectively for almost a twenty percent difference. Comparing sex, there was only 2.4% difference between the male TSB and the female TSB (see Figures 1 and 2). The females UTSB had almost 10% more body fat compared to the males.

The male TSB had a 10% higher body fat when compared to the male CTRL. The female TSB had a 4% higher body fat difference when compared to the female CTRL group.

**OGTT**

The Mean fasting blood glucose in TSB subjects was 89.5 mg/dl, which is comparable to UTSB. After consuming the glucose load, mean blood glucose was 127, 124, 111, and 62 mg/dl at 30, 60, 90, and 120 min, respectively in TSB (see Figure 3).
Discussion

In the present case study, several health-related components were measured in one trained male and one trained female subject, both with spina bifida. Their results were compared with results from previous research that compared obese able-bodied with obese spina bifida subjects. The present study found that the trained subjects were more fit than their untrained counterparts.

Spina bifida is one of the most prevalent birth defects that also can cause some degree of paralysis of the lower body (Jallo & Becske, 2005). From denervation studies, it is known that GLUT 4 decrease dramatically (Block, Menick, Robinson, & Buse, 1991; Duckworth et al., 1980; Mortensen-Lauritzen et al., 2008). In the condition of spina
bifida, there is less skeletal muscle compared to able-bodied individuals and not only is CHO uptake is compromised, but there is decreased storage capacity for dietary CHO. As state previously, skeletal muscle GLUT-4 content is important for whole-body glucose homeostasis (Friedman, Sherman, Reed, Elton, & Dohm; Tsao, Burcelin, Katz, Huang & Charron, 1996). Due to denervation, there may be an impairment in both insulin and contraction stimulated glucose uptake in skeletal muscle (Brooks, Fahey, & Baldwin 2005), leading to a shift in storage of CHO from skeletal muscle to adipose (Cortright, et al., 2006). This may also partially explain the high prevalence of metabolic syndrome in this population (Dopler-Nelson et al., 2007).
Individuals with spina bifida have less skeletal muscle than able-bodied individuals which compromises whole-body glucose disposal. For example, the average able-bodied individual weighs 70 kg and muscle represents 40% of total body mass, this translates to 28 kg of skeletal muscle. The average male child with spina bifida weighs on the average of 61 kg. However, if most individuals with spina bifida are only 20% muscle, this would translate to only 12 kg muscle (Doppler-Nelson) compromising whole-body carbohydrate disposal. It has been demonstrated in rats that denervation of skeletal muscle results in a decrease of GLUT4. GLUT4 is the major glucose transport protein in skeletal muscle. If spina bifida is considered a condition of denervation, then the skeletal muscle of individuals with spina bifida has much less GLUT4, compromising the ability of muscle to take up carbohydrate (glucose). Skeletal muscle in able-bodied,
non-diabetic individuals is responsible for virtually all post-prandial carbohydrate 
disposal.

Physical inactivity results in decreased mitochondrial activity. This leads to the 
accumulation of intramyocellular triacylglycerol (IMTG) (Lowell & Shulman, 2005). It 
has been well established that the accumulation of IMTG interferes with insulin 
signalling (Koves, et al., 2008: Lowell & Shulman, 2005). If skeletal muscle is insulin 
resistant, dietary carbohydrate must be taken up by other tissues (e.g. adipose) (Cortright, 
et al., 2006; DeFronzo, Bonadonna, & Ferannini, 1992). To summarize, most individuals 
with spina bifida have less skeletal muscle, which very likely has less GLUT4, and is also 
insulin resistant. Taken together, these three factors lead to a state of a very compromised 
state of glycemic control in individuals with spina bifida.

Further, with less active skeletal muscle (both due to denervation and to 
physical inactivity) in people with spinal cord dysfunction can account partially for a 
lower VO₂peak that is often observed in people with spina bifida (Buffart, van den Berg-
Emons, van Wijlen-Hempel, Stam, & Roebroeck, 2008; Dopler-Nelson, et al., 2007; 
Widman, Abresch, Styne, & McDonald, 2007). However, the results from the present 
case study suggest that lower values of aerobic capacity are to some degree a result of 
deconditioning. These results concur with results from Buffart, et al. (2008). The able-
bodied male and female controls and the male and female TSB had comparable results 
for aerobic capacity and PO.

Body fat was 10% lower in male TSB compared to their male CTRL 
counterparts and less than 4% higher in the female TSB vs. the female CTRL group. Both 
the male and female TSB and the male and female CTRL were all within a normal,
healthy body fat percentage. This further supports the idea that poor body composition that is often observed in people with spina bifida is related to physical inactivity.
CHAPTER V

SUMMARY, CONCLUSIONS, AND RECOMMENDATIONS

Two trained subjects, aged 20 and 30, with spina bifida participated in an investigation to examine the relationship between aerobic fitness and adiposity in trained subjects with spina bifida who use a wheelchair as their primary means of mobility compared with untrained spina bifida subjects from a previous study.

Aerobic fitness was evaluated via VO$_{2\text{peak}}$ on an arm crank ergometer. A gas collection and analysis technique was performed to determine VO$_{2\text{peak}}$. Body composition was measured by way of DXA, and glucose disposal was determined by way of OGTT after a 12 hour fast.

The TSB had healthier values than the UTSB. Causality cannot be established and results must be interpreted with caution due to the small sample size. However, we can infer from the results that physical activity produces a positive health outcome for people with spina bifida.

Conclusion

Overweight and obesity is a serious problem for people with spinal cord dysfunction and is independent of disability. A sedentary lifestyle can be attributed to the issues with excess weight. Using VO$_{2\text{peak}}$ as a measure of aerobic capacity in trained
subjects with spina bifida, they exhibited normal healthy values, had a healthy BMI and glucose disposal compared to untrained subjects with spina bifida. The results from this case study show there is suggestive evidence of a relationship between aerobic fitness and adiposity in people with spina bifida.

Individuals with spina bifida respond positively to physical fitness as indicated by increased VO$_2$peak, maximum power output, and healthy/normal body composition. Cardiovascular disease is the leading cause of death for people with spinal cord dysfunction. This study has suggestive clinical significance with regard to preventing risk for the development of chronic disease in people with spina bifida using exercise. This was only a case study. More detailed research with this population will allow more valid inferences.

Recommendations for Future Research

There are few studies examining people with spina bifida, physical fitness, and health. Therefore, the results from this study may be useful in future research in this area.

1. Mechanistic evaluation needs to be carried out. For example, is the onset of overweight/obesity due to partitioning of fuel stores to adipose because of the lack of skeletal muscle in spina bifida patients or is there a lack of GLUT4 in the skeletal muscle of spina bifida patients. If so, are GLUT4 levels comparable to sedentary able-bodied individuals, and would exercise training increase the amount of GLUT4 in skeletal muscle of SB patients, and therefore normalize the post-prandial glycemic response. Further, is insulin signaling normal or is it also disrupted.
2. It will be important to determine exercise amounts, modes and intensities of exercise that will elicit health benefits to prevent chronic disease for people with spina bifida.

3. A significant limitation in this study, and others, is the small sample size. In order to have internal and external validity, statistical power, and to make population inferences, a large number of subjects are needed.

4. The age of onset of overweight and obesity will be important to determine in the spina bifida population for prevention. This will be important to determine at what age to implement an exercise/physical activity program, as well as nutrition counseling.
REFERENCES
REFERENCES


STATEMENT OF INFORMED CONSENT

INFORMED CONSENT TO PARTICIPATE IN A RESEARCH STUDY

California State University, Chico
Department of Kinesiology
Chico, CA 95938

Title of Research: Insulin Resistance and Spina Bifida

Principal Investigator: Kerri A. Vanderbom

A. PURPOSE AND BACKGROUND

Obesity has become a world wide epidemic. The World Health Organization (WHO) estimates that there are 1 billion overweight adults and approximately 300 million obese adults globally\(^1\). In the physically disabled population, people with paralysis experience a change in body composition: a loss of lean body mass, skeletal muscle and an increase in adiposity\(^2\). Most persons with spinal cord dysfunction are dependent on the use of a wheelchair, thereby decreasing their capacity for physical activity. According to the Spina Bifida Association of America, beyond the age of six, approximately 50% are overweight and by adolescence and adulthood, 50% are obese\(^3\).

Most of the research examining overweight and obesity for people with spinal cord dysfunction focuses on adults with acquired injuries and not congenital disabilities. The purpose of this study is to assess the relationship between physical fitness and adiposity in active (not overweight or obese) youth with spina bifida who use a wheelchair as their primary means of mobility as compared with overweight/obese able-bodied controls and an overweight/obese spina bifida group (UCD data). The outcomes will measure glucose and insulin levels by way of an oral glucose tolerance test (OGTT), body composition measured using a dual energy x-ray absorptimetry (DXA), VO\(_{2\text{peak}}\) using an arm crank ergometer and metabolic cart, and anthropometric measurements.


B. PROCEDURES

Description of the study

If you participate, we will ask you to perform the tests listed below with the number of times listed for each test.

You will be required to visit the Exercise Physiology Lab two times and the North State Imaging clinic one time over a period of approximately 8 weeks. The length of the visits will vary from 1 hour to approximately 3 hours.

On the first day, you will arrive at the exercise lab in Yolo hall after fasting for 12 hours. You will have an oral glucose tolerance test (OGTT). I will verbally remind you of the process that will be taking place. I will confirm that you fasted for 12 hours and verify that consent from an adult (if a minor) has been obtained. Vital signs and weight will be taken. The registered nurse will insert an intravenous catheter into your non-dominant arm into the antecubital vein. A zero time (baseline) blood sample will be drawn. Then, you will be given a glucose solution to drink. It will be 1.75 g of glucose per kilogram of body weight, with a maximum dose no more than 75g. You will be instructed to drink the solution within 5 minutes. One milliliter of blood will be drawn every 30 minutes for 2 hours (base line, 30, 60, 90, 120 min) for a total of 5 draws. After the testing, the RN will remove the IV. Final blood glucose level will be checked using a portable glucose meter to assure glucose is within an acceptable range.

A DXA scan will be performed to measure total body composition (fat mass, soft lean tissue mass, total bone mineral content, and percentage body fat). The following anatomical regions will be measured: right arm, left arm, trunk/pelvis, right leg, left leg, head plus neck. You will be asked to meet in the morning at the North Valley Imaging clinic. You will be instructed to wear comfortable, loose clothing, and to avoid wearing garments that have zippers, belts, or buttons made of metal. You may be asked to remove some your clothing and to wear a gown during the exam. You may be asked to remove any jewellery, eyeglasses, and anything else that is metal that may interfere. You will be allowed to eat normally on the day of the exam, but should not take calcium supplements at least 24 hours before the exam.

On the second day, body composition (fat-mass and lean-mass) will be measured using seven-site skinfold calipermetry. Lange skinfold calipers will be used to measure skinfolds at seven sites: chest, axilla, triceps, subscapula, abdomen, suprailiac, and thigh (all on the right side). You should not exercise prior to the skinfold test. Following the skinfold test will be an incremental exercise test using an arm crank ergometer to assess VO2peak to determine aerobic fitness. You will have the protocol explained prior to the testing. You will be allowed to crank for five minutes to familiarize yourself with the equipment and procedure. You will be positioned so that the crank axis is at shoulder level at a distance that allows slight bend in the elbow when the arm is extended. You will be asked to maintain 70 rpm throughout the testing. One minute of resting data will be collected, followed by 3 minutes of unloaded cranking. After the three minutes, the work load will increase 10 watts per minute until you feel you cannot cycle any longer.
You will be asked to wear a headgear with a mouthpiece so that measurements can be taken using your breath.

Participants: Four to 10 young healthy men and women with spina bifida will be evaluated using four different measurements: DXA, OGTT, VO2peak, skinfolds and other basic anthropometric measurements.

After answering questions concerning medical history and signing an informed consent, subjects will undergo body composition assessment (DXA), skinfolds, and other basic anthropometric measurements, an OGTT, and one maximal (peak) oxygen consumption test.

Exercise Task: Subjects will arrive at the lab in the morning following a 12-hr overnight fast and undergo an OGTT. Subjects will have a total body DXA scan. Exercise trial involving VO2peak assessed by indirect calorimetry. Exercise power output (PO) will be assessed using an arm crank ergometer (ACE).

Assessments: Energy substrate oxidation (VO₂, VCO₂, RER), blood glucose concentration, and heart rate.

Blood Sampling Schedule: From the antecubital vein, 1 ml of blood will be withdrawn at rest and every 30 minutes for two hours. A total of five blood samples will involve sampling of a total of 5 ml blood.

C. RISKS AND CONFIDENTIALITY

Drawing blood from the hand may cause pain, bruising, bleeding, light-headedness and, on rare occasions, infection, blood clots or scarring.

There may be some risks associated with the performance of VO₂peak test, such as exhaustion, increased blood pressure, heart rate, disorders of heart rhythm, and in very rare cases heart attack and death. I understand that there is a risk of injury, heart attack, or even death as a result of my performance of this test, but knowing those risks, it is my desire to proceed to take the test as herein indicated.

If any such complications arise, Dr. Azevedo, who has over 20 years of experience in exercise stress testing as well as CPR training, will be present during the sessions. The participant will be asked about medical history to help minimize these risks. If injured, the participant will seek a medical referral at their own expense. The participant is obliged to tell the researcher of any medical conditions that may impact performance or any discomforts felt during the study. The participant is free to withdraw from this study at any time.

In case of emergency: I understand there are certain changes which may occur during the exercise test. They include abnormal blood pressure, fainting, disorders of heart beat, and very rare instances of heart attack. I understand that every effort will be made to minimize problems by preliminary examination and observation during testing. In the
event of an emergency, the exercise test will be terminated; appropriate EMS will be
activated (e.g. calling 911 if deemed appropriate).

**Confidentiality:** Confidentiality may not be maintained. For example subjects may
discuss their experiences during the Ability First Youth Sports Camp as they attend camp
together. However, no individual identities will be used in any reports or publications
resulting from the study. All information will be given codes and stored separately from
any names or other direct identification numbers or letters of participants. Research
information will be kept in locked files in Dr. Azevedo’s laboratory at all times. Only
investigators on this study will have access to the files and only those with an essential
need to see names will have access to that particular file. For example, in case of the
participant’s VO\textsubscript{peak} reading is clinically questionable for the researcher; the advisors of
the investigator can see the participant’s name and file for medical prescription. After the
study is completed and all data will be stored on the researcher’s personal computer
disks, the original information with no identification about a participant will be held for
one year after the final study is published, and then destroyed. If study is not published,
then data will be held for five years (assuming the publishing process has been exhausted,
i.e. manuscript has been rejected by one journal and new attempts have been made at
another journal).

**D. DIRECT BENEFITS**

There may be no direct benefit from participating in this study. The purpose of the study
is to determine whether there are physiological differences when comparing youth with
spina bifida that are fit versus youth with spina bifida that are overweight or obese and to
overweight or obese controls without spina bifida or any other physical disability.

**E. COSTS**

North Valley MRI & North State Imaging is donating their time and equipment.

**F. COMPENSATION**

**G. ALTERNATIVES**

The alternative is not to participate in the research.

**H. QUESTIONS**

The participant has spoken to Kerri McMurtry. All questions should be directed to Kerri
McMurtry by phone (XXXX), or email: xxxxx.com, or in writing at xxx Little Ave.
Chico, CA 95928.

**I. CONSENT**

The participant has been given a copy of this consent form to keep.
PARTICIPATION IN THIS RESEARCH IS VOLUNTARY. Free to decline to participate in this research study, or to withdraw your participation at any point, without penalty. The decision whether or not to participate in this research study will have no influence on your present or future status at California State University Chico.

I have read the above information. In signing this consent, I am not waiving any legal claims, rights, or remedies. I consent to voluntarily participate in this study. A copy of this consent form will be signed and given to me. The above procedures have been explained and demonstrated to me and I agree to participate in them.

Signature _____________________________  Date: __________
Research Participant

Signature _____________________________  Date: __________
Researcher
APPENDIX B
MEDICAL AND EXERCISE HISTORY

I.D. Number ____________________________ DATE __________________________

BIRTH DATE _______________ AGE _______ HEIGHT _______ WEIGHT _______

1. How often do you exercise? ______________ times/week
2. On average, what is the duration of a typical exercise session for you? _____________ min/session
3. Describe the intensity of your exercise (circle one)
   1 = none
   2 = light (e.g. casual pushing, golf)
   3 = moderate (e.g. brisk pushing, cycling, swimming)
   4 = heavy (e.g. high intensity sport activity)
4. What types of exercise do you engage in and how much do you do each session? (circle all that apply)
   1 = none
   2 = pushing _______ miles or minutes _______ sessions/week
   3 = intense pushing _______ miles or minutes _______ sessions/week
   4 = swimming _______ yards or minutes _______ sessions/week
   5 = cycling _______ miles or minutes _______ sessions/week
   6 = team sports (basketball, softball, soccer, etc.) _______ minutes _______ sessions/week
   7 = racquet sports _______ minutes _______ sessions/week
   8 = weight training _______ minutes _______ reps/set _______ sets/session _______ sessions/week
   9 = other ________________________________________________________________
5. How much time per week do you spend exercising? ___________ hours/week
6. Do you measure your heart rate during exercise? ___________
   If yes:
   a. How high does it get during your typical workout? _______ beats/min
   b. What heart rate is maintained throughout most of your workout? _______ beats/min
7. How long have you had a regular exercise program? _______
8. What condition or shape do you consider yourself to be in now (in terms of physical fitness)?
   1 = poor
   2 = fair
   3 = good
   4 = excellent
9. Do you or have you ever smoked? ________
   If yes: How long ago? ________ For how many years? ________ How many packs/day ________
10. How much and what type of alcohol do you consume in an average week?

11. Has a close blood relative had or died from heart disease or related disorders (Heart Attack, Stroke, High Blood Pressure, Diabetes etc.)?
   1 = Mother
   2 = Father
   3 = Brother - Sister
   4 = Aunt - Uncle
   5 = Grandmother - Grandfather
   6 = None
   If yes- Give ages at which they died or had the event and the problem they had.
12. Have you ever had your cholesterol measured?
   1 = yes
   2 = no
   If yes- write the date and value (or if it was normal or abnormal)

13. Indicate which of the following apply to you (circle all that apply).
   1 = high blood pressure
   2 = high blood fats or cholesterol
   3 = cigarette smoking
   4 = known heart disease or abnormalities
   5 = family history of heart disease (parents or siblings before age 50)
   6 = sedentary lifestyle
   7 = stressful lifestyle at home or at work
   8 = diabetes mellitus
   9 = gout (high uric acid)
   10 = obesity

14. Any medical complaints now (illness, injury, limitations)?
   1 = yes        If yes, describe completely ________________________________
   2 = no         ________________________________________________________

15. Any major illness in the past?
   1 = yes        If yes, describe completely ________________________________
   2 = no         ________________________________________________________

16. Any surgery or hospitalization in the past?
   1 = yes        If yes, describe completely ________________________________
   2 = no         ________________________________________________________

17. Are you currently taking any medications (prescription or over-the-counter: including birth control)?
   1 = yes        If yes, list drugs and dosages ______________________________
   2 = no         _______________________________________________________ 

18. Are you allergic to any medications?
   1 = yes        If yes, list medications _________________________________
   2 = no         _______________________________________________________ 

19. Have you ever had any neurological problems?
   1 = yes        If yes, describe completely ________________________________
   2 = no         _______________________________________________________

20. Do you now have, or have you ever had, any of the following? (circle all that apply)
   1 = heart murmurs
   2 = any chest pain at rest
   3 = any chest pain upon exertion
   4 = pain in left arm, jaw, neck
   5 = any palpitations
   6 = fainting or dizziness
   7 = daily coughing
   8 = difficulty breathing at rest or during exercise
   9 = any known respiratory diseases
   10 = any bleeding disorders or problems with bleeding
Please describe fully any items you circled ____________________________________________
________________________________________________________________________________
________________________________________________________________________________
________________________________________________________________________________

21. Do you now have, or have you ever had, any of the following? (circle all that apply)
1 = any bone or joint injuries
2 = any muscular injuries
3 = muscle or joint pain following exercise
4 = limited flexibility
5 = any musculoskeletal problems which might limit your ability to exercise
Please describe fully any items you circled ____________________________________________
________________________________________________________________________________
________________________________________________________________________________
________________________________________________________________________________

22. If you are a female, are you, or could you be pregnant presently?
1 = Yes
2 = No

In case of emergency, please contact: _________________________________________
Parent/Guardian Name: ____________________________________________________
Parent/Guardian Address: __________________________________________________
Parent/Guardian Phone Number: _____________________________________________
Primary Physician’s Name: _________________________________________________
Clinic & Address: ________________________________________________________
Physician’s Phone Number: _________________________________________________

I have read and understand the above questions. I have answered them to the best of my knowledge:
Participant/Guardian Name Printed: ______________________________ Date________
Participant Signature: _________________________________________ Date________
May 30, 2007

Kerri McMurtry
346 Little Ave.
Gridley, CA 95948

Dear Kerri McMurtry,

As the Chair of the Campus Institutional Review Board, I have determined that following your Full Board review, no further modifications are needed in your research proposal entitled "INSULIN RESISTANCE IN SPINA BIFIDA". This clearance allows you to proceed with your study.

I do ask that you notify our office should there be any further modifications to, or complications arising from or within, the study. In addition, should this project continue longer than the authorized date, you will need to apply for an extension from our office. When your data collection is complete, you will need to turn in the attached Post Data Collection Report for final approval. Students should be aware that failure to comply with any HSRC requirements will delay graduation. If you should have any questions regarding this clearance, please do not hesitate to contact me.

Sincerely,

[Signature]

John Mahoney, Ph.D., M.S.
Human Subjects in Research Committee

Attachment: Post Data Collection Report

cc: John Azevedo (330)
HUMAN SUBJECTS IN REVIEW COMMITTEE
Post Data Collection Questionnaire

Under Federal law relating to the protection of Human Subjects, this report is to be completed by each Principal investigator at the end of data collection.

Please return to: Diane Smith, HSRC Assistant
Graduate and International Programs
Student Services Center (SSC), Room 440
CSU, Chico
Chico, CA 95929-0875

Or Fax to: Diane Smith, 530-898-6889

Name: Keri A. VanderJohm (NCHU)  Chico State Portal ID: KAVX
Phone(s) (530) 876-5851 Email: kam-ha08ski@hotmail.com
Faculty Advisor name (if student): Jack Renode Phone: 518-

College/Department: KINESIOLOGY

Title of Project: INSULIN RESISTANCE & SPINAL BIRDA

Date application was approved (mo/yr): / Date collection complete (mo/yr): /

How many subjects were recruited? 2 How many subjects actually completed the project? 2

*HARM* Did subjects have severe reactions or extreme emotional response? NO

If yes, please attach a detailed explanation: N/A

Your signature: Keri A. VanderJohm Date: 12/17/08

*Final clearance will not be granted without a complete answer to this question.

Approved By: John Mahoney, Chair Date: 12-17-08

********************************************************************************************

VERy IMPORTANT: If you will or have used this research in your project or thesis you are required to provide a copy of this form (with John Mahoney's signature in place) to your graduate committee.

Do you want a photo copy of this form mailed to you? YES

If yes, provide address: 124 NW 7TH ST. 97330
Corvallis, OR 97330

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