AN ABSTRACT OF THE THESIS OF

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Title: The Relationship Between the Plasma Catecholamine, Lactate and Ventilatory Responses to Incremental Exercise in Individuals with Spinal Cord Injury

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This investigation was designed to examine the plasma catecholamine, lactate and ventilatory responses to incremental exercise in individuals with spinal cord injury (SCI). Three men with spinal cord injuries (SCI) above the 6th throacic vertebrae (T6) (Quad; age=30.2±4.9 yrs) and four men with SCI below T6 (Para; age=27.8±8.3 yrs) volunteered to participate. All subjects were at least six months post injury and active in various forms of wheelchair sports. Each subject performed a peak oxygen uptake ($\dot{V}O_2pk$) exercise test on a friction braked arm ergometer. Workloads were increased 6 and 8 Watts every 3 minutes for the Quads and Paras, respectively. The Quads cranked at 60 rpm's and the Paras cranked at 70 rpm's. Forearm venous blood samples were taken following 20 minutes at rest and at the end of each work stage, and subsequently analyzed for norepinephrine (NE), epinephrine (EPI), and lactate (LA) content. Ventilatory parameters were measured in 20 second intervals throughout testing. Heart rate (HR) was determined during the second minute of each work stage. Unpaired t-tests indicated that the Paras

exhibited significantly greater ($p \leq 0.05$) peak values for $\dot{V}O_2$, $\dot{V}E$, HR, LA, NE and EPI compared to the Quads ($\dot{V}O_2$=2.2±0.2 vs 1.2±0.1 $l \cdot min^{-1}$; $\dot{V}E$=103.8±16.27 vs 51.2±3.25 $l \cdot min^{-1}$; HR=195.5±4.09 vs 133.0±18.45 $beats \cdot min^{-1}$; LA=7.2±0.4 vs 2.7±0.2 mM; NE=3.1±1.0 vs 0.4±0.1 ng/ml; EPI=0.5±0.2 vs 0.1±0.01 ng/ml). While some subjects exhibited thresholds in ventilation (Tv), lactate (Tla), and catecholamines (Tne and Tepi), this was not consistent between or within subjects. Correlations between NE-EPI, NE-LA, and EPI-LA were r=0.93; r=0.79; r=0.72 in the Paras and r=0.21; r=0.33; r=0.35 in the Quads. The strong relationships between NE, EPI, and LA in the Paras were similar to those previously reported in able-bodied athletes. However, the relatively weak association between these factors in the Quads indicates that, while some function exists, the sympathoadrenal response to exercise is significantly impaired. These results suggest that the location of the spinal injury plays an important role in the sympathoadrenal and metabolic responses to exercise. Estimation of Tv, Tla, Tepi and Tne in individuals with SCI requires further investigation.

Relationship Between the Plasma Catecholamine, Lactate and Ventilatory Responses to Incremental Exercise in Individuals with Spinal Cord Injury

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DEDICATION

This project is dedicated to my parents Thomas and Norma and my family Regina and Ken, Tommy and Cheri, Linda and Ted, Laurie and Danny, Dawn, Amber, Laurel, Marissa, Andrea, Hillary, Matthew, Brad and Amy. They have always supported me emotionally, spiritually, and physically and have provided me with the confidence and security necessary for continuance of my academic career. God has blessed me with a family filled with unselfish, unending, and unconditional love and for this I am truly grateful.

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TABLE OF CONTENTS

TABLE OF CONTENTS (CONT.)

LIST OF FIGURES

LIST OF TABLES

Relationship Between the Plasma Catecholamine, Lactate and Ventilatory Responses to Incremental Exercise in Individuals with Spinal Cord Injury

CHAPTER I

INTRODUCTION

The research involving responses to exercise in individuals with spinal cord injury has developed significantly throughout the past decade. This continued development includes improvements in factors such as methodological procedures and interpretation of results, as well as attempts to confront difficult physiological questions regarding this population. These investigations have provided valuable information concerning basic responses to exercise in those with spinal cord injury and have prompted growing interest in the physiological capabilities of individuals with various disabilities.

However, while invasive studies of metabolic responses to exercise are common in the able-bodied, scientists have been cautious in pursuit of similar research questions in people with spinal injury. Previously, participation in physical activity for those following spinal trauma was limited, due to factors such as inaccessibility to fitness programs, lack of fitness programs for this population, and ignorance of the physical abilities of those with spinal injury. These factors, combined with the challenge of finding subjects or subjects that were willing to withstand the rigors of physiological testing, made it difficult to obtain a sufficient quantity of subjects. Further, the cardiorespiratory and training responses to exercise in

these individuals needed to be established before more invasive biochemical factors could be examined.

The cardiorespiratory and training responses to exercise in those with spinal cord injury are well documented (Hjeltnes, 1988; Shephard, 1988; Hoffman, 1986; Figoni, 1984; Davis, Kofsky, Kelsey & Shephard, 1981). Others have reported similar, but diminished cardiorespiratory exercise and training responses in this population compared to the able-bodied (Hjeltnes, 1988; Shephard, 1988; Hoffman, 1986; Figoni, 1984; Davis et al., 1981). There are many physiological complications resulting from spinal trauma that limit cardiorespiratory and biochemical responses to exercise. A primary variable in the decreased physiological capacity is the interruption of sympathetic nervous system activity (SNS) (Hjeltnes, 1988; Shephard, 1988; Hoffman, 1986; Figoni, 1984; Davis et al., 1981). The SNS, through the chemical mediators norepinephrine and epinephrine, serves many important biological functions, the most recognized of these being the fight or flight reaction. In response to physical activity, the SNS controls heart rate, blood pressure, substrate mobilization and utilization, and redirection of blood flow. If the SNS is impaired, then all of these factors are affected, and consequently so are responses to physical activity. Despite the obvious importance of understanding the SNS response to exercise in those with SCI, there is minimal data available on this topic.

Another area of research that has received relatively little attention in the scientific literature is the lactate response to exercise in people with spinal injury. Lactate dynamics during exercise is the subject of continuing interest in the able-bodied population. In general, the increased lactate production during maximal exercise is thought to represent a substrate cycle shift to non-oxidative glycolysis. The point at which lactate concentration begins to rise

nonlinearly is termed the lactate threshold and is used as a determinant of exercise intensity and as a tool for identifying optimal submaximal training. Two studies have documented the lactate threshold response in those with spinal cord injury (Lakomy, Campbell & Williams, 1987; Flandrois, Grandmontagne, Gerin, Mayet & Eyssett, 1986). The controversial relationship between the lactate and ventilatory thresholds (Brooks, 1985; Davis, 1985) has not been debated in this population.

As previously mentioned, the increased lactate response during exercise is associated with non-oxidative glycolysis. However, other metabolic processes, including liver and muscle glycogenolysis, are indirectly responsible for lactate production. Glycogenolysis is stimulated by catecholamines and this implies that lactate production is affected by SNS activity. Studies using infusion or ß-blockade of catecholamines in animals have shown that the SNS is directly related to lactate production (Stainsby, Sumners & Eitzman, 1985; Stainsby, Sumners & Andrew, 1984; Cain, 1969). This relationship was only recently demonstrated in humans (Mazzeo & Marshall, 1989). It is of particular interest to examine this relationship in a physiological system where the SNS is impaired.

Purpose

The purpose of this study was threefold. First, to examine the plasma catecholamine, lactate and ventilatory responses to incremental arm ergometry exercise in individuals with various levels of spinal cord injury. Second, to determine if a relationship existed between the plasma catecholamine, lactate and ventilatory responses to incremental exercise in this population. Third, to evaluate if there were differences in the plasma

catecholamine, lactate and ventilatory responses to incremental exercise between individuals with spinal cord injuries above and below the 6th thoracic vertebrae (T6).

Significance of the Study

To date, the majority of studies addressing physiological responses to exercise in individuals with spinal cord injury have focused on cardiorespiratory parameters (Hjeltnes, 1988; Shephard, 1988; Hoffman, 1986; Figoni, 1984; Davis et al.,1981). Relatively few investigators have attempted to assess the metabolic responses to exercise in this population. While there is some evidence concerning peak blood lactate concentration in individuals with spinal cord injury (Burkett et al., 1988; Hjeltnes, 1986; Taylor, McDonnell & Brassar, 1986; Gass & Camp, 1979), there is relatively little information on lactate threshold (Lakomy et al., 1987; Flandrois et al., 1986). Additionally, there have been no attempts to assess the relationship between the lactate and ventilatory thresholds in people with spinal trauma.

The fact that individuals with spinal injury have a diminished SNS is well accepted. However, data on this phenomenon have traditionally focused on resting levels (Claus-Walker & Halstead, 1982; Claus-Walker, Carter, Ferrante & Singh; 1977-78; Mathias, Christensen, Corbett, Frankel & Spalding, 1976; Debarge, Christensen, Corbett, Eidelman, Frankel & Mathias, 1974; Frewin, Levitt, Myers, Co & Downey, 1973; Naftchi, Lowman, Sell & Rusk,1972; Claus-Walker, Vallbona, Carter & Lipscomb, 1971; Munro & Robinson, 1960), immediate post-injury responses (Claus-Walker et al., 1977-78; Frewin et al., 1973), and tilt table responses (Frewin et al., 1973). Only one investigation addressing the catecholamine response to exercise in those with

spinal injury has been identified (Fitzpatrick, McKay & Ready, 1990). These authors used submaximal exercise to examine circulating catecholamines in quadriplegics and paraplegics. This information is extremely important, but there exists a void in the literature concerning the catecholamine response to incremental, maximal exercise in this population.

The present study attempted to fill the previously mentioned void in the literature by examining the plasma catecholamine, lactate and ventilatory responses to incremental exercise in individuals with spinal cord injury. Also, these data provided information on the influence of plasma catecholamines on the lactate threshold, which has been demonstrated to be significant in able-bodied athletes (Mazzeo & Marshall, 1989). Finally, this investigation was novel in that both individual and group data were interpreted and presented. The preponderance of reported literature classifies subjects according to status as quadriplegic or paraplegic (Hjeltnes, 1988; Shephard, 1988; Hoffman, 1986; Figoni, 1984; Davis et al.,1981). However, the amount of sympathetic nervous system activity that is preserved following a spinal injury varies according to the level, type, etiology and length of lesion (Hjeltnes, 1988; Shephard, 1988; Hoffman, 1986; Figoni, 1984; Davis et al.,1981). This is particularly true for those with spinal lesions at and above T6. The adrenal medulla, which is responsible for the majority of epinephrine production is sympathetically innervated by nerves extended from this area. Without this primary stimulus, the adrenal medulla must rely on other compensatory mechanisms, such as hypoxia and hypoglycemia, for initiation of epinephrine production (Mazzeo, 1991). If the lesion is below T6, then plasma epinephrine concentration should resemble able-bodied values. Therefore, it is inappropriate to make group analyses of exercise responses in

individuals with different types, levels, etiologies and time lengths of spinal lesions.

Statement of Problem

The following research questions were addressed in this investigation.

1. What is the lactate response to incremental exercise in individuals with spinal cord injury?

2. At what percentage of peak oxygen uptake does the lactate threshold occur in individuals with spinal cord injury?

3. At what percentage of peak oxygen uptake does the ventilatory threshold occur in individuals with spinal cord injury?

4. What is the catecholamine response to incremental exercise in individuals with spinal cord injury?

5. At what percentage of peak oxygen uptake does the catecholamine threshold occur in individuals with spinal cord injury?

6. What is the relationship between the lactate and ventilatory thresholds in individuals with spinal cord injury?

7. What is the correlation between the catecholamine and lactate response to incremental exercise in individuals with spinal cord injury?

8. With regard to research questions 1-7, are there differences between individuals with spinal injuries above T6 as compared to those with spinal injuries below T6?

Delimitations

This study was delimited to seven physically active males with various levels of spinal cord injury. Individuals with lower limb disabilities (those

that do not effect the spinal cord) resulting from congenital, amputation, or disease pathologies, were not included as subjects. This study also was delimited to arm ergometry exercise, which is often considered to have less practical application as compared to wheelchair ergometry.

Limitations

The results of this study cannot be generalized across people with spinal injuries. However, individual subject data trends can be compared to others with the same type, length, etiology and level of injury.

Definition of Terms

The abbreviations of the terms defined below are utilized throughout the text to facilitate brevity. An attempt is made to use person first terminology as frequently as possible.

Spinal Cord Injury (SCI): Individuals with various levels of spinal cord injury, resulting from a direct insult to the spinal column.

Peak oxygen uptake ($\dot{V}O_2pk$): The highest recorded level of oxygen consumption during the final stages an incremental exercise test.

Ventilatory Threshold (Tv): The point at which ventilation begins to rise nonlinearly with increasing workload.

Lactate Threshold (Tla): The point at which lactate begins to rise nonlinearly with increasing workload.

Catecholamine Threshold (Tne and Tepi): The point at which the catecholamines, norepinephrine (Tne) and epinephrine (Tepi), begin to rise nonlinearly with increasing workload.

Quadriplegic (Quad): For the purposes of this study, is an individual with an incomplete or complete spinal lesion above the 6th thoracic vertebrae.

Paraplegic (Para): For the purposes of this study, is an individual with an incomplete or complete spinal lesion below the 6th thoracic vertebrae.

Tetraplegic: An individual with a spinal injury that results in paralysis of all four limbs.

CHAPTER II

REVIEW OF LITERATURE

The participation of individuals with spinal cord injury (SCI) in sport and recreation has gained support and acceptance in the past decade. The passing of federal legislation requiring improved accessibility for persons with disabilities will serve to promote continued and increased physical activity in this population. Therefore, knowledge associated with physiological responses to exercise must advance along with this increased involvement in physical activity. The current body of literature focuses on the basic physiologic responses to maximal and submaximal exercise in those with SCI. These basic physiologic responses include factors such as heart rate, blood pressure, cardiac output, and oxygen consumption. However, there is comparatively little information concerning the biochemical responses to exercise in these individuals. Of particular interest is the compensatory activity of the sympathetic nervous system (SNS). When the integrity of the spinal column is disrupted, SNS activity is also disrupted. The SNS utilizes the catecholamines norepinephrine and epinephrine as powerful physiological regulators. These biogenic amines aid the body's adjustment to exercise through such mechanisms as the redirection of blood flow, substrate mobilization, and increased heart rate. If the spinal column and, consequently, SNS function is damaged, then physiological adaptation to exercise is compromised. The current knowledge base of physiological responses to exercise in individuals with SCI must be augmented through investigation of complex biochemical activities.

A brief review of the literature concerning physiological responses to upper body exercise (UBE) in both those with spinal injury and the able-bodied will be presented in this chapter. Attention will focus upon the available information addressing catecholamine and lactate responses to UBE in these two populations.

Physiological Responses to Upper Body Exercise in the Able-Bodied

A large number of studies investigating the physiological responses to UBE have reported similar findings, despite variations in methodologies. Factors such as oxygen uptake ($\dot{V}O_2$), power output, heart rate, blood pressure, ventilation, ventilatory threshold (Tv) and cardiac output are lower or similar for maximal UBE compared to various modes of maximal lower body exercise (LBE) (Louhevaara, Sovijarvi, Ilmarinen & Teraslinna, 1990; Sawka, Foley, Pimental & Pandolf, 1983; Davis, Vodak, Wilmore, Vodak & Kurtz, 1976; Reybrouk, Heigenhauser & Faulkner, 1975; Davies & Sargeant, 1974; Stenberg, Åstrand, Ekblom, Royce & Saltin, 1967). The differences between UBE and LBE are attributed to the comparatively smaller muscle mass utilized in upper body activities (Shephard, Bouhlel, Vandewalle & Monod, 1988; Sawka, 1986; Franklin, 1985).

While the cardiovascular responses to UBE are consistent throughout the literature, scientific reports regarding the responses of metabolic parameters such as blood lactate (BLa) and catecholamines are less clear. Pimental, Sawka, Billings & Trad (1984) examined the BLa response during four 60 minute exercise sessions. Nine, untrained male subjects performed both arm crank and bicycle ergometry at an intensity of 60% exercise-specific peak $\dot{V}O_2$ ($\dot{V}O_2$pk). In addition, subjects performed arm crank and bicycle

ergometry at an intensity associated with an absolute value of 1.60 $l \cdot min^{-1}$. The findings indicated that BLa was significantly higher during the absolute arm exercise compared to the absolute bicycle exercise. This was not surprising since the subjects were working at a higher percentage of $\dot{V}O_2pk$ during absolute arm compared to absolute bicycle exercise. There was no difference in BLa response between the two relative exercise bouts.

Hooker, Wells, Manore, Philip & Martin (1990) reported results in agreement with those of Pimental et al. (1984), using a similar subject population. They examined the BLa response to 30 minutes of submaximal arm crank (AC) and leg cycle ergometry (LC1) at a power output corresponding to 70% arm and leg $\dot{V}O_2pk$, respectively. These responses were compared to the BLa activity during leg cycle ergometry at a power output corresponding to 70% arm $\dot{V}O_2pk$ (LC2). The authors detected no difference between BLa concentrations during AC and LC1 at the same relative intensity. However, BLa concentrations were higher during the AC and LC1 work bouts compared to LC2. This is due to the fact that the subjects were exercising at higher percentages of $\dot{V}O_2pk$ during AC and LC1 compared to LC2. These studies indicate that BLa responses are similar during submaximal arm and leg exercise at the same relative intensity.

Conversely, Davies and Sargeant (1974) reported lower BLa levels for arm compared to leg work expressed as a relative percentage of $\dot{V}O_2$. Their research design required that eight males, with an undefined training status, complete a one arm, two arm and combined arm/leg maximal exercise test over a range of unspecified work intensities. In accordance with the findings of Pimental et al. (1984), and Hooker et al. (1990), BLa concentration for a given absolute $\dot{V}O_2$ was greater for arm than leg exercise. Freyschuss and Strandell (1967) conducted a study aimed at determining the arterial and

venous BLa concentration and differences in arm, leg and combined arm/leg exercise in the supine position. Three physically active males were trained on three modes of exercise until they could perform the highest work load at a steady state heart rate below 170 beats·min^{-1}. Each subject performed two different work loads for 6-7 minutes. The net lactate production was markedly less and slightly less in arm exercise compared to leg and combined arm/leg exercise, respectively. When expressed in relation to a given oxygen uptake, arm exercise arterial BLa levels were higher compared to those of leg and combined arm/leg exercise. This was attributed to the relatively smaller muscle mass used for arm exercise and, thus, a reduced ability for large amounts of total lactate production compared to leg exercise. Since combined arm/leg activity utilizes proportionately more muscle mass than either arm or leg exercise, it should follow that combined arm/leg exercise would result in greater total lactate levels. The authors reasoned that the slightly different total lactate levels for arm and combined arm/leg exercise in the present study were representative of better lactate clearance rates in combined arm/leg exercise.

Louhevaara et al. (1991), employed a standing arm crank activity versus bicycle ergometry to determine BLa responses to maximal and submaximal exercise in twenty-one untrained men. The BLa responses to exercise at submaximal workloads of 50 and 100 Watts were significantly higher for arm than cycle exercise. Maximal exercise BLa was also higher during arm compared to cycle exercise. The findings related to submaximal lactate response concur with those reported by Sawka (1986) in his comprehensive review of the physiology of upper body exercise. However, the higher maximal lactate values for arm compared to leg exercise illustrated in the Louhevaara et al. (1991) study contrast with those summarized by

Sawka (1986). The researchers explained the disparity in these results by emphasizing blood sample site. Blood was sampled from a forearm vein during both exercise bouts. The blood sampled during arm exercise reflected blood draining directly from the active muscle, thus indicating an immediate lactate response. The blood sampled during leg exercise was distal to the active muscle, thus indicating a more diluted lactate response. This hypothesis is not substantiated by Pimental et al. (1984) who found identical lactate concentrations from hand and foot sampling sites during arm crank exercise.

The discrepancies between these research findings can be attributed to many diverse methodologic designs, primarily different modes of UBE. In addition to the insufficient literature available on the lactate response to UBE, there has been no description of the lactate threshold (Tla) during UBE in the able-bodied.

It is well documented in lower body exercise (LBE) that catecholamine levels increase gradually with increasing workload (Mazzeo, 1991, Brooks & Fahey, 1984). At a workload approximating 50-70% of maximal $\dot{V}O_2$ ($\dot{V}O_2max$), the catecholamine response begins to increase nonlinearly (Brooks & Fahey, 1984). There have been very few attempts to determine if this catecholamine response is similar in UBE.

Early work by Davies et al. (1974) compared the catecholamine responses during one leg, two leg and arm exercise over a wide range of nonconstant intensities, including maximal levels. Four untrained males performed each work interval for 10 minutes. The catecholamine responses demonstrated similar patterns for each type of activity. At lower levels of exercise, the catecholamine response remained stable, but at a certain intensity, catecholamines increased rapidly. The absolute $\dot{V}O_2$ at which

catecholamines increased rapidly was dependent upon active muscle mass. However, when catecholamine response was expressed as a percentage of $\dot{V}O_2pk$, individual differences for each exercise disappeared, and the patterns for each type of activity changed. Despite the alteration in response pattern, the rapid increase in catecholamine response occurred at approximately 60% $\dot{V}O_2pk$ for all three types of exercise. There was a close relationship between catecholamine and lactate responses, but this association was dependent on the mode of exercise. The authors concluded that the catecholamine response during exercise corresponded with circulatory stress and represented the body's ability to maintain systemic blood pressure in reaction to increased metabolic demands.

Hooker et al. (1990) evaluated the epinephrine response during UBE and LBE. As described previously, nine active males performed submaximal UBE and LBE at 70% of exercise-specific $\dot{V}O_2pk$ (AC and LC1) and LBE at an absolute level equal to 70% UBE (LC2) $\dot{V}O_2pk$. There were no differences in the plasma epinephrine concentrations between AC and LC1. Additionally, epinephrine was greater during both AC and LC1 compared to LC2. It was surmised that the epinephrine response was more dependent upon relative exercise intensity than exercising muscle mass. This finding is in direct contrast with the previously mentioned work of Davies et al. (1974).

Physiological Responses to Exercise in Individuals With Spinal Cord Injury (SCI)

When examining the available literature associated with exercise and individuals with SCI, there are many elements to consider. These include: (1) differences between people with SCI and the able-bodied; (2) differences in training status; (3) differences between lesion levels; and (4) differences between wheelchair and arm crank ergometry. All of these factors will be addressed in this section.

There is sufficient evidence indicating that maximal and submaximal cardiovascular responses to exercise in those with SCI are diminished compared to the able-bodied (Davis, 1993; Figoni, 1993; Hjeltnes, 1988; Shephard, 1988; Hoffman, 1986; Figoni, 1984; Davis et al., 1981). However, the aerobic capacity of individuals with SCI can be improved with training (Davis, Plyley & Shephard, 1991; Davis & Shephard, 1988; Eriksson, Lofstrom & Ekblom, 1988; Taylor et al., 1986; Gass et al., 1980). This was further illustrated by Zwiren and Bar-Or (1975), who demonstrated that wheelchair athletes had significantly higher $\dot{V}O_2pk$ levels compared to sedentary able-bodied people.

Additionally, as the level of injury increases in severity, the cardiovascular responses decrease (Hjeltnes, 1988; Figoni, 1984). Eriksson et al. (1988) designed a study to examine the maximal exercise responses in upper body trained able-bodied athletes, untrained able-bodied individuals, and trained and untrained paraplegics and quadriplegics with complete and incomplete injuries. All subjects performed a $\dot{V}O_2pk$ test on a wheelchair ergometer. Paraplegics were able to tolerate larger increments in work rate than quadriplegics. Results from the maximal exercise tests showed that

$\dot{V}O_2pk$ and maximal ventilation were inversely related to level of spinal lesion. Alternatively, ventilation per liter of $\dot{V}O_2$ was greater for quadriplegics compared to paraplegics. Peak oxygen uptake differences between trained and untrained subjects increased at lower levels of spinal injury. For instance, trained quadriplegics had aerobic capacities comparable to that of untrained paraplegics. Untrained subjects with incomplete injuries demonstrated greater aerobic capacities than untrained peers with complete lesions. However, this situation was reversed when the subjects with complete injuries were trained. Both untrained and trained able-bodied individuals exhibited $\dot{V}O_2pk$ levels higher than all subjects with SCI. The conclusions from this research investigation were clear. Quadriplegics and paraplegics differed in physiological responses to exercise. The authors reasoned that these variations were due to the smaller amount of available muscle mass and greater loss of sympathetic activity in quadriplegics compared to paraplegics. The results of Eriksson et al. (1988) have been supported by others (Burkett, Chisum, Stone & Fernhall, 1990; van Loan, McCluer, Loftin & Boileau, 1987; Coutts, Rhodes & McKenzie, 1983).

It is often difficult to compare physiological findings in the SCI population because there is a disparity among published reports with regard to methodology. The use of wheelchair or arm crank ergometry has been well debated (Shephard, 1990). Wicks, Lymburner, Dinsdale & Jones (1977-78) attempted to determine the differences between maximal physiological performance using both wheelchair and arm crank ergometry. Five subjects with various lesion levels and training status and two able-bodied individuals completed three multistage maximal exercise tests: (1) arm crank ergometry; (2) wheelchair ergometry with a low resistance setting to simulate wheeling on a hard surface; and (3) wheelchair ergometry with a high

resistance setting to simulate wheeling over a rough surface. Protocol for each test was assigned according to lesion level. There were no differences between the three exercise modes on maximum values of $\dot{V}O_2$, heart rate, and ventilation for all subjects. The mechanical efficiency among subjects using arm crank ergometry was fairly constant, but fluctuated greatly using wheelchair ergometry. The findings of Wicks et al. (1977-78) were criticized because they did not use similar protocols for each mode of exercise nor report power output figures.

Glaser, Sawka, Brune & Wilde (1980) designed a study aimed at correcting the inconsistencies in the aforementioned study. Six subjects with spinal injuries and seven able-bodied subjects performed discontinuous exercise tests on both an arm crank and wheelchair ergometer. The beginning power outputs for both activities corresponded to 75% of each subject's age-predicted maximum heart rate with subsequent work rate increases of 60 kpm. Work stages were four minutes in duration followed by seven minute rest periods. The average number of work stages completed were 2.2 (8.8 minutes) and 2.7 (10.8 minutes) for wheelchair and arm crank ergometry, respectively. Similar to the results of Wicks et al. (1977-78), the present study demonstrated no differences in $\dot{V}O_2pk$ or maximal ventilation between the two exercise modes. Physical work capacity, maximal heart rate, and maximal lactate values were significantly higher for arm crank than wheelchair ergometry for all subjects. The researchers concluded that comparable muscle masses were used in both types of exercise, as represented by the consistent $\dot{V}O_2pk$ values. However, the 36% lower physical work capacity during wheelchair ergometry indicated that this activity was metabolically less efficient than arm crank ergometry. Although wheelchair ergometry is deemed more specific than arm crank ergometry, the latter imposes less

physical stress on the individual. This statement has been further substantiated by Sawka, Glaser, Wilde and von Luhrte (1980) and Wicks, Oldridge, Cameron and Jones (1983).

Diminished SNS activity is identified as the primary limiting factor in individuals with SCI (Hjeltnes, 1988; Shephard, 1988). The SNS establishes homeostatic control through the neurotransmitter and hormonal responses of norepinephrine and epinephrine, respectively. Norepinephrine is primarily released from the SNS nerve endings, while the majority of epinephrine is released from chromaffin tissue in the adrenal medulla. Norepinephrine concentration in the blood is approximately four times that of epinephrine in able-bodied individuals. When interruption of the SNS occurs, as in spinal injury, these controls will be compromised, particularly when adrenal medulla function is affected.

Munro and Robinson (1960) designed a descriptive study to compare resting norepinephrine and epinephrine levels in the following populations: (1) healthy able-bodied people; (2) individuals with SCI ranging from the 4th cervical (C4) to 3rd lumbar (L3) vertebra and; (3) able-bodied subjects before and after bilateral adrenalectomy. All SCI subjects had recovered from their initial injury. The research findings indicated that subjects with spinal lesions above the 6th thoracic vertebrae (T6) had significantly lower norepinephrine and epinephrine levels compared to the able-bodied, thus identifying the region above T6 as the source of adrenal medulla sympathetic innervation. There was no difference in catecholamine levels between subjects with lesions below T6 and the able-bodied. There was no measurable epinephrine in the plasma following bilateral adrenalectomy, indicating that the adrenal medulla is a major contributor of epinephrine. The authors attributed the continued presence of epinephrine in the plasma of those with

lesions above T6 to indemnificating factors, such as sympathetic reflex activity at the spinal level, the existence of extra-medullary chromaffin tissue as a source of epinephrine, or direct stimulation of the adrenal medulla by other metabolites. Other investigators have supported these early findings by Munro and Robinson (1960). Claus-Walker and Halstead (1982); DeBarge et al. (1978); Frewin et al. (1973); Naftchi et al. (1972); Claus-Walker et al. (1971) have also reported plasma catecholamine levels in the low to normal range following spinal trauma of various degrees. Further, these catecholamine levels remained low as a consequence of chronic injury.

It has been suggested that during the recovery period following spinal injury, the body becomes increasingly sensitive to available catecholamines (Frewin et al., 1973). Speculation about this increased sensitivity suggests increased ß-receptor density and increased renal production to maintain blood pressure. While the increased renal production is a plausible conclusion, the hypothesis of increased ß-receptor density has not been substantiated in humans.

To date, Fitzpatrick et al. (1989) have provided the only published results addressing the catecholamine response to exercise in those with SCI. They compared the metabolic responses to prolonged submaximal exercise in four quadriplegic and four paraplegic athletes. Subjects wheeled for two hours at 75% of $\dot{V}O_2max$. Results showed that quadriplegics demonstrated lower resting norepinephrine levels compared to paraplegics. Norepinephrine levels increased in both groups during exercise. Circulating epinephrine levels were lower in quadriplegics compared to paraplegics during exercise. The authors concluded that, as a consequence of lower catecholamines during exercise, quadriplegics have a decreased ability to utilize fat as a fuel source during prolonged exercise.

It is logical to assume that the pattern of BLa response to UBE in the able-bodied can also be applied to those with SCI. However, with regard to the fact that sympathetic stimuli effects the production of BLa production (Mazzeo & Marshall, 1989; Stainsby et al., 1985; Stainsby et al., 1984) and that sympathetic activity is diminished in those with SCI, it can be hypothesized that the decreased catecholamine production reduces the BLa response in the spinally injured. This would be particularly true for those with injuries above T6. Epinephrine stimulates lipolysis as well as muscle and liver glycogenolysis by activating hormone sensitive lipase and adenylate cyclase, respectively (Brooks & Fahey, 1984). Lactate is an eventual by-product of glycogenolysis. Previous discussion indicated that epinephrine activity is decreased in people with spinal lesions above T6. Therefore, the BLa production would also be expected to be reduced. However, in individuals with spinal lesions below the T6 level, BLa levels should resemble able-bodied values. Unfortunately, investigations on the BLa response in people with SCI are varied in methodology and therefore preclude the formation of definite conclusions.

Burkett et al. (1988) examined the BLa response to maximal and supramaximal exercise in twenty trained and untrained males and females with various types of SCI. Each subject performed a maximal exercise test on a wheelchair ergometer. Ten minutes following the maximal test, a two minute supramaximal test at 80% of $\dot{V}O_2$, was completed to determine if a true maximal level had been achieved. Finger capillary BLa samples were taken prior to exercise and 4 minutes post maximal and supramaximal exercise. Resting lactate levels were higher compared to those found in the able-bodied. Postexercise BLa values were lower than than those reported for able-bodied subjects. Male subjects had higher resting lactate concentrations

compared to females. However, the authors were somewhat contradictory in their interpretations of able-bodied and SCI responses. They referred to the results of Walters (1985) who determined the BLa responses to exercise in able-bodied 13-17 year old male and female athletes. Trained able-bodied females showed maximal BLa values twice that of females with SCI, while trained able-bodied males' maximal lactate responses were lower than trained males with SCI. Burkett et al. (1988) stated that subjects with SCI in their study had higher resting and lower maximal BLa concentrations compared to the able-bodied subjects in the Walters study (1985). They attributed these discrepancies to the higher workloads associated with wheelchair ambulation and the smaller muscle mass utilized in wheelchair propulsion. The comparisons made by Burkett et al. (1988) between their SCI subject pool and the many studies on able-bodied BLa responses they referenced are clearly unwarranted. Subjects were not matched with regard to age, number, and training status. Further, there were no similarities in test protocols which elicited the BLa responses. Therefore, the conclusions of Burkett et al. (1988) must be interpreted with caution.

Eriksson et al. (1988) determined lactate responses following maximal exercise using a previously mentioned research protocol. Maximal BLa levels were lower in quadriplegics compared to paraplegics and the able-bodied. There were no training differences in BLa among quadriplegics. Trained paraplegics had higher maximal BLa concentrations than untrained paraplegics and the able-bodied, while the able-bodied and untrained paraplegics demonstrated equivalent lactate levels. The higher BLa values for trained paraplegics can be attributed to their ability to exercise at higher work levels. Hjeltnes (1986) also investigated the maximal BLa response in newly injured paraplegics and tetraplegics. Two-hundred male and female subjects

each performed maximal arm crank ergometry. The authors reported BLa concentrations between 5.5 and 11.4 mmol/l, which were similar to those reported by Taylor et al. (1986); Wicks et al. (1983); Glaser et al. (1980); and Gass and Camp (1979).

Two studies have addressed the issue of the lactate threshold (Tla) in individuals with SCI. Flandrois et al. (1986) compared the Tla response to maximal arm crank exercise in nine paraplegic and nine able-bodied, physically active males. The paraplegics were subdivided according to high-level and low-level lesions. The lactate threshold occurred at 63%, 59%, and 43% of $\dot{V}O_2max$ for high-level paraplegics, low-level paraplegics and able-bodied subjects, respectively. This indicated that since changes in central cardiovascular functions in those with SCI are limited by reduced SNS activity, improvements in aerobic capacity are manifested through adaptations in cellular metabolic capability. Additionally, Lakomy et al. (1987) utilized wheelchair ergometry to determine the BLa response to maximal exercise in paraplegic and tetraplegic athletes. Each subject performed a maximal exercise test and a five kilometer time trial. Blood lactate samples were taken after each of the five stages performed in the maximal exercise test. A 4 mmol/l lactate value is often used as an indicator of Tla in able-bodied populations. The investigators found a high correlation between the 4 mmol/l lactate value and the average speed the athletes wheeled during the five kilometer time trial. This suggested that the 4 mmol/l lactate concentration was the highest level of exercise intensity the athletes with spinal injury could work using primarily oxidative fuel sources.

Summary

Examination of the literature clarifies the need for more extensive research into the biochemical responses to maximal exercise in individuals with SCI. The catecholamine response to maximal exercise in this population has not been addressed and therefore necessitates inquiry. While there has been a limited attempt to quantify the lactate threshold in those with SCI, these studies failed to relate the lactate threshold to the ventilatory threshold. Finally, since the catecholamine, lactate and ventilatory responses have been shown to be coincidental and possibly interrelated in the able-bodied, it is of interest to determine if individuals with SCI exhibit a similar response.

CHAPTER III

METHODS

The methodologic procedures that were utilized in this investigation are presented in this chapter. The chapter is divided into sections addressing subjects, experimental design, data collection and statistical analysis.

Subjects

Four males diagnosed with injuries above the 6th thoracic vertebra (T6) level (Quad) and three males diagnosed with injuries below the T6 level (Para) volunteered to participate. Specific subject characteristics are presented in Table 1. All subjects were physically active and recruited from wheelchair basketball teams, track clubs or other athletic organizations for those with spinal injuries in the Oregon Willamette Valley area. Each subject was informed about the test protocol and read and signed a written informed consent document, previously approved by the Oregon State University Institutional Review Board (Appendix A).

Table 1

Subject Characteristics

Subject	Age (yrs.)	Weight(kg)	Injury Description
1	36	65.6	C7/Incomplete; 9 years post
2	28	86.0	T2/Incomplete; 7 years post
3	27	58.5	C7/Complete; 6 years post
4	40	74.0	T12/Complete; 20 years post
5	22	64.0	T10-12/Incomplete; birth
6	23	66.0	T12/Complete; 3 years post
7	26	57.0	T10/Incomplete; 15 years post
mean±SE	28.9±6.7	67.3±3.8	

Experimental Protocol

All exercise testing was performed in the morning following an overnight fast to control for substrate levels in the blood. Subjects were asked to refrain from vigorous activity 24 hours before testing. Upon arrival to the laboratory, the subjects were weighed, provided an explanation of the experimental protocol, and allowed time for questions and answers concerning the informed consent. Following the question and answer period, subjects were asked to sign the informed consent document prior to actual participation in the study. A licensed phlebotomist inserted the catheter into a forearm vein and described the blood drawing process. Subjects rested for 20

minutes and, during this time, were provided further explanation regarding laboratory protocol. The principal investigator performed the blood draws, while trained personnel assisted in the following: (1) monitoring the metabolic cart; (2) collecting ratings of perceived exertion and heart rate; (3) placing blood samples in appropriate tubes, as well as vortexing and spinning the blood; and (4) helping the subject maintain cadence during the blood draw, which will be described in further detail.

Each subject performed an incremental, peak oxygen uptake test ($\dot{V}O_2pk$) on a previously calibrated, friction-braked Monark arm ergometer. Crank axis height was established at shoulder level and crank distance was adjusted to allow for slight elbow flexion upon arm extension The test protocol varied according to the level of spinal injury. In general, individuals with spinal lesions classified as Quad pushed at a rate of 60 revolutions per minute (RPM) with an increase in work increments of 6 Watts every 3 minutes. Ace bandages were utilized to secure hands to the arm crank grip, for subjects with quadriplegia who had limited grip function. Individuals with spinal lesions classified as Para pushed at a rate of 70 revolutions with an increase in work increments of 8 Watts every 3 minutes. Initial workloads were determined by the investigator and based on individual activity levels. Subjects who were deemed to be more physically fit started the exercise test at a higher workload than subjects who were deemed less physically fit. This was necessary to prevent extended test sessions in individuals who had a greater tolerance for the test protocol. Subjects continued to exercise until they could no longer maintain cadence or until volitional exhaustion.

Measurement of Oxygen Consumption

Oxygen consumption ($\dot{V}O_2$) was measured through open circuit spirometry and indirect calorimetry using a Sensormedics 2900 metabolic cart system (Sensormedics Corporation, Yorba Linda, CA). Exhaled air was monitored continuously for concentrations of oxygen and carbon dioxide. Exhaled ventilatory volume was measured through a mass flowmeter. The metabolic data were reported in 20 second intervals. The metabolic cart gas analyzers and mass flowmeter were calibrated prior to testing using two known gas concentrations and a 3 liter syringe, respectively.

Measurement of Heart Rate

Heart rate (HR) was monitored throughout exercise using electrocardiography and a standard V5, 3 electrode system. A polar pulse monitor was also used as a back-up measure.

Measurement of Blood Parameters

Blood was sampled following 20 minutes of rest and during the last minute of each workload, in 10 ml volumes, obtained through a 21 gauge angiocatheter, equipped with a 3-way stopcock, inserted into a forearm vein. The angiocatheter was flushed between sampling with heparinized saline to prevent clotting. To facilitate sampling, the subject stopped pushing with the catheterized arm, while the remaining arm continued to crank. A laboratory technician assisted the subject in maintaining cadence until the end of sampling (Hooker et al., 1990). This protocol was chosen because it was

relatively continuous and more conducive to sampling of blood parameters than ventilatory parameters. Prior to commencement of the research project, it was acknowledged by the experimenter that the ventilatory data resulting from this protocol would probably not yield a measurable Tv. The lactate and catecholamine data were considered to be a priority and sacrifice of the Tv data was accepted as a consequence.

For lactate determinations, approximately 1 ml of blood was placed into tubes prepared with 4.5 ml of 8% perchloric acid ($HClO_4$) to deproteinize the blood. The lactate tubes were weighed before and after blood sampling to obtain the actual blood volume. For catecholamine determinations, the remaining blood sample was placed in tubes prepared with a small amount of reduced glutathione to prevent the oxidation of the catecholamines and two drops of heparin to prevent clotting. All tubes were vortexed immediately after each blood sample.

Plasma norepinephrine (NE) and epinephrine (EPI) levels were determined by high performance liquid chromatography (HPLC) with electrochemical detection (Bio-Rad HPLC pump, Model 1330; Bio-Rad electrochemical detector, Model 1340 and Shimatzu C-R3A Integrator), as specified using the modified method of Hallman, Farnebo, Hamberger (1978). After centrifugation, 25 µl dihydroxy-bensylamine (DHBA) was added to the supernatant as an internal standard. The pH was adjusted to above 8.0 with 1 ml of 1.5 M Tris buffer (pH 8.6 in 2% EDTA). Twenty-five mg of acid-washed alumina (AAO) was added to each sample, followed by 10 minutes of vortexing. The alumina was washed twice with 3.0 ml of deionized water and aspirated 3 times. The catecholamines were extracted with 100 µl of 0.1 M HClO4 with 10 minutes of vortexing. One hundred microliters of each sample was injected into the HPLC column (Bio-Rad C-18 Reverse Phase,

150x4 mm) and eluted with an ion pair mobile phase (6.8 g sodium acetate, anhydrous, 1.2 g sodium heptane sulfonate, 0.80 g sodium EDTA, 45 ml acetonitrile, adjusted to a pH of 4.8 with glacial acetic acid). Samples were compared with known NE and E standards. Plasma levels of NE were calculated using the following equation:

$$[NE]unknown = \frac{\text{NE peak ht. of unknown/DHBA peak ht.}}{\text{NE peak ht. of std./DHBA peak ht.}} \times [NE]$$

Plasma epinephrine concentrations were calculated by substituting EPI values in place of NE values in the above equation. The catecholamine analysis was performed at the University of Colorado Exercise Biochemistry Laboratory.

Plasma lactate levels were analyzed using the method of Hohorst (1963). The glycine-hydrazine assay mixture was prepared by combining 8.44 glycine U.S. P., 5.85 g hydrazine sulfate A.R., 0.22 g EDTA-Na2 and 67.4 ml 2N NaOH. This was added to 100 ml of distilled water, mixed and refrigerated. Immediately prior to assay, 0.500 g NAD+ and 0.125 ml of LDH suspension (from rabbit muscle, Type II, Sigma Chemical Co., L-2500) was added to the assay mixture and the final volume brought to 150 ml with distilled water. The pH of the assay mixture was 9.5. One hundred microliter of the sample was pipeted into test tubes, and 1.0 ml of the assay mixture added. Duplicate samples were compared against blanks of 100 µl of 8% HClO4 combined with 1.0 ml assay mixture. The samples and blanks were vortexed and then placed into a 37°C water bath for 30 minutes with continuous, gentle shaking. The tubes were cooled for 5-10 minutes and sampled (Perkin-Elmer uv/vis Spectrophotometer). Lactate levels were determined by the reduction of

NAD+. Reduction of NAD+ to NADH causes the proportional increase in the optical density at 340 nM.

[LACTATE] μMol/ml=delta ExFxV/(exd)

where delta E is the change in optical density

F is the sample dilution factor

V is the dilution of filtrate in the cuvette

d is the light path of the cuvette in cms

[LACTATE] = (O.D. sample - O.D. mean blank) xFxV/6.23

The lactate analysis was performed at the University of Colorado Exercise Biochemistry Laboratory.

Determination of Ventilatory, Lactate and Catecholamine Thresholds

Ventilatory threshold (Tv) was determined by ventilatory ($\dot{V}E$) parameters obtained during the $\dot{V}O_2$pk test. An increase in the ventilatory equivalents for O_2 ($\dot{V}E/\dot{V}O_2$) without an increase in the the ventilatory equivalents for CO_2 ($\dot{V}E/\dot{V}CO_2$), and a nonlinear increase in $\dot{V}E$ will provide an indication of where the Tv occurs (Green, Hughson, Orr & Ranney, 1983). The lactate and catecholamine thresholds (Tla and Tne, Tepi) were determined by multisegmental regression lines.

Statistical Analysis

Unpaired t-tests were used to determine if differences existed in the plasma catecholamine, lactate, and ventilatory responses to incremental exercise, as well as total exercise time, between subjects with spinal lesions above T6 and those with lesions below T6. Pearson-product moment correlations were performed to determine the relationships between Tv-Tla, Tla-Tne, Tla-Tepi, NE-LA, EPI-LA, and NE-EPI for each subject. The significance of the correlations were determined from regression coefficients. Visual inspection of the data was used to describe individual differences for each dependent measure.

CHAPTER IV

RESULTS AND DISCUSSION

The experimental results and statistical analysis of the data are presented in this chapter. Both individual subject, as well as group data are reported. The results are evaluated and discussed in relation to previously reported literature. An explanation of the data patterns that were observed is offered.

Peak Exercise Responses

The peak performance times were (mean ± SE) 27.3±4.2 minutes and 19.1±3.7 minutes for those with injuries below the 6th thoracic vertebra level (T6) (Para) and above the T6 level (Quad) groups, respectively. These times were significantly different at $p \leq 0.05$. The mean peak norepinephrine (NE), epinephrine (EPI) and lactate (LA) values for the Quad and Para groups are presented in Table 2.

Table 2

Peak NE, EPI, and LA Exercise Responses

	Exercise Time (min)	NE (ng/ml)	EPI (ng/ml)	LA (mM)
Para	27.3±4.2*	3.1±1.0*	0.5±0.2*	7.1±0.5*
Quad	19.1±3.7	0.4±0.1	0.1±0.01	3.2±0.4

values are mean ± SE

*Significant difference between groups at $p \leq 0.05$

There was no significant difference in resting levels of NE (0.3±0.05 vs 0.4±0.14), EPI (0.03±0.01 vs 0.08±0.04), and LA (0.8±0.04 vs 0.8±0.04) between the Quad and Para groups, respectively ($p \leq 0.05$). The mean peak ventilatory ($\dot{V}E$), oxygen uptake ($\dot{V}O_2$), respiratory exchange ratio (RER) and heart rate (HR) responses are presented in Table 3. The Para group, compared to the Quad group, exhibited significantly ($p \leq 0.05$) higher peak responses for all parameters, with the exception of RER.

Table 3

Peak $\dot{V}E$, $\dot{V}O_2$, RER and HR Exercise Responses

	$\dot{V}E$ ($l \cdot min^{-1}$)	$\dot{V}O_2$ ($l \cdot min^{-1}$)	RER ($\dot{V}O_2/\dot{V}CO_2$)	HR ($beats \cdot min^{-1}$)
Para	103.8±16.27*	2.2±0.2*	1.12±0.02	195.5±4.09*
Quad	51.2±3.25	1.2±0.01	1.07±0.02	133.0±18.45

values are mean ± SE
*Significant difference between groups at $p \leq 0.05$

As the severity of spinal injury increases there is a concomitant increased loss of function. This increased loss of function is manifested through decreased active muscle mass and decreased sympathetic nervous system (SNS) activity. The reduction in SNS activity has pronounced debilitating effects on physiological and metabolic factors such as cardiac output, heart rate, ventilatory capacity, and various substrate pathways. Therefore, the greater peak responses in $\dot{V}E$, $\dot{V}O_2$, HR, exercise time and LA for the Para compared to the Quad group are not surprising. The results from the present study are in agreement with data from previous research, indicating that there is an inverse relationship between injury level and responses to peak exercise. (Wells & Hooker, 1993; Eriksson et al., 1988; Flandrois et al., 1986; Taylor et al., 1986; Wicks et al., 1983; Glaser et al., 1980; Gass & Camp 1979). It is difficult to compare the current values of the aforementioned variables with those found in the literature. Subjects with spinal injury vary greatly with regard to injury type, severity, length and

etiology. Also, it is difficult to ascertain the extent of neural activity that each subject possesses. This is important because of the powerful influence neural activity has on metabolic and physiologic functioning. However, the ventilatory data from the current study are in general accord with other investigations that employed similar subject pools (Flandrois et al., 1986; Wicks et al., 1983; Gass & Camp, 1979). Alternately, the peak LA values from the present research are lower than the LA data reported in other investigations that also utilized active subjects (Eriksson, et al., 1988; Flandrois et al., 1986; Gass & Camp; 1979). The lower LA levels seen in the present study, compared to the other studies, may be attributed to the variable levels of fitness among subjects. The subjects who participated in previous research endeavors were reportedly more involved in consistent training than the subjects in the current study. Their capacity for LA production was greater due to their ability to work at higher power outputs. Several of the subjects who participated in the present study were active, but not necessarily trained athletes.

Because this is the first study to investigate the peak exercise responses of NE and EPI in individuals with spinal cord injury (SCI), no comparisons can be made between the present data and other sources. However, Fitzpatrick et al. (1989) have shown that during prolonged submaximal exercise at 75% $\dot{V}O_2max$, Quads exhibit lower NE and EPI levels compared to Paras. The current findings correspond with those of Fitzpatrick et al. (1989). The Paras had significantly greater peak NE and EPI responses compared to the Quads. This heightened response is representative of the greater amount of neural functioning in the Paras. This information lends further support to the observation that as the severity the spinal lesion increases, there is a decrease in sympathoadrenal function.

Ventilatory Parameters

The ventilatory threshold (Tv) was not detectable in every subject. Typically, an increase in the ventilatory equivalents for O_2 ($\dot{V}E/\dot{V}O_2$) without an increase in the the ventilatory equivalents for CO_2 ($\dot{V}E/\dot{V}CO_2$), and a nonlinear increase in $\dot{V}E$ will provide an indication of where the Tv occurs. The general trend among subjects in the present study was for the ventilatory equivalents and $\dot{V}E$ to increase linearly (Figures 1, 2, 3, and 4), thus establishment of a Tv for the majority of the subjects was not possible.

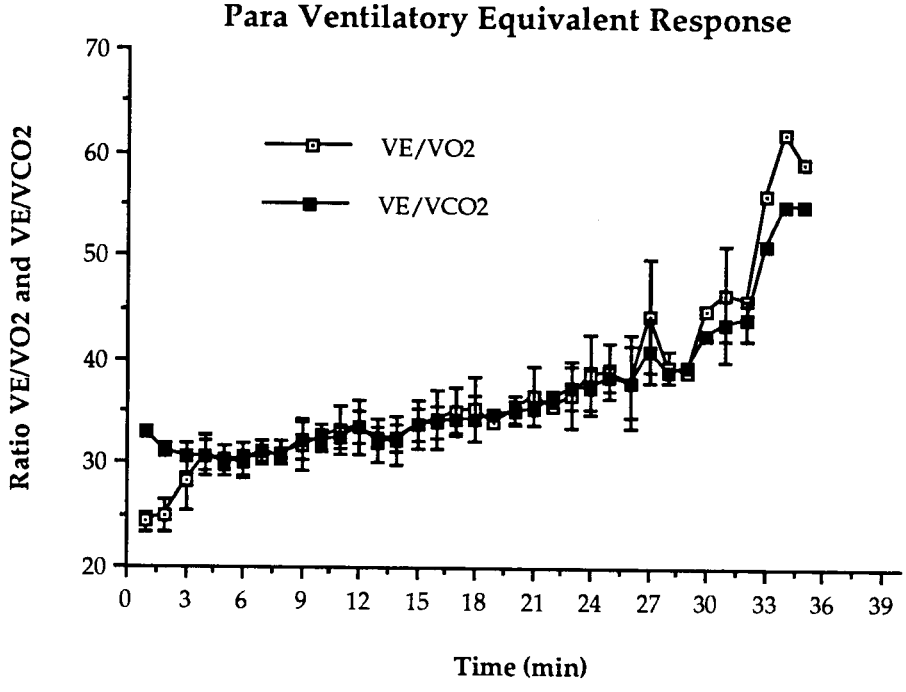

Figure 1. Ventilatory equivalents for O_2 and CO_2 in the Para group.

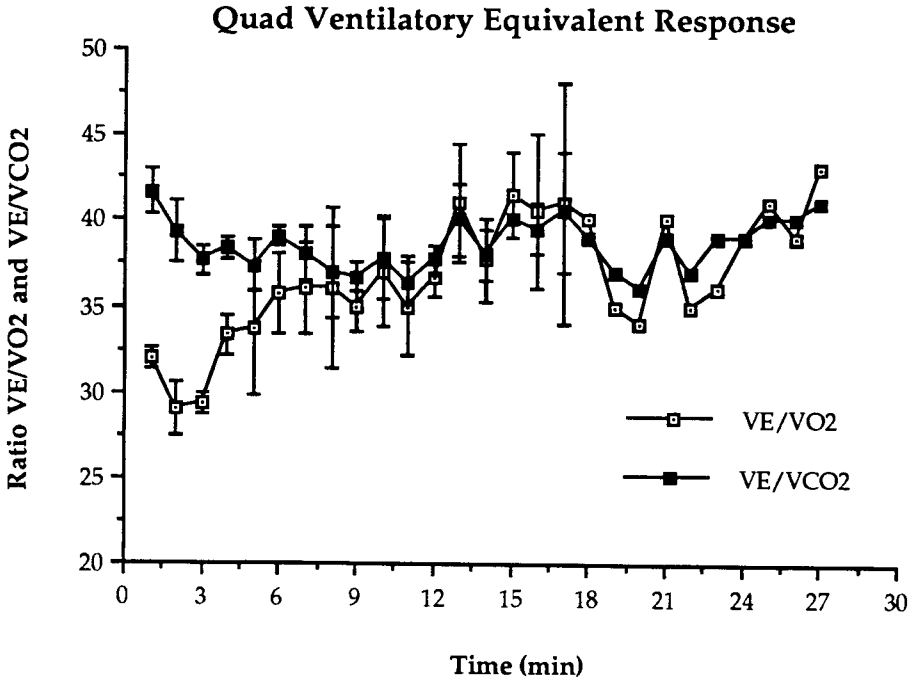

Figure 2. Ventilatory equivalents for O_2 and CO_2 in the Quad group.

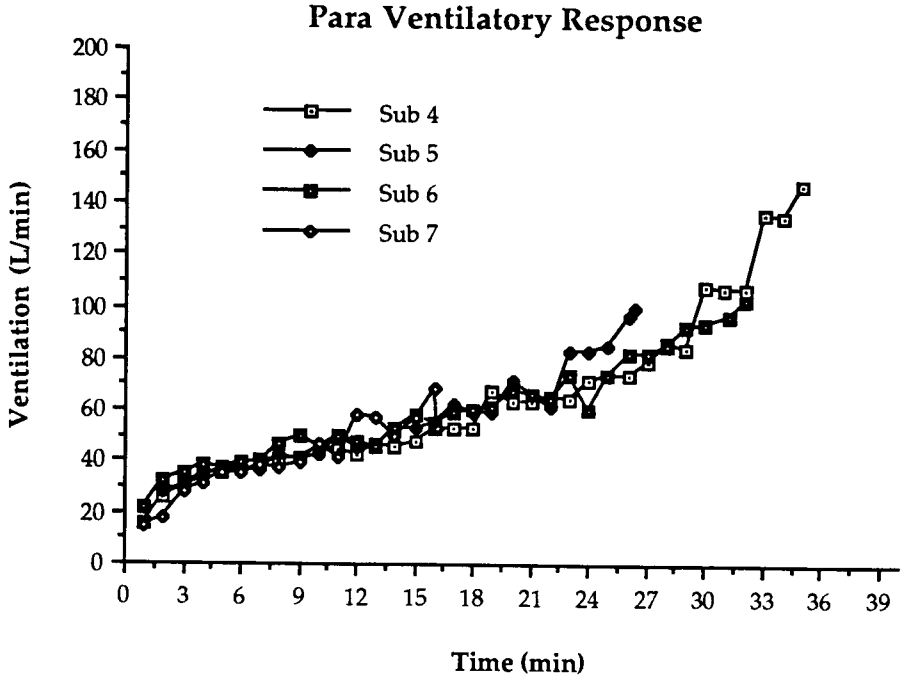

Figure 3. Ventilatory response for each subject in the Para group.

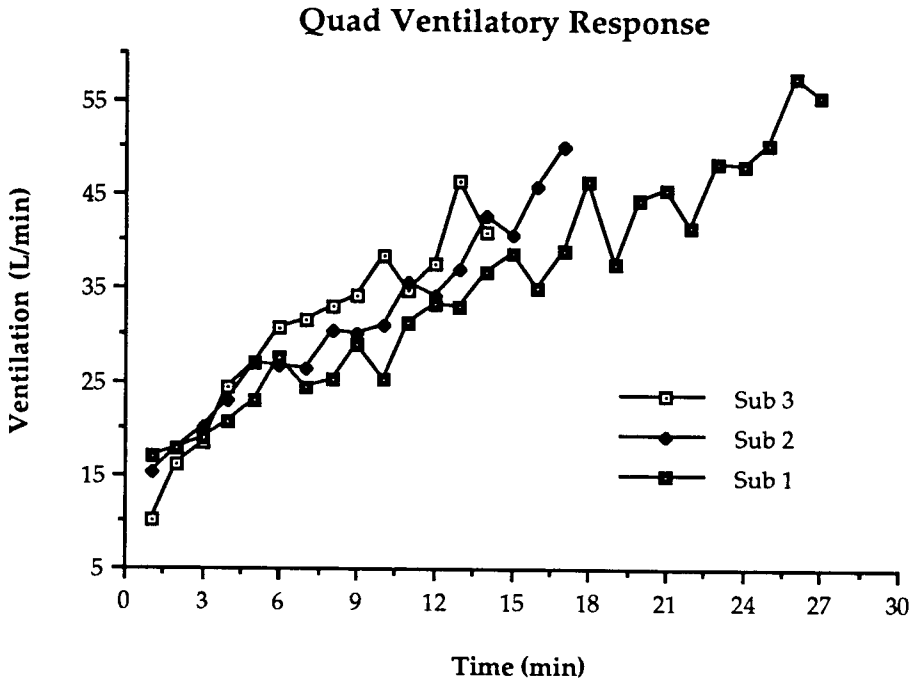

Figure 4. Ventilatory response for each subject in the Quad group.

As stated in Chapter III, it was acknowledged prior to beginning the study that the exercise protocol was specific to sampling blood parameters and may undermine the ability to detect the Tv from the ventilatory data The catecholamine and lactate data were given priority and lack of clear and consistent Tv data was accepted as a consequence. The investigator reasoned that consistent $\dot{V}E$ data might be obtained because $\dot{V}E$ would decrease only during minute 3, when the subject brought his arm off the arm crank. At this time there would be a decreased neural stimulus to the motor cortex and thus a decrease in $\dot{V}E$. When the subject returned his arm to the arm crank, $\dot{V}E$ would increase accordingly. This suggested, therefore, that minute 3 should

be excluded from the data inspection as being unrepresentative of the true exercise $\dot{V}E$ response. Unfortunately, the extent and timing of the decrease in $\dot{V}E$ during minute 3 was not consistent among the subjects and $\dot{V}E$ did not increase immediately following minute 3 for all subjects. There was a large variability in the $\dot{V}E$ response, with $\dot{V}E$ sometimes decreasing during minute 2, increasing during minute 3, or staying constant following minute 3. This variability possibly can be explained by the amount of assistance the subjects received from the laboratory aids. A strong effort was made to communicate with the subjects regarding how much assistance was required. Despite these efforts, the assistance the subjects received appeared to have been variable from stage to stage and from subject to subject. Appendix C contains graphs of individual $\dot{V}E$ and ventilatory equivalent data.

There was a departure in linearity of $\dot{V}E$ for Subject 4 in the Para group (Figure 5). This subject's $\dot{V}E$ data were used to estimate Tv.

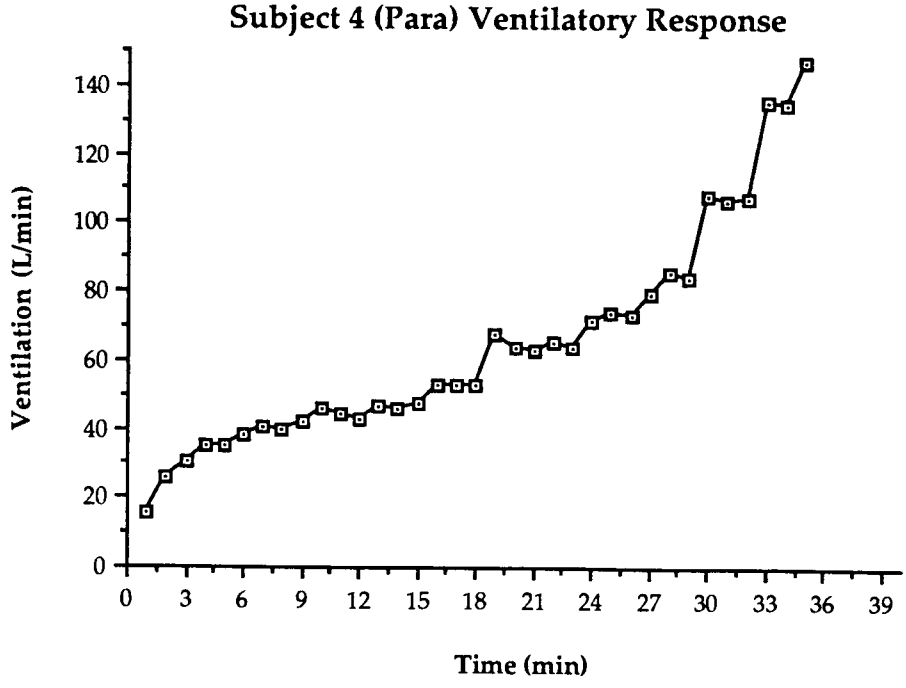

Figure 5. **Ventilatory response for Subject 4 in the Para group.**

The results indicated that Subject 4's Tv occurred at approximately minute 29 of the exercise session. This corresponded to a $\dot{V}O_2$ of 2.14 $l \cdot min^{-1}$, which was equivalent to 86% of the subject's $\dot{V}O_2pk$. While the breakpoint in Subject 4's $\dot{V}E$ responses appears to be clear, it may merely represent respiratory compensation and not the Tv.

Previous research has not attempted to estimate a Tv in individuals with SCI. To date, only two studies have examined this phenomenon in the able-bodied using arm crank ergometry (Davis et al., 1976; Reybrouck et al., 1975). Davis and colleagues (1976) had subjects perform arm cranking, leg cycling and treadmill walk-running, in order to determine the validity of gas

exchange parameters as an indirect measure of lactic acidosis (Tla). To determine where the Tv occurred these authors used the point of departure in linearity of $\dot{V}E$, $\dot{V}O_2$, RER and F_{EO_2} together with the linearity in the $\dot{V}E$ and $\dot{V}CO_2$. Blood samples were taken to establish at which point there was an abrupt increase in LA production. However, blood LA response was only measured during a separate leg cycling exercise session. Blood was not sampled during arm cranking or walking. There was a strong correlation between the gas exchange parameters and the blood LA response (r=0.95), so the gas exchange parameters could be used as indirect measures of Tla. These researchers found that the Tv was significantly lower in arm cranking compared to the other modes of exercise. Also the test-retest reliability of measuring Tv in arm cranking was moderate (r=0.77). Davis et al. (1976) attributed the lower Tv in arm crank exercise to: (1) the smaller amount of available muscle mass in the arms; (2) specificity of training; and (3) variations in motor unit recruitment patterns between the different types of exercise. The results of Davis and associates (1976) must be interpreted with caution. It is logical that the Tv would occur earlier in arm cranking compared to leg cycling and walking, due to the explanations the authors provided. However, since determinations of Tla were not made during arm cranking, extrapolation of the leg cycling correlations to arm cranking is unwarranted.

The results of Reybrouck et al. (1975) are in agreement with those of Davis et al. (1976). Reybrouck and associates observed that during arm crank exercise, the Tv occurred at a lower percentage of $\dot{V}O_2max$ compared to leg cycling and combined arm-leg exercise. The authors focused their discussion on the differences between leg cycling and combined arm-leg exercise and did not submit any hypotheses regarding the lower Tv in arm exercise.

Davis et al. (1976) used a protocol where subjects cranked at 50 rpm and workload was increased 0.25 kp each minute. Reybrouck et al. (1975) had subjects exercise for 4 minutes at 0, 30, 45 and 60 Watts. Additionally, studies investigating maximal exercise responses in individuals with SCI have used short work stages (Eriksson, et al., 1988; Burkett, et al., 1990; Coutts et al., 1983). Studies investigating Tv in the able-bodied have typically used one-two minute stages (Green et al., 1983; Podolin, Munger & Mazzeo, 1991; Davis et al., 1976; Reybrouck et al., 1975). Mazzeo and Marshall (1989) used 3 minute stages to determine Tv during running and cycling. The protocol in the present study used small workload increases and 3 minute stages and, while necessary for blood sampling purposes, may not have been conducive to eliciting a Tv in the population studied. The reason for this is unclear, but it may be difficult to elicit a Tv during arm ergometry, regardless of work stage length. Other researchers have not attempted to demonstrate a Tv in individuals with SCI. Factors such as exercise protocol and the inherent limitations associated with spinal trauma may be possible explanations of the the lack of Tv in this population.

The lack of a Tv in the Quads is not surprising. First, Subjects 2 and 3 did not have enough data points, due to their short exercise times, to clearly establish a Tv. Second, Quads may have lower ventilatory capacity related to their disruptions in ventilatory musculature innervation, which may cause variations in breathing patterns (Coutts et al., 1983). Coutts et al. (1983) reported that the $\dot{V}E/\dot{V}O_2$ for the tetraplegics and high level paraplegics in their study were similar to those reported in the able-bodied. This suggested that ventilation was not limiting the availability of O_2. The $\dot{V}E/\dot{V}O_2$ values in the present study (Quad=46±1.5; Para=51±4.4) were similar to those reported by Coutts et al. (1983) for a comparable subject population. Thus,

limitations in ventilation may not have been a singular factor in the lack of Tv in the Quads, but instead a contributing factor.

It is not apparent why only Subject 4 exhibited a Tv (Figure 5). Subject 4 had a low lesion level, was one of the more fit subjects in the study and had the greatest peak exercise time. However, Subject 4 was similar to Subject 6 regarding the fitness and lesion level. Thus, it would follow that Subject 6 would also exhibit a Tv, but this was not the case. It is difficult to rationalize why a Tv occurred for Subject 4, but not with the other subjects. The only clear justification appears to be subject variability. A critical difference between subjects was the completeness of the spinal lesion. This probably had a significant effect on the data. This statement is supported by Hjeltnes (1986) who found the greatest variations in responses to exercise among tetraplegics with incomplete lesions. With an incomplete spinal injury it is difficult to assess the amount of neural activity that has remained intact. The subjects in this study provided anecdotal information regarding sensory and motor function. Unfortunately, there was no medical information documenting actual neural functioning. Also, it would be difficult to establish actual metabolic activity without extensive medical evaluation.

Lactate Response

Multisegmental regression lines were used to determine the lactate threshold (Tla). While all subjects, with the exception of Subject 4, did not demonstrate a Tv, the Tla was more easily discernable for Subjects 5 and 6 in the Para group (approximately 40 and 72 Watts for Subjects 5 and 6, respectively) (Figure 6). Graphs of individual LA responses are presented in Appendix E.

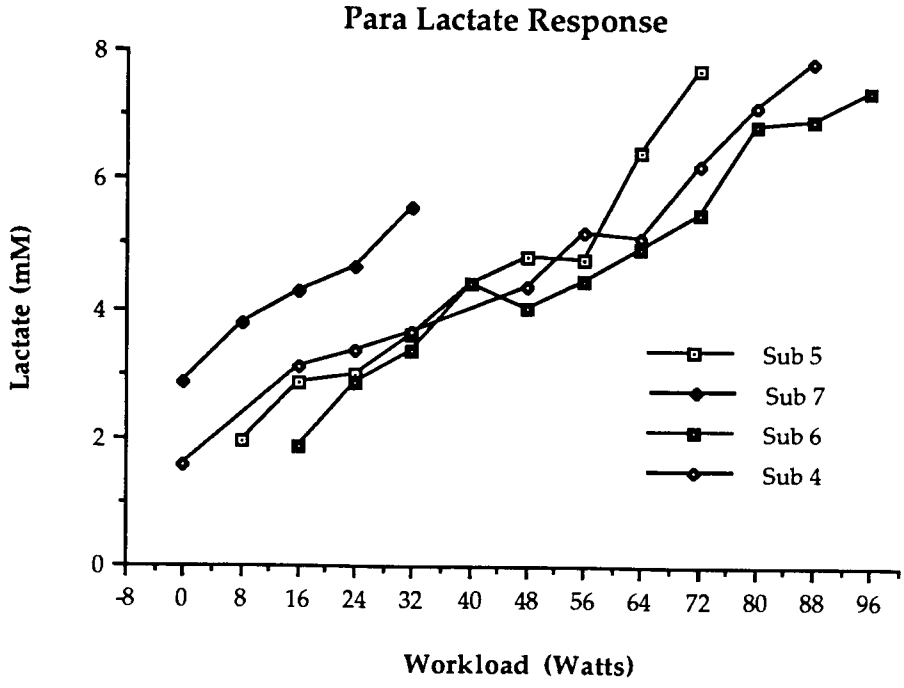

Figure 6. Lactate response for each subject in the Para group.

The regression lines did not intersect in Subject 4's data. Visual inspection, however, implies that Tla occurred at a workload of 64 Watts (Figure 6). In the Quad group, Subject 1 exhibited a Tla that occurred at approximately 36 Watts. A clear lactate breakpoint was not visible in Subjects 2 and 3 (Figure 7).

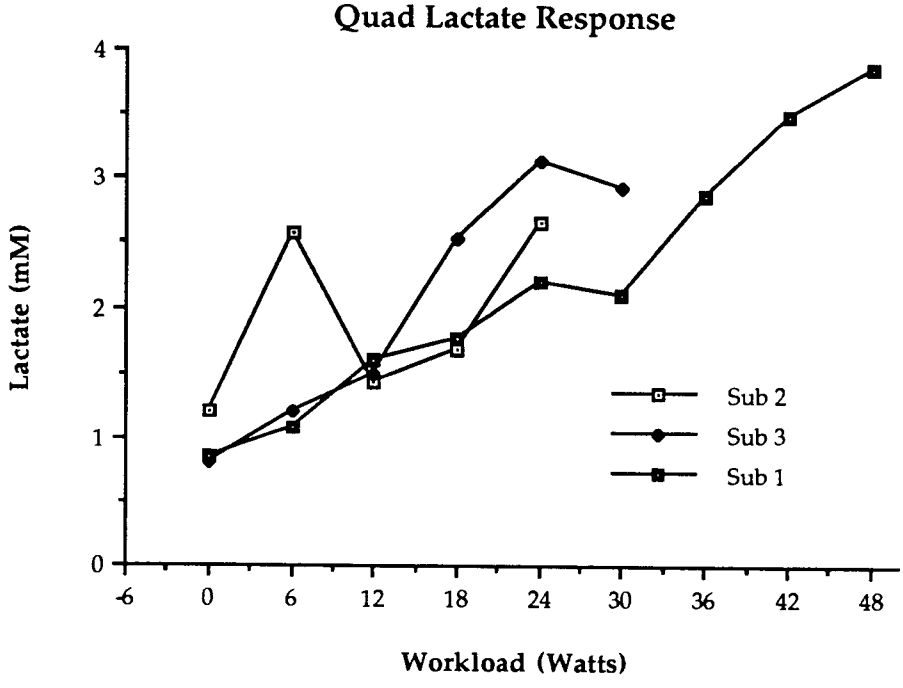

Figure 7. **Lactate response for each subject in the Quad group.**

In general, the Para subjects demonstrated a curvilinear increase in lactate with an increase in workload (Figure 6). An evaluation of the Para group lactate response indicated a Tla at approximately 64 Watts (Figure 8).

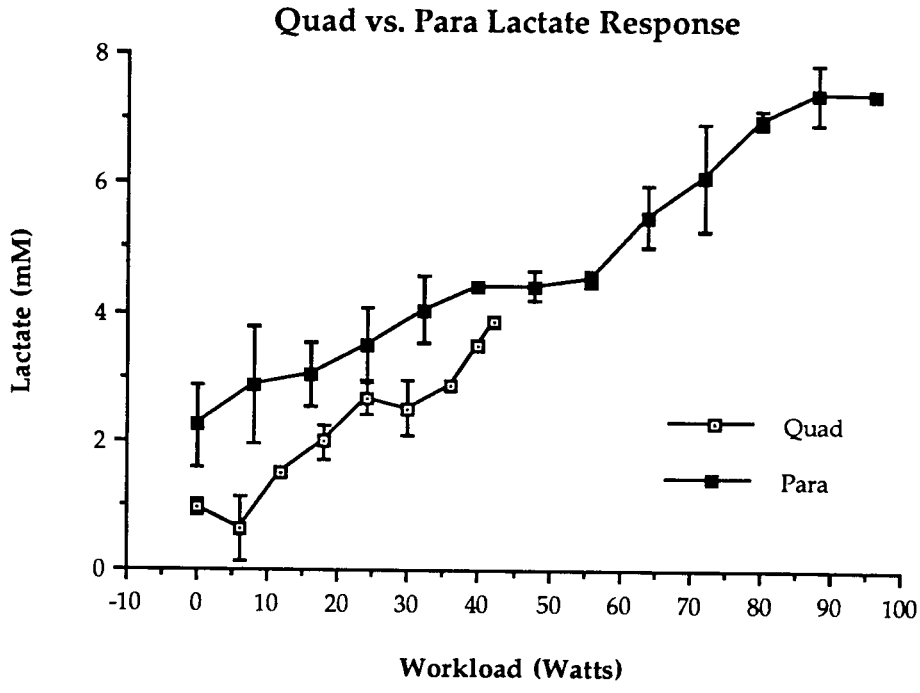

Figure 8. **Lactate response for the Quad and Para groups.**

The lactate response in the Quad subjects appeared to be linear and thus, no Tla could be interpreted (Figure 8). Additionally, the lactate response to increasing workload was attenuated in the Quad group compared to the Para group (Figure 8). The Tla data are summarized in Table 4.

Table 4

Individual Lactate Threshold Response

Subject	Clear Breakpoint	Workload (Watts)	Percentage $\dot{V}O_2pk$
Sub 1 (Quad)	yes	36	78%
Sub 2 (Quad)	no		
Sub 3 (Quad)	no		
Sub 4 (Para)	yes (visually)	64	90%
Sub 5 (Para)	yes	40	67%
Sub 6 (Para)	yes	72	73%
Sub 7 (Para)	no		
Values are mean±SE		53.0±8.9	77.0±4.9

Flandrois et al. (1986) compared the difference in Tla between high level Paras, low level Paras and able-bodied subjects. All subjects performed a maximal arm crank ergometry test which involved 15 Watt increments in workload every 2.5 minutes. They found that Tla occurred at a significantly greater percentage of $\dot{V}O_2max$ in the high level Paras compared to the low level Paras and the able-bodied. Their discussion of these results emphasized the specificity in arm training of the Paras compared to the able-bodied subjects. Since there is less circulatory adaptations to training in individuals with SCI, the training effect has more impact on cellular metabolic capacity. The cellular metabolic adaptation to training manifests itself in an increased ability to maintain balance between the rate of appearance and rate of disappearance of lactate. This is represented by a delayed Tla (Flandrois et al., 1986).

Lakomy et al. (1987) designed an investigation examining some of the physiological factors associated with endurance performance, particularly the Tla. They utilized a 4 mmol/l value as an indicator of Tla. Subjects performed a $\dot{V}O_2$max test and a 5 kilometer (km) submaximal time trial on a wheelchair ergometer. The authors found a strong relationship between the 4 mmol/l value and the average pushing speed during the 5 km test (r=0.87). They concluded that wheelchair athletes pace themselves at an intensity just below the Tla. This is the highest level of submaximal exercise the athlete can perform and still utilize primarily oxidative fuel sources that would ultimately delay fatigue.

The results of the current study concur somewhat with those of Flandrois et al. (1986). It is curious that multisegmental analysis did not reveal a Tla for Subject 4. This does not seem logical considering his demonstration of a Tv. Visual inspection of his data (Figure 6) identifies a Tla occurring at approximately 64 Watts and 90% of $\dot{V}O_2$pk. The Tv for Subject 4 occurred at 86% of $\dot{V}O_2$pk. These data imply that there may be a relationship between the Tla and Tv in Subject 4. However, the association between theses two factors is viewed as coincidental and not causal (Podolin et al., 1991; Mazzeo & Marshall, 1989; Brooks, 1985). The coincidental nature of the Tla and Tv is further substantiated by the exhibition of a Tla, but not a Tv in Subjects 5, and 6. As mentioned previously, these subjects had a fitness level similar to Subject 4 and would be expected to display similar responses. However, the Tla appeared at a lower percentage of $\dot{V}O_2$pk in Subjects 5 and 6, compared to Subject 4. Subject 4 was better able to maintain a consistency in LA turnover before increased exercise intensity caused an imbalance in the rate of LA appearance and disappearance. This suggests that Subject 4 had a higher training status than Subjects 5 and 6, although his $\dot{V}O_2$pk was not

substantially higher. The Tla for the Paras in the present study occurred at a higher percentage of $\dot{V}O_2pk$ compared to the Paras in the study by Flandrois and colleagues (1986). Differences in exercise protocol, training status and variability of subjects could explain the disparity in the results of Flandrois et al. (1986) and the present study.

Subject 1 was the only Quad to demonstrate a Tla. This is not surprising since Subject 1 had been training aerobically and consistently for wheelchair road races. In contrast, Subjects 2 and 3 were quad rugby players, which requires anaerobic training. Consequently, Subjects 2 and 3 were less aerobically fit than Subject 1 and were unable to perform the exercise test for a time period that would produce sufficient data points for determination of a Tla. Subject 1 did not display a Tv, therefore it can be surmised that there was a dissociation between Tla and Tv in this individual. Although the individual LA response appeared to increase linearly with increasing workload (Figure 7), the LA pattern in Subjects 2 and 3 was somewhat variable. The Tla for Subject 1 occurred at a higher percentage of $\dot{V}O_2pk$ compared to similar subjects in the study by Flandrois et al. (1986). Again, differences in exercise protocol, training status and variability of subjects could explain the disparity in the results of Flandrois et al. (1986) and the present study.

The Quad group showed an attenuated LA response with increasing workload, compared to the Paras. As discussed in the previous section on peak exercise responses, the decrease in active muscle mass for the Quads compared to the Paras would result in reduced catecholamine and LA concentrations (Eriksson et al., 1988).

Catecholamine Response

The lack of available literature examining the NE responses to exercise in individuals with SCI makes it difficult to analyze the current findings relative to other findings. Multisegmental regression lines were used to determine the catecholamine threshold for NE (Tne) and EPI (Tepi) in the Quad and Para groups. There was a clearer breakpoint in NE compared to LA for each subject in the Para group (Figure 9). Graphs of individual NE responses are presented in Appendix E.

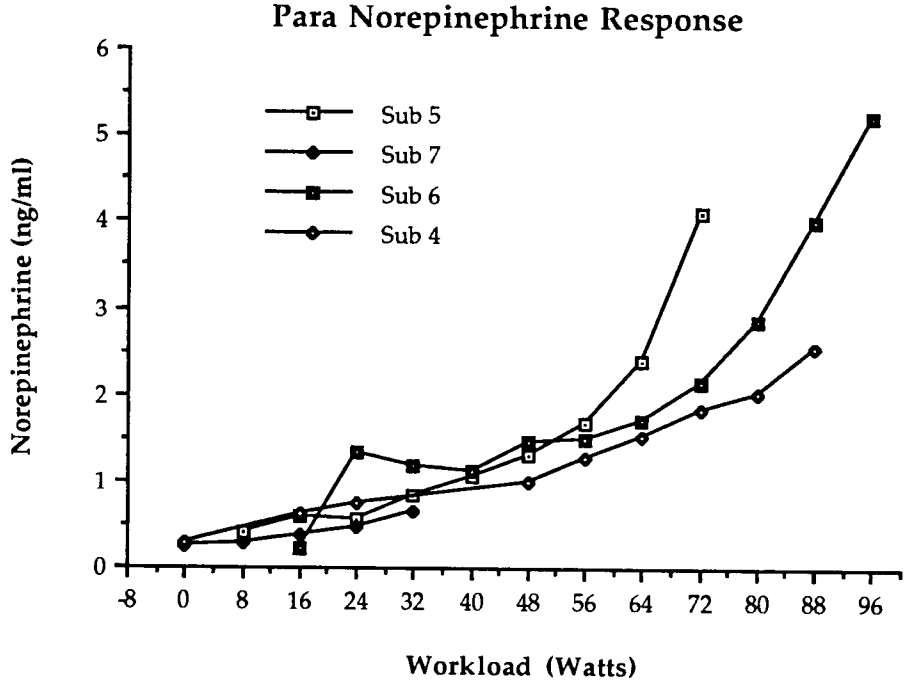

Figure 9. Norepinephrine response for each subject in the Para group.

Also, the Tla response did not coincide with the Tne response for the Paras (Tables 4 and 5).

Table 5

Individual Norepinephrine Threshold Response

Subject	Clear Breakpoint	Workload (Watts)	Percentage $\dot{V}O_2pk$
Sub 1 (Quad)	no		
Sub 2 (Quad)	no		
Sub 3 (Quad)	no		
Sub 4 (Para)	yes	48	78%
Sub 5 (Para)	yes	48	75%
Sub 6 (Para)	yes	64	77%
Sub 7 (Para)	yes	16	74%
Values are mean±SE		44.0±10.1	76.0±0.91

Norepinephrine is primarily responsible for alpha receptor mediated actions such as gluconeogenesis and liver glycogenolysis. Although other mechanisms through which NE could influence LA production may exist, it appears that liver glycogenolysis is the most feasible in this situation. Theoretically, the exercise duration of this study was not long enough to utilize liver glycogen stores as a fuel source. Since there is little available information outlining the substrate compensatory actions of the body after spinal trauma, absolute conclusions regarding this topic cannot be made. While Subjects 4, 5, and 6 demonstrated both a Tla and a Tne, these two variables did not coincide.

The Tne in the Para groups occurred between 75-80% $\dot{V}O_2pk$ for all subjects (Table 5), while no Tne occurred in the Quads. The NE response to exercise with increasing workload was variable and no predictable pattern could be interpreted in the Quad group (Figure 10).

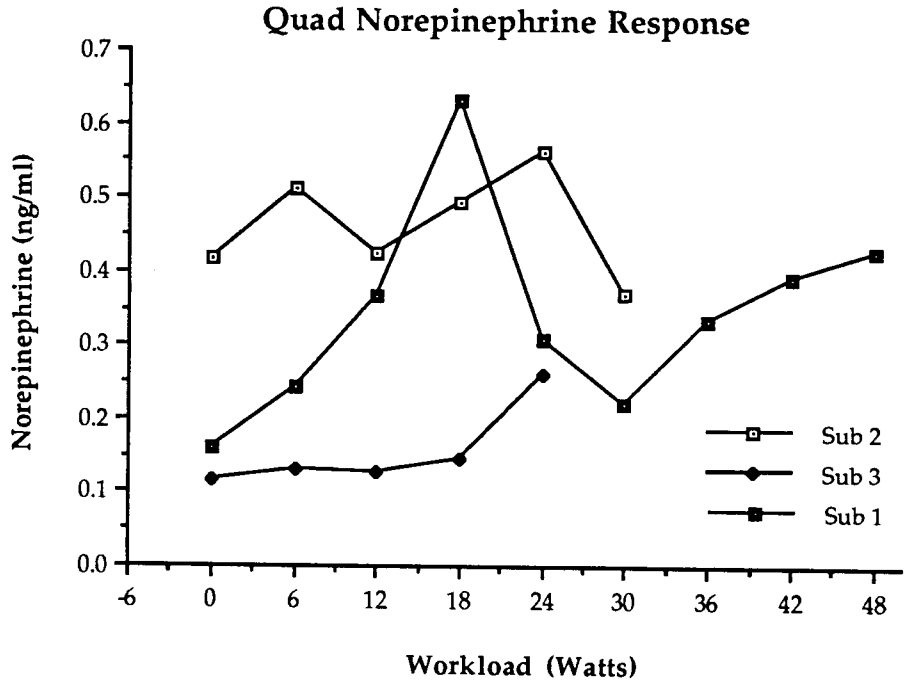

Figure 10. Norepinephrine response for each subject in the Quad group.

The Quads exhibited an attenuated response compared to the Paras, in which NE appeared to vary little from resting levels (Figure 11).

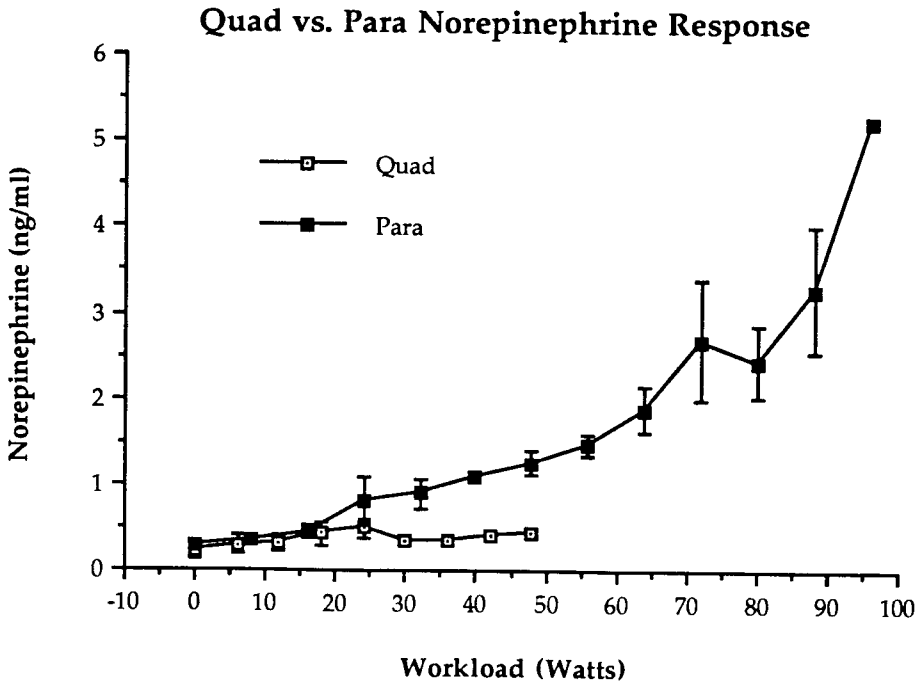

Figure 11. Norepinephrine response for the Quad and Para groups.

Further analysis revealed that there was no significant difference between the initial and final NE values in the Quads. The variable pattern of the NE response in the Quads indicated that their sympathetic drive is impaired. The differences in subject lesion level and completeness of the injury make it difficult to draw conclusions about the NE response in the Quads. The low heart rate response in these subjects suggests that their attenuated NE response significantly alters chronotropic functioning.

Subjects 4, 5, 6 and 7 possessed low level lesions. Their apparent retention of some neural activity allowed their NE responses to resemble those of the able-bodied. Additionally, the "normal" maximal heart rate

responses in this group denote that their sympathetic activity was sufficient to promote high level chronotropic functioning (Table 3). The Paras display a similar, albeit attenuated, NE response (Figure 11) to acute exercise compared to the reported able-bodied literature (Mazzeo, 1991). Therefore, Paras are more similar than dissimilar to the able-bodied with respect to their NE response.

Again, the lack of available literature examining the peak EPI responses to exercise in individuals with SCI makes it difficult to analyze the current findings. The EPI and NE responses to incremental exercise were similar in the Para group. Both variables increased in a curvilinear pattern with increasing workload, which has been reported in literature on the NE responses in the able-bodied (Mazzeo, 1991). Breakpoints in EPI occurred at approximately 48 Watts in Subject 5, at 64 Watts in Subject 6, and at 48 Watts in Subject 4. In accordance with the Tne, the Tepi occurred between 75-80% $\dot{V}O_2pk$ for the three subjects who exhibited this response. The Tepi data are summarized in Table 6. Graphs of individual EPI responses are presented in Appendix E.

Table 6

Individual Epinephrine Threshold Response

Subject	Clear Breakpoint	Workload (Watts)	Percentage $\dot{V}O_2pk$
Sub 1 (Quad)	no		
Sub 2 (Quad)	no		
Sub 3 (Quad)	no		
Sub 4 (Para)	yes	56	80%
Sub 5 (Para)	yes	48	75%
Sub 6 (Para)	yes	56	77%
Sub 7 (Para)	no		
Values are mean±SE		53.3±2.7	77.3±1.5

There was no regression line intersection in Subject 7, thus no Tepi could be interpreted (Figure 12).

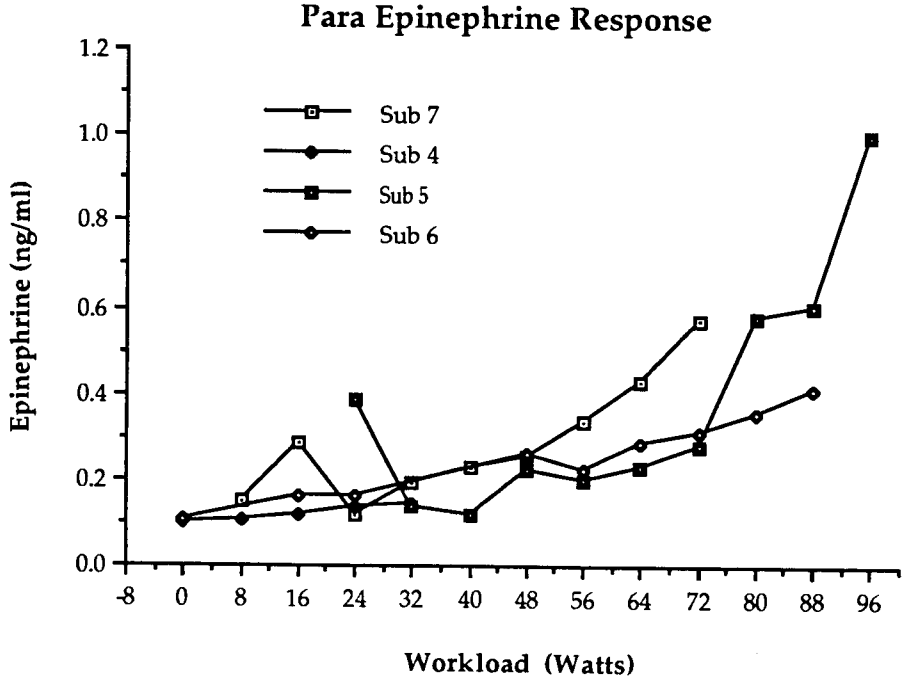

Figure 12. Epinephrine response for each subject in the Para group.

It is unclear why Subject 7 exhibited a Tne, but not a Tepi. This subject was considerably less fit than the other Paras. However, a reasonable explanation of why this would inhibit an inflection in Tepi is unavailable.

There was little association between Tla and Tepi in the Paras (Tables 4 and 6). Lactate production is regarded as an acceptable estimate of glycogenolysis (Cartier & Gollnick, 1985). Glycogenolysis (muscle and liver) is stimulated through EPI activation of the adenylate cyclase system (Brooks & Fahey, 1984). Lactate is a product of glycogenolysis. Consequently, EPI activity can also be estimated through LA production (Mazzeo & Marshall, 1989; Stainsby et al., 1985). Mazzeo and Marshall (1989) and Podolin et al. (1991) have identified a strong relationship between Tepi and Tla in the able-bodied. Since there was a disparity in the Tepi and Tla in the subjects in the present study, conclusions analogous to those of Mazzeo and Marshall (1989) and Podolin et al. (1991) cannot be made.

Similar to the NE response, the EPI response to exercise with increasing workload was variable and no predictable pattern could be interpreted in the Quad group (Figure 13).

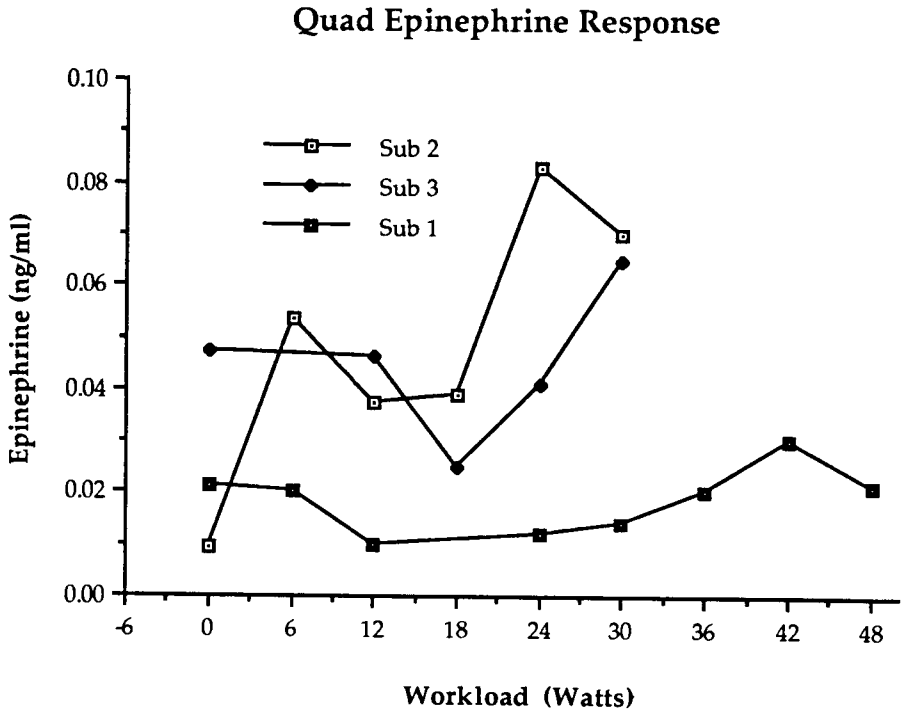

Figure 13. Epinephrine response for each subject in the Quad group.

Gray and Beetham (1957), stated that EPI levels are inconsistent among able-bodied individuals and vary greatly from an acute increase to no measurable change. The marked variability in EPI response in the able-bodied would be even more pronounced in individuals whose EPI secretion agent was disrupted.

The Quads exhibited an attenuated response, compared to the Paras, in which EPI appeared to vary little from resting levels (Figure 14).

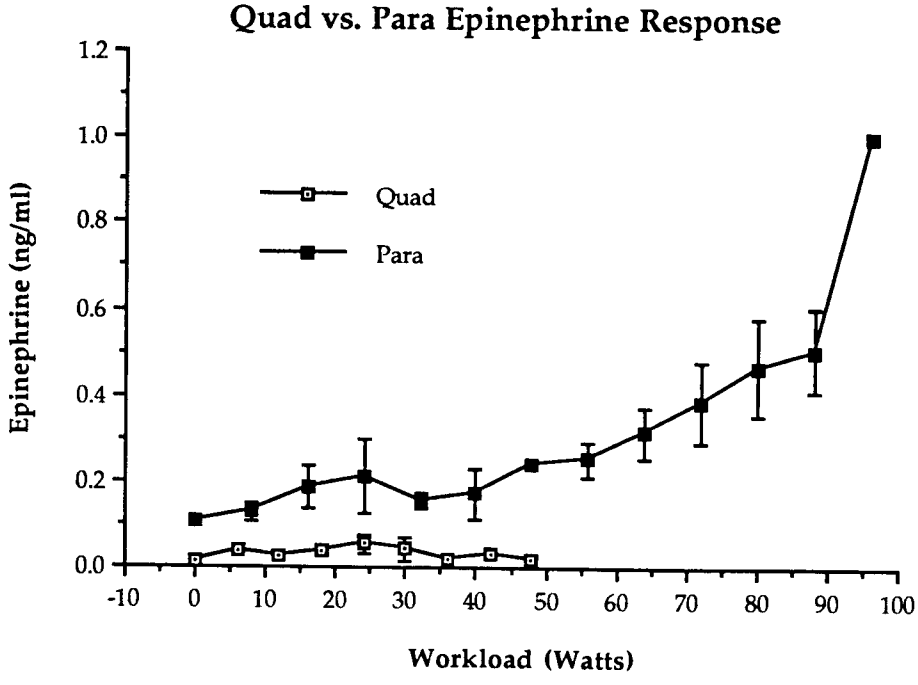

Figure 14. Epinephrine response for the Quad and Para groups.

Further analysis revealed that there was no significant difference between the initial and final EPI values in the Quads. These data concur with Fitzpatrick et al. (1991) who reported lower circulating levels of EPI in Quads compared to Paras during prolonged, submaximal exercise.

Howley (1976) demonstrated variable EPI responses with increasing workloads using a walking protocol. Six males completed three 15 minute submaximal exercise tests at workloads that corresponded to 50%, 65% and 80% of relative $\dot{V}O_2max$. Norepinephrine increased with increasing workloads, but the EPI response was variable, with one subject demonstrating little change from resting levels. While the results of Howley (1976)

regarding the EPI response to exercise of increasing workload are similar to those of the Quads in the present study, other scientists maintain that NE and EPI follow the same pattern during exercise of increasing intensity (Mazzeo, 1991; Mazzeo & Marshall, 1989).

It is evident that the diminished EPI response in the Quads results from disruptions in adrenal innervation. The area of the 6th thoracic vertebrae has been identified as the primary area of adrenal medulla innervation (Munro & Robinson, 1960; Hjeltnes, 1986). Interruption in this innervation causes impairment in EPI secretion. Epinephrine, acting mainly through ß-mediated receptors, has powerful effects on factors such as vasodilation, cardiac acceleration, muscle and liver glycogenolysis, and lipolysis (Mazzeo, 1991). The attenuated EPI response in Quads indicates that all of these factors were significantly diminished in these individuals. However, Quads do exhibit some EPI response. The mechanism behind this is unclear, but several theories may be suggested. The adrenal medulla may be receiving some type of compensatory neural stimulus that has not been observed in previous medical studies. Also, it is quite plausible that the Quads with incomplete injuries (Subjects 1 and 2) possessed adrenal innervation that was not disrupted during their injury. Hypoxia and hypoglycemia have been identified as specific factors that may influence EPI secretion (Mazzeo, 1991). The reduced ventilation and cardiac output seen in quadriplegics may induce hypoxia, but this has not yet been clarified. The subjects may have been hypoglycemic since they were performing the exercise session after an overnight fast, but lack of glucose data prohibits consideration of this mechanism as a definite contributing factor.

Table 7 provides a summary comparison of those subjects who exhibited threshold values for LA, NE and EPI. Subjects who did not

demonstrate threshold values for any of the variables were not included in the table. The threshold values are reported according to the percentage of peak $\dot{V}O_2$ at which the threshold occurred.

Table 7

Summary of LA, NE, and EPI Threshold Values

Subject	LA Threshold	NE Threshold	EPI Threshold
Sub 1 (Quad)	78%	--	--
Sub 4 (Para)	90% (visual)	48%	80%
Sub 5 (Para)	67%	48%	75%
Sub 6 (Para)	73%	64%	77%
Sub 7 (Para)	--	16%	--

Values are % of $\dot{V}O_2pk$

Correlations Between Norepinephrine, Epinephrine and Lactate

Pearson-product moment correlations revealed that there were strong correlations between NE-LA, EPI-LA, and NE-EPI for the Para group (Table 8). There were weak correlations between NE-LA and NE-EPI, and EPI-LA for the Quad group (Table 8). The strengths and weaknesses of these relationships are further illustrated in Figures 15-20. Illustration of the correlations are presented in Appendix F.

Table 8

Correlations Between Norepinephrine, Epinephrine and Lactate for the Quad and Para Groups

Group	NE - EPI	NE - LA	EPI - LA
Para	0.93*	0.79*	0.72*
Quad	0.21	0.28	0.35

*Significant correlation at $p \leq 0.05$

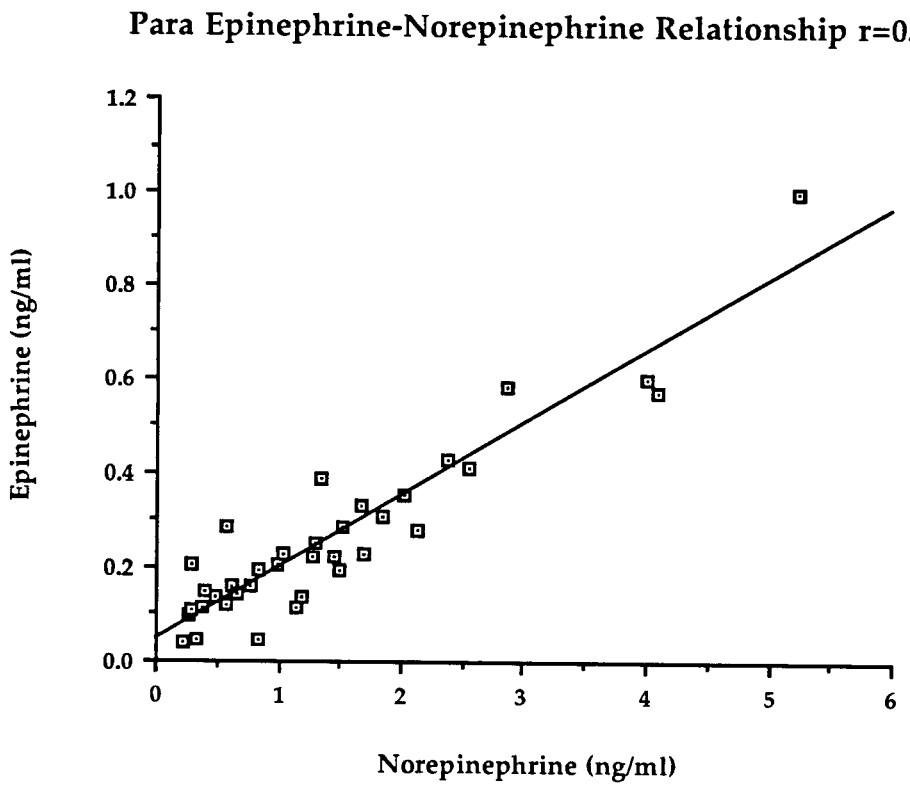

Figure 15. Relationship between norepinephrine and epinephrine in the Para group.

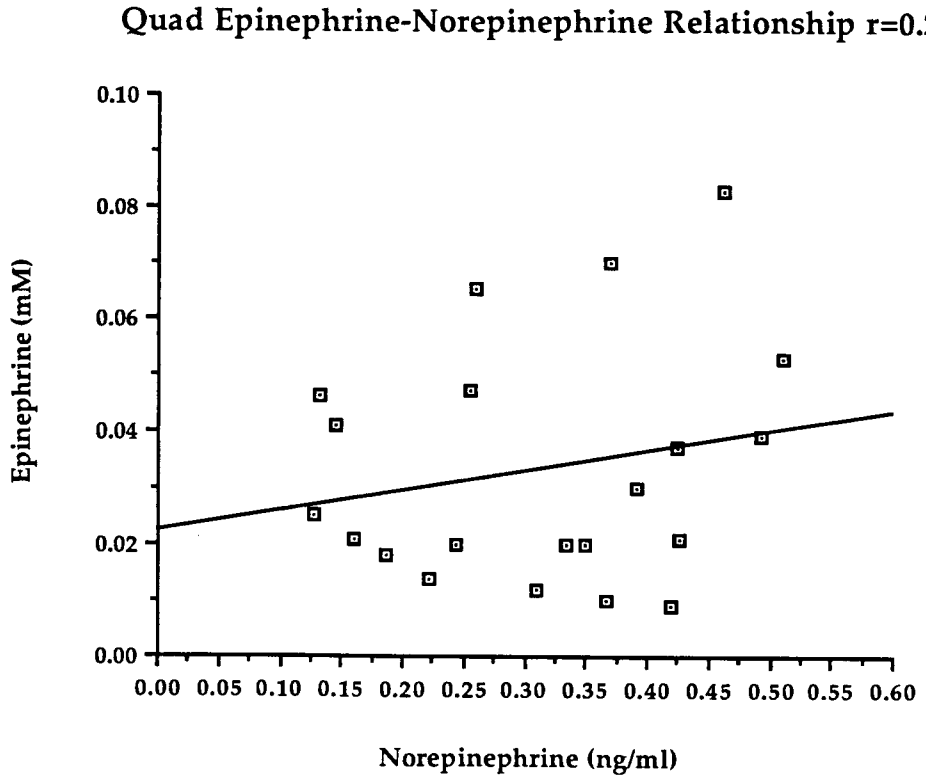

Figure 16. Relationship between norepinephrine and epinephrine in the Quad group.

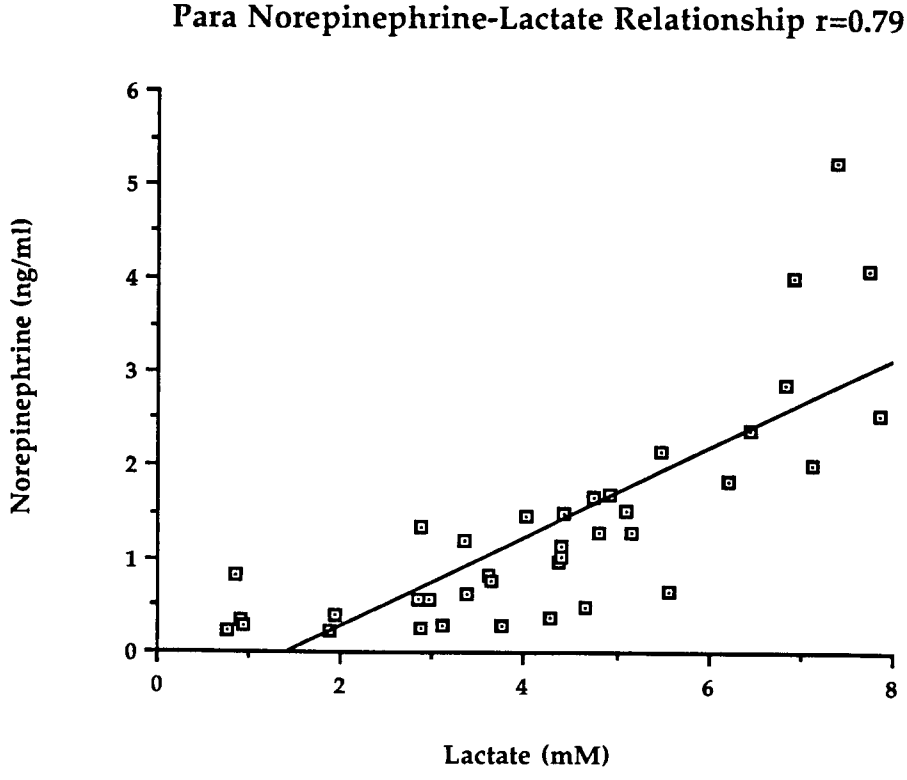

Figure 17. Relationship between norepinephrine and lactate in the Para group.

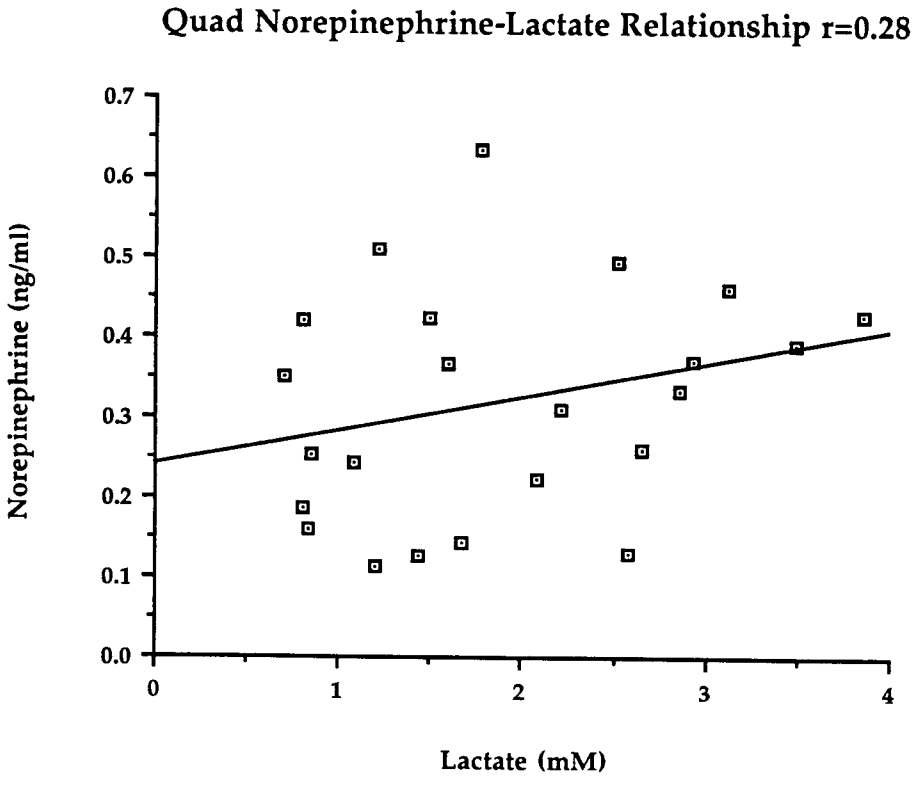

Figure 18. Relationship between norepinephrine and lactate in the Quad group.

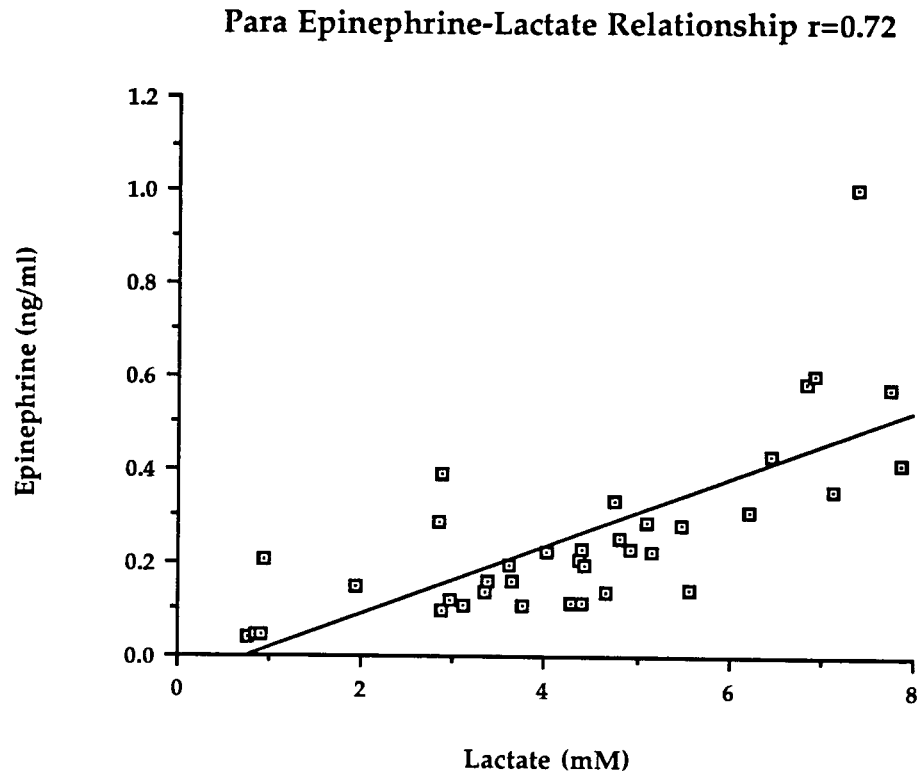

Figure 19. Relationship between epinephrine and lactate in the Para group.

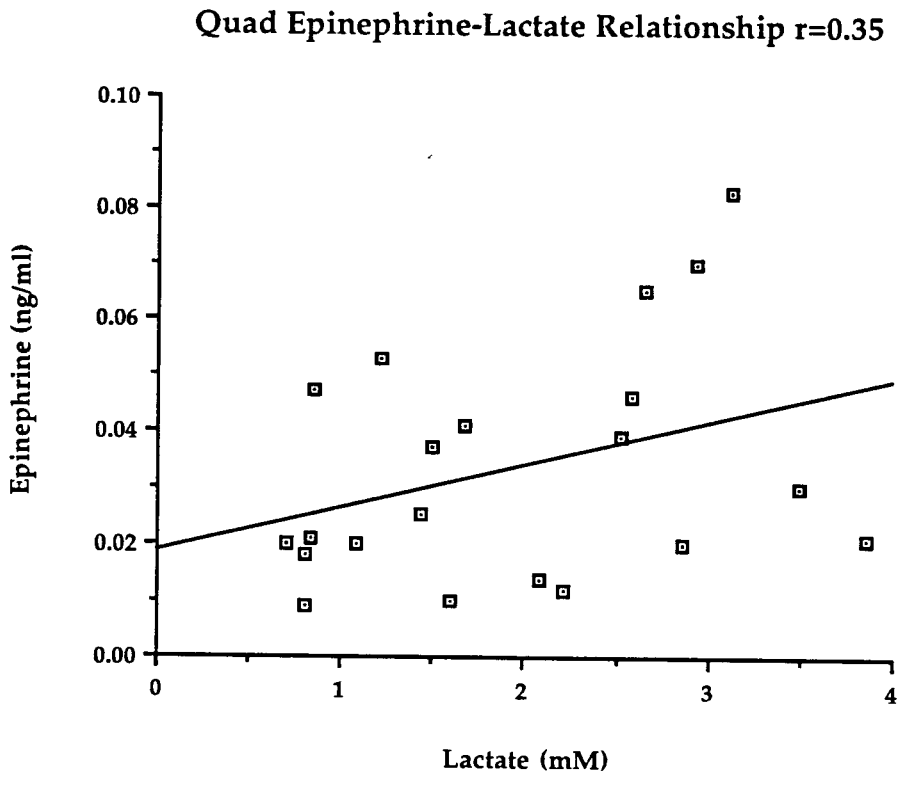

Figure 20. **Relationship between epinephrine and lactate in the Quad group.**

It is well documented that there is an exponential increase in catecholamines (NE and EPI) with an increasing workload in acute exercise. During this time, the ratio of NE to EPI (in which NE is typically 3-4 times greater than EPI) remains constant (Mazzeo, 1991). Thus, it is accepted that the catecholamine response to acute exercise is primarily controlled by NE (Mazzeo, 1991). In the present study, the peak NE response was approximately 6 times and 4 times greater than the peak EPI response for the Para and Quad groups, respectively. It is interesting that the ratio of NE-EPI was greater in the Paras, since they should be capable of more EPI secretion than the Quads. A possible explanation is that the Paras have more neural

drive and are capable of more NE production. The strong relationship between NE-EPI in the Paras corresponds to that found in the able-bodied (Mazzeo, 1991) (Figure 15). However, the large variability in the catecholamine response in the Quads precludes such an association (Figure 18).

Mazzeo and Marshall (1989) reported a strong correlation between Tne and Tla (r=0.98) and Tepi and Tla (r=0.97) in able-bodied runners and cyclists. As mentioned previously, catecholamines activate glycogenolysis. Epinephrine plays a more powerful role in this process, but NE is a contributing factor. Since LA is viewed as a marker of glycogenolysis and catecholamine activity, the thresholds for these variables should be associated. Data from the present study did not yield consistent thresholds for the variables studied. Therefore, no relationships between Tla, Tne and Tepi were established. However, correlations between NE, EPI and LA patterns revealed that these factors are significantly related in the Paras, but not the Quads (Table 7). Although the correlations for the Paras are lower than those reported by Mazzeo and Marshall (1989), a cause and effect mechanism between NE-LA and EPI-LA, as seen in the able-bodied, can be postulated in the Paras. This indicated that the Para metabolic response to acute exercise is somewhat similar to the able-bodied (Figures 15 & 16). Conversely, the absence of correlations between NE, EPI and LA in the Quads (Table 7), indicates that there is no cause and effect relationship in these parameters for this group. If catecholamines appear to have no effect on LA production in the Quads, then other factors must be employed to activate glycogenolysis in this population. The primary compensatory mechanism may be intracellular Ca++. In the able-bodied, this ion acts rapidly during the transition from rest to exercise, to activate glycogenolysis. Once the catecholamines are released,

the Ca++ mediated mechanism is superseded by catecholamine activity (Brooks & Fahey, 1984). It is conceivable that when catecholamine functioning is impaired, the Ca++ mediated mechanism undertakes greater control of glycogenolysis. To date, this hypothesis has not been examined in humans.

Another compensatory mechanism may be the up-regulation of the available ß-receptors, resulting in an increased sensitivity to available catecholamines. This up-regulation has been shown to occur with short and long term exercise (Maki, Kontula & Harkonen, 1990). Also, there may be an increased density of ß-receptors that is associated with high aerobic capacity (Maki et al., 1990). Alternatively, there may be a decrease in ß-receptor density, similar to that found in individuals with Duchenne muscular dystrophy (Maki et al., 1990). These ideas are purely speculative.

CHAPTER V

SUMMARY, CONCLUSIONS and RECOMMENDATIONS

Summary

The purpose of this study was threefold. First, to determine if there were differences in the plasma catecholamine, lactate and ventilatory responses to incremental exercise in individuals with spinal cord injuries (SCI) above (quadriplegic) and below (paraplegic) the 6th thoracic vertebrae (T6). Second, to determine if a relationship existed between these variables in those with SCI. Third, to evaluate if there were differences in these variables between individuals with SCI above and below T6.

Three males classified as quadriplegic and four males classified as paraplegic completed a peak oxygen uptake exercise test on an arm ergometer. Blood samples were taken and analyzed for catecholamine (NE and EPI) and lactate (LA) concentrations every three minutes during the exercise session. Ventilatory parameters were measured throughout the testing. The design of this study was essentially descriptive, and cause and effect conclusions regarding the data generated from this research are unwarranted. The findings do provide additional evidence that people with SCI above T6 have attenuated plasma catecholamine, lactate and ventilatory responses to incremental exercise, compared to those with SCI below T6. Although generalizations of this information to other individuals with SCI must be made with caution, it is evident from this study that SCI above T6 results in significantly impaired sympathoadrenal function, whereas individuals with SCI below T6 demonstrate plasma catecholamine, lactate and ventilatory

patterns similar to the able-bodied. The results of the present study can be best summarized by addressing the problem statements that were outlined in Chapter I.

What is the lactate response to incremental exercise in individuals with spinal cord injury?

The group means for quadriplegics and paraplegics illustrate an increasing, linear lactate response with an increase in workload. Quadriplegics had an attenuated response compared to paraplegics. Individual data identified a curvilinear lactate response for Subjects 1, 4, 5, and 6.

At what percentage of peak oxygen uptake does the lactate threshold (Tla) occur in individuals with spinal cord injury?

Only Subjects 1, 4, 5, and 6 demonstrated a Tla, as determined from multisegmental regression lines. The Tla occurred at 78%, 90%, 67%, and 73% of $\dot{V}O_2pk$ for Subjects 1, 4, 5, and 6, respectively. Subjects who displayed a Tla were three paraplegics and one quadriplegic who were, based on their $\dot{V}O_2pk$ values, physically trained. This suggests that training status had an impact on the ability to exhibit a Tla in the population studied.

At what percentage of peak oxygen uptake does the ventilatory threshold (Tv) occur in individuals with spinal cord injury?

The Tv was only observable in Subject 4. It is not clear why Subject 4 demonstrated a Tv and Subjects 5 and 6, who were of similar training status, did not demonstrate a Tv. The Tv for Subject 4 occurred at 86% of $\dot{V}O_2pk$. It is reasonable to conclude that the exercise protocol utilized in the present study was not conducive to eliciting a Tv in the current population .

What is the catecholamine (NE and EPI) response to incremental exercise in individuals with spinal cord injury?

The group means illustrate that the paraplegics demonstrated an increasing, curvilinear response with an increase in workload for NE and EPI. Quadriplegics had an attenuated response in NE and EPI, that varied little from resting values, compared to paraplegics.

At what percentage of peak oxygen uptake does the catecholamine threshold (Tne and Tepi) occur in individuals with spinal cord injury?

A Tne was observable in Subjects 4, 5, 6, and 7. A Tepi was observable in Subjects 4, 5, and 6. The Tne and Tepi occurred between 75-80% VO_2pk in subjects who displayed this response. It is not clear why Subject 7 displayed a Tne and not a Tepi. Typically, these two responses are closely related. All subjects who demonstrated catecholamines thresholds were in the paraplegic group.

What is the relationship between the lactate and ventilatory thresholds in individuals with spinal cord injury?

The exhibition of Tv and Tla was inconsistent among subjects. Consequently, establishing a relationship between Tv and Tla was not possible. Visual inspection of the data revealed a similar, linear increase in the ventilatory and lactate responses to incremental exercise in paraplegics and quadriplegics. This would suggest that there may be a relationship between these two variables, although this relationship was not statistically verified.

What is the correlation between the catecholamine (NE and EPI) and lactate (LA) response to incremental exercise in individuals with spinal cord injury?

There were significant relationships between NE-EPI (0.93), NE-LA (0.79) and EPI-LA (0.72) in the paraplegic group. This suggested that the sympathoadrenal system in these individuals was unimpaired. There were no significant relationships between these variables in the quadriplegic group, indicating that the sympathoadrenal system in these individuals is disrupted and may be insufficient to provide adjustment to the stresses of exercise.

Impairment of the sympathoadrenal system, as a consequence of SCI above T6, has far-reaching, debilitating effects. Examples include: (1) decreases in cardiac functioning, specifically chronotropic and inotropic activity; (2) disruption in vasoconstriction and vasodilation, which affects redirection of blood flow and thermoregulation; and (3) alterations in metabolic pathways of substrate mobilization such as gluconeogenesis, glycogenolysis (liver and muscle), and lipolysis. It has been well documented that as the level of SCI

increases in severity, the body's ability to respond to exercise decreases (Wells & Hooker, 1990; Shephard, 1988). This is logical since there is a progressive loss of sympathetic activity with increasing SCI severity.

Despite the reduced responses to exercise, quadriplegics continue to participate in physical activity. Their participation goes beyond the limited sport and recreational activities that were previously promoted for individuals with SCI. Quadriplegics, and also paraplegics, are currently engaging in endurance and contact activities at high levels of competition. Many of these individuals have garnered respect as trained athletes. Considering the seriously impaired physiological structure associated with quadriplegia, it is of interest to understand how individuals with high level SCI adapt, so they can effectively adjust to the stresses inherent in vigorous exercise.

The results from this study clarify that the sympathoadrenal system in quadriplegics is dysfunctional, as identified through impaired catecholamine activity. This information can then be utilized to hypothesize how individuals with quadriplegia compensate for the significant disruption in these powerful metabolic and physiologic regulators. The subjects in this study with SCI above T6 were identified as quadriplegics, but individuals with SCI who are medically classified as high-level paraplegics may also experience sympathoadrenal deficiencies. It was suggested in Chapter IV that mechanisms which previously played a secondary role in various metabolic pathways may be recruited to take on a primary role. This seems logical, since some type of compensatory activity must be initiated. However, current knowledge is insufficient to draw any firm conclusions regarding these compensatory mechanisms.

The present research clarifies that paraplegics are capable of successful adjustment to exercise. This was particularly true for Subjects 4, 5, and 6, who were in better physical condition than Subject 7. Paraplegics' physical responses to exercise are similar but diminished compared to the able-bodied (Davis, 1993). As a consequence of paralyzed lower limbs, the diminished exercise responses associated with paraplegia are generally attributed to circulatory hypokinesis and decreased venous return, (Davis, 1993). Findings from an investigation by Hooker and Wells (1990) conveyed that sympathetic nervous system impairment in paraplegia has no obvious effects on physiological or metabolic functioning during prolonged exercise. With physical training, the differences in exercise responses between paraplegics and able-bodied are lessened (Davis, 1993). Zwiren and Bar-Or (1975) found no significant differences in $\dot{V}O_2max$ between wheelchair athletes and able-bodied athletes when $\dot{V}O_2max$ was expressed in $ml \cdot kg \cdot min^{-1}$. Regrettably no control group of able-bodied individuals was evaluated in the present study, but a review of previous literature allows for adequate comparisons.

Conclusions

The findings from this study have generated the following conclusions:

1. Individuals with SCI above T6 demonstrate attenuated, ventilatory, physiological, adrenal and sympathetic responses to incremental exercise.

2. Metabolic pathways that are primarily activated by catecholamines must rely on other compensatory mechanisms for stimulation in individuals with SCI above T6.

3. Individuals with SCI below T6 demonstrate sympathoadrenal responses similar to those previously reported in the able-bodied.

4. Subject variability made determination of threshold values for ventilation, catecholamines and lactate difficult in the population studied.

Practical Implications

The results from the Tv and Tla are beneficial for individuals with SCI who are interested in physical training. The Tv has yet to be verified as a valid, indirect measure of exercise intensity (related to Tla) for those with SCI. The Tv is often employed in able-bodied athletes for this purpose. Additional research is required before the Tv can be utilized in athletes with SCI. The NE, EPI and LA data provide new insight into the sympathoadrenal responses to exercise in individuals with SCI. This will help scientists explore further the compensatory mechanisms that occur in those with SCI, particularly individuals with injuries above T6. Eventually, new training practices associated with factors such as nutrition, training intensity and training frequency may be developed for individuals with SCI.

Recommendations for Future Research

This study was novel in attempting to address the previously outlined problem statements. Early research has not examined the plasma catecholamine, lactate and ventilatory responses to incremental exercise in individuals with SCI above and below T6. Therefore, the methodological procedures and results from this investigation can be used as a foundation for

1. Replication of this study requires a larger subject pool. If possible, subjects should be grouped according to lesion level (above and below T6), gender and training status.

2. Separate protocols for blood and ventilatory parameters may be necessary. Ventilatory thresholds may be elicited with shorter work stages than were employed in the present study. If separate protocols were used, comparisons could still be made between Tv and Tla, when expressed as a percentage of $\dot{V}O_2max$.

3. It would be interesting to examine further the impaired metabolic responses to exercise in individuals with different lesion levels above T6. Specifically, dividing subjects according to medical classification (class IA, IB, IC, and II).

4. A focus on the compensatory mechanisms of the quadriplegic response to exercise is essential. This requires more invasive investigative techniques. The use of animal models may be required to answer basic questions such as adrenal function after spinal trauma and changes in ß-receptor density and sensitivity after spinal trauma.

5. Beta and alpha receptor blockade are specific methods of examining the significance of catecholamine activity, particularly EPI, in the adjustment of individuals with SCI to exercise. Comparison of blockade and non-blockade exercise sessions would reveal new information on how individuals with SCI compensate for impaired sympathoadrenal function.

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APPENDICES

APPENDIX A

Statement of Informed Consent

Relationship between the plasma catecholamine, blood lactate and ventilatory responses to incremental exercise in individuals with spinal cord injury

Investigators: Georgia Frey, MS, John Dunn, EdD and Jeffrey McCubbin, PhD

Purpose: The purpose of this investigation is to examine the relationship between the plasma catecholamine (adrenalin and noradrenaline), blood lactate and ventilatory responses to incremental exercise in individuals with various levels of spinal injury.

Significance: There is no available literature addressing the sympathetic nervous system (where adrenalin and noradrenaline are produced) response to exercise in those with spinal cord injury. Additionally, no study has examined the blood lactate (as a measure of intensity) or ventilatory (volume of air taken in by the lungs) thresholds in this population. Evaluating these variables will yield important information concerning the diminished sympathetic response in this population, as well as, the effect it may have on lactate production, substrate utilization (fats and carbohydrates) and circulatory (blood) adjustments to exercise. These data will aid the study participants in developing training programs. It will also give them more knowledge about their body's physiological responses to exercise.

Participation in this study will require one laboratory visit. The approximate time for each session will be two hours.

The following procedures have been explained to me in lay terms and I have been given the opportunity to ask questions concerning the testing, research objectives, possible hazards, as well as potential benefits of participation. I hereby authorize Georgia Frey, MS, John Dunn, EdD and Jeffrey McCubbin, PhD, and such assistants they may select to administer the following:

1. **Test of Peak Oxygen Consumption ($\dot{V}O_2pk$)**

   I will undergo an incremental exercise test which has two objectives. One, to determine the peak aerobic capacity (how much oxygen the body can use) of my body and two, to ascertain the dramatic rise in my ventilatory and blood parameters in response to exercise of increasing intensity. The test will require exercise on an arm crank ergometer at a

certain level of revolutions per minute. The intensity of the exercise effort will be increased every three minutes by increasing the resistance to cranking. The test shall be terminated when I feel I can no longer sustain the effort necessary to complete another increment. The test may also be terminated if I feel excessive fatigue or discomfort, and if any possible clinical abnormalities are observed in my electrocardiogram (EKG).

My oxygen consumption will be measured while I breathe room air through a mouthpiece. I will also wear a noseclip so that all my exhaled air can be collected. The discomfort in this procedure is minimal. My heart rate will be continuously monitored using an electrocardiograph (EKG) system. Trained laboratory personnel, certified in CPR and basic cardiac life support, will administer the exercise test.

2. Blood Collection

I understand that blood samples will be taken while I am resting before the exercise test, and then during the last minute of each work stage during the test. The blood is drawn from a disposable, sterile, short needle called a butterfly, (an indwelling venous catheter), inserted and fastened to a prominent forearm vein. This procedure shall be performed by experienced and trained Human Performance Laboratory personnel. Approximately 6 ml of blood will be drawn for each sample. The total amount of blood taken for analysis should not exceed 60ml (about 1/4-1/2 cup). These blood samples will later be analyzed to determine lactate (lactic acid) and catecholamine (adrenalin and noradrenaline) concentrations.

It has been explained to me that many factors such as food, caffeine, physical activity and medication may affect my blood parameters. Therefore, I will report to the laboratory in the morning after an overnight fast and will not partake in physical activity, other than that required for daily living, 24 hours before the exercise test. If possible, I will refrain from taking medication that has a documented, significant affect on catecholamine activity 24 hours prior to the test. However, if I cannot discontinue this type of medication 24 hours prior to testing I will be excluded from the study.

3. Risks/Benefits to the Subject

Risks: I understand that there exists no data documenting the risks associated with peak exercise testing in populations with spinal cord injury. However, I have been informed that the risks in large varied

populations are minimal (approximately .5 deaths per 10,000 exercise tests). Since I am young, healthy and active and have no documented symptoms of heart disease the risk will be considerably less. Emergency procedures have been established and CPR personnel are available to deal with unusual situations which may arise. I can normally expect to experience breathlessness, and general fatigue, during the graded exercise test, but I can signal the test to be terminated when I feel too exhausted to continue.

There are risks and discomfort inherent in the venous blood drawing. A small amount of pain will be experienced as a needle is inserted into the vein. There exists a 5% chance that a bruising of the skin may occur and a less than 1 in 1000 risk that a bruise will become infected. However, since sterile blood drawing techniques will be used and the procedure will be performed by qualified personnel these risks will be much less. Heparin is an anticoagulant that is used to flush the catheter to prevent blood clotting. The amount of heparin actually introduced into the bloodstream is negligable (perhaps a drop), but there is a very remote possibility of an allergic reaction to the heparin. Therefore, safety precautions will require that I stay for approximately one hour after completion of the exercise test to observe for possible allergic reactions to the heparin. Finally, some arm muscle stiffness and soreness may exist for one to two days following the $\dot{V}O_2$peak test.

Persons at increased risk for Hepatitis B or HIV (commonly called AIDS) should not donate blood or any other body fluids and therefore should not participate in this investigation. Persons at increased risk include men who have had sexual contact with another man since 1977, persons who have used intravenous drugs and persons who have had sexual contact with either a member of one of these groups or a person who has AIDS.

Benefits: I will benefit from my participation in this study by helping contribute to the understanding of the exercise responses in individuals with spinal cord injury. This investigation will provide information concerning the sympathetic nervous system activity during exercise in individuals whose sympathetic nervous system has been damaged. I will gain knowledge concerning my physical fitness level and I can utilize this knowledge for athletic training purposes.

4. Confidentiality

The information obtained during this investigation will be treated as privileged and confidential. The data will be used for statistical analysis and scientific purposes with my right to privacy retained. I

will be referred to as a numerical figure, randomly assigned to me at the onset of the study, on all reports and publications of this data. Access to this data will only be available to the researchers in this study. Following final publication of literature, the code list of numerical references and corresponding names will be destroyed.

5. **Freedom of Consent**

I have been thoroughly informed and understand the nature and purpose of this investigation. The researchers have made it clear that they will answer all questions or concerns that I may have. My participation in this study is completely voluntary. I am free to deny my consent at any time without prejudice or loss of benefits guaranteed by my participation. Questions concerning my rights has a subject can be directed to the Institutional Review Board for the Protection of Human Subjects at the Research Office of Oregon State University. I understand that Oregon State University does not provide a research subject with compensation or medical treatment in the event the subject is injured as a result of participation in a research project. Questions concerning the study may be directed to Georgia Frey 737-3402, John Dunn 737-0732 or Jeffrey McCubbin 737-5921.

I have thoroughly read this statement of informed consent and agree to participate in this study.

_____ _____

Subject's Signature **Date**

_____

Subject's Address and Phone Number

_____ _____

Witness Signature **Date**

Medical Questionnaire

Please answer the following questions to the best of your knowledge.

Questions Related to Cardiac Heart Disease Risk Factors

Do you or have you had any of the following:

1. High blood pressure (above 160/90)

   (Y) (N) (?)

2. Elevated blood cholesterol (above 240mg/dl)

   (Y) (N) (?)

3. Cigarette smoking

   (Y) (N) (?)

4. Family history of heart disease prior to age 50

   (Y) (N) (?)

6. Diabetes Mellitus (Insulin dependent)

   (Y) (N) (?)

Questions Related to Medication

1. Are you currently taking any physician prescribed medication?

   (Y) (N) (?)

2. If you answered "yes" to question 7, please list the name of the medication and what it is prescribed for in the space provided below (you are under no obligation to answer this question).

Questions related to Blood Drawing

1. Have you ever been diagnosed with a bleeding problem (e.g. hemophilia)?

   (Y) (N) (?)

2. Have you ever been diagnosed as being allergic to the anticoagulant heparin?

   (Y) (N) (?)

I, the undersigned, realize that this medical questionnaire is used solely for the purpose of screening potential participants for heart disease risk factors and medication that may conflict with catecholamine activity. I understand that this procedure is for my own protection.

_____ _____

Subject's Signature **Date**

APPENDIX B

INDIVIDUAL SUBJECT AND GROUP VENTILATORY DATA

Subject 1 (Quad)

Time (min)	$\dot{V}O_2$ ($l \cdot min^{-1}$)	$\dot{V}E$ ($l \cdot min^{-1}$)	RER ($\dot{V}O_2/\dot{V}CO_2$)	$\dot{V}E/\dot{V}O_2$	$\dot{V}E/\dot{V}CO_2$
1	0.551	17.1	0.72	31	43
2	0.577	17.8	0.74	31	42
3	0.637	19.1	0.77	30	39
4	0.673	20.7	0.83	31	37
5	0.808	22.9	0.81	28	35
6	0.862	27.5	0.84	32	38
7	0.760	24.3	0.90	32	36
8	0.868	25.2	0.90	29	32
9	0.892	28.9	0.93	32	35
10	0.801	25.3	0.92	32	34
11	1.308	31.2	0.97	30	34
12	0.957	33.3	0.96	35	36
13	0.926	32.9	0.97	35	37
14	1.093	36.5	0.92	33	36
15	0.983	38.7	0.92	33	36
16	0.970	35.0	0.96	36	38
17	1.164	39.0	0.90	34	37
18	1.155	46.2	1.02	40	39
19	1.077	37.5	0.95	35	37
20	1.308	44.3	0.93	34	36
21	1.146	45.6	1.01	40	39
22	1.179	41.6	0.95	35	37
23	1.342	48.2	0.93	36	39
24	1.219	48.1	1.02	39	39
25	1.234	50.4	1.01	41	40
26	1.467	57.3	0.98	39	40
27	1.282	55.3	1.05	43	41

APPENDIX B (CONT.)

Subject 2 (Quad)

Time	$\dot{V}O_2$	$\dot{V}E$	RER	$\dot{V}E/\dot{V}O_2$	$\dot{V}E/\dot{V}CO_2$
(min)	($l \cdot min^{-1}$)	($l \cdot min^{-1}$)	($\dot{V}O_2/\dot{V}CO_2$)		
1	0.480	15.3	0.76	32	43
2	0.589	17.9	0.76	30	40
3	0.669	20.2	0.80	30	38
4	0.672	22.9	0.88	34	39
5	0.828	26.8	0.87	32	37
6	0.748	26.6	0.92	35	39
7	0.757	26.4	0.94	35	37
8	0.901	30.2	0.90	34	38
9	0.822	30.0	0.99	36	37
10	0.862	31.0	0.99	36	37
11	1.010	35.6	0.96	35	37
12	0.883	34.0	1.01	39	38
13	0.904	36.9	1.06	41	39
14	1.109	42.7	1.02	39	38
15	0.917	40.7	1.10	44	40
16	1.025	45.7	1.10	45	41
17	1.034	50.1	1.08	48	44

Subject 3 (Quad)

Time	$\dot{V}O_2$	$\dot{V}E$	RER	$\dot{V}E/\dot{V}O_2$	$\dot{V}E/\dot{V}CO_2$
(min)	($l \cdot min^{-1}$)	($l \cdot min^{-1}$)	($\dot{V}O_2/\dot{V}CO_2$)		
1	0.309	10.1	0.83	33	39
2	0.613	16.1	0.73	26	36
3	0.658	18.4	0.78	28	36
4	0.693	24.4	0.91	35	39
5	0.650	27.0	1.05	41	40
6	0.764	30.7	1.00	40	40
7	0.768	31.5	1.01	41	41
8	0.738	32.9	1.09	45	41
9	0.930	34.1	0.97	37	38
10	0.902	38.4	1.02	43	42
11	0.867	34.7	1.04	40	38
12	1.036	37.5	0.93	36	39
13	0.988	46.2	1.05	47	44
14	0.994	40.8	0.99	41	41

APPENDIX B (CONT.)

Subject 4 (Para)

Time (min)	$\dot{V}O_2$ ($l \cdot min^{-1}$)	$\dot{V}E$ ($l \cdot min^{-1}$)	RER ($\dot{V}O_2/\dot{V}CO_2$)	$\dot{V}E/\dot{V}O_2$	$\dot{V}E/\dot{V}CO_2$
1	0.686	15.5	0.70	23	32
2	1.151	25.6	0.73	22	31
3	1.286	30.2	0.82	24	29
4	1.311	34.9	0.91	27	29
5	1.242	35.0	0.97	28	29
6	1.473	38.1	0.91	26	28
7	1.431	40.1	0.95	28	30
8	1.439	40.0	0.97	28	29
9	1.573	41.7	0.92	26	29
10	1.536	45.6	0.98	30	30
11	1.531	44.4	0.96	29	30
12	1.629	42.8	0.91	26	29
13	1.613	46.4	0.95	29	30
14	1.604	46.1	0.95	29	30
15	1.765	47.5	0.92	27	29
16	1.811	52.6	0.95	29	30
17	1.680	53.1	1.00	32	32
18	1.857	52.9	0.94	29	30
19	1.933	67.6	1.03	35	34
20	1.860	63.5	1.03	34	33
21	2.033	63.1	0.97	31	32
22	1.806	65.4	1.03	36	35
23	2.007	64.0	0.93	32	34
24	2.161	71.2	0.96	33	34
25	1.947	73.6	1.03	38	37
26	2.153	73.4	0.96	34	35
27	2.232	79.0	0.99	35	36
28	2.103	85.7	1.05	41	39
29	2.135	84.0	0.98	39	40
30	2.379	108.0	1.05	45	43
31	2.107	106.7	1.07	51	47
32	2.346	107.0	0.98	46	46
33	2.427	135.3	1.09	56	51
34	2.182	134.6	1.13	62	55
35	2.479	147.1	1.08	59	55

APPENDIX B (CONT.)

Subject 5 (Para)

Time	$\dot{V}O_2$	$\dot{V}E$	RER	$\dot{V}E/\dot{V}O_2$	$\dot{V}E/\dot{V}CO_2$
(min)	($l \cdot min^{-1}$)	($l \cdot min^{-1}$)	($\dot{V}O_2/\dot{V}CO_2$)		
1	*incomplete data for minute 1*				
2	0.959	28.0	0.89	29	33
3	0.940	30.0	0.98	32	33
4	1.096	33.4	0.96	31	32
5	1.257	37.4	0.95	30	31
6	1.119	36.4	1.02	33	32
7	1.164	36.3	0.96	31	33
8	1.354	42.1	0.98	31	32
9	1.196	39.9	1.01	33	33
10	1.361	42.1	0.98	31	32
11	1.532	49.8	0.99	33	33
12	1.284	45.2	1.02	35	35
13	1.426	46.1	0.98	32	33
14	1.633	52.4	0.99	32	33
15	1.504	52.4	1.03	35	34
16	1.610	54.8	0.99	34	34
17	1.821	62.5	1.00	34	34
18	1.578	59.2	1.05	38	36
19	1.748	59.5	0.97	34	35
20	1.872	71.7	1.04	38	37
21	1.660	66.3	1.08	40	37
22	1.701	61.0	0.97	36	37
23	1.899	82.5	1.07	43	41
24	1.791	82.7	1.13	46	41
25	2.008	84.6	1.02	42	41
26	2.230	96.5	1.03	43	42
26.4	1.830	99.0	1.16	54	47

APPENDIX B (CONT.)

Subject 6 (Para)

Time (min)	$\dot{V}O_2$ ($l \cdot min^{-1}$)	$\dot{V}E$ ($l \cdot min^{-1}$)	RER ($\dot{V}O_2/\dot{V}CO_2$)	$\dot{V}E/\dot{V}O_2$	$\dot{V}E/\dot{V}CO_2$
1	0.860	21.9	0.75	26	34
2	1.227	32.3	0.87	26	30
3	1.048	35.0	1.01	34	33
4	1.054	37.9	1.05	36	34
5	1.325	37.7	0.92	29	31
6	1.210	39.7	1.02	33	32
7	1.231	39.6	0.99	33	33
8	1.518	46.5	0.96	31	32
9	1.293	49.4	1.03	38	37
10	1.298	45.9	1.01	35	35
11	1.622	49.5	0.94	31	32
12	1.366	48.1	1.03	35	34
13	1.487	45.2	0.94	30	32
14	1.821	52.9	0.94	29	31
15	1.500	57.5	1.08	38	36
16	1.688	54.8	0.96	32	34
17	1.851	58.8	0.95	32	33
18	1.556	60.3	1.06	39	37
19	1.828	60.7	0.95	33	35
20	2.003	37.8	0.97	34	35
21	1.724	66.4	1.04	39	37
22	1.826	64.4	0.95	35	37
23	2.059	73.1	0.97	35	37
24	1.661	60.0	1.01	37	37
25	2.017	73.8	0.99	37	37
26	2.195	81.5	1.00	37	37
27	1.872	81.9	1.08	44	40
28	2.208	84.7	0.97	38	39
29	2.393	92.2	.099	39	39
30	2.089	93.7	1.07	45	42
31	2.278	96.0	1.04	43.	41
32	2.259	102.2	1.07	47	42

APPENDIX B (CONT.)

Subject 7 (Para)

Time	$\dot{V}O_2$	$\dot{V}E$	RER	$\dot{V}E/\dot{V}O_2$	$\dot{V}E/\dot{V}CO_2$
(min)	($l \cdot min^{-1}$)	($l \cdot min^{-1}$)	($\dot{V}O_2/\dot{V}CO_2$)		
1	0.609	14.4	0.71	24	33
2	0.766	18.0	0.77	23	31
3	1.213	28.2	0.86	23	27
4	1.060	31.2	1.04	29	28
5	1.049	35.4	1.16	34	29
6	1.215	35.6	1.06	29	28
7	1.250	38.4	1.06	31	29
8	1.079	37.1	1.14	34	30
9	1.304	39.3	1.00	30	30
10	1.380	46.8	1.06	34	32
11	1.047	41.7	1.14	40	35
12	1.522	58.1	1.06	38	36
13	1.500	57.0	1.08	38	35
14	1.256	49.3	1.10	39	36
15	1.625	57.2	0.99	35	36
16	1.640	68.1	1.10	42	38
16.2	1.245	52.4	1.12	42	38

APPENDIX B (CONT.)

Group means ± SE (Para)

Time (min)	$\dot{V}O_2$ (L/min)	$\dot{V}E$ (L/min)	RER ($\dot{V}O_2/\dot{V}CO_2$)	$\dot{V}E/\dot{V}O_2$	$\dot{V}E/\dot{V}CO_2$
1 (n=3)	0.718 ±0.07	17.3±2.34	0.72±0.02	24±0.88	33±0.58
2(n=4)	1.029±0.11	25.9±3.00	0.81±0.04	25±1.58	31±0.63
3	1.120±0.08	30.9±1.46	0.92±0.05	28±2.78	30.5±1.5
4	1.130±0.61	34.4±1.41	0.99±0.03	31±1.93	31±1.35
5	1.219±0.06	36.4±0.69	0.99±0.03	30±1.32	30±0.58
6	1.254±0.08	37.4±0.91	1.00±0.03	30±1.70	30±1.16
7	1.268±0.06	38.6±0.85	0.99±0.03	31±1.03	31±1.03
8	1.350±0.10	41.4±1.98	1.00±0.04	31±1.23	31±0.75
9	1.342±0.08	42.6±2.32	0.99±0.02	32±2.53	32±1.80
10	1.396±0.05	45.1±1.03	1.01±0.02	33±1.19	32±1.03
11	1.433±0.13	46.4±1.98	1.01±0.05	33±2.39	33±1.04
12	1.451±0.08	48.6±3.36	1.01±0.03	34±2.60	34±1.56
13	1.507±0.04	48.7±2.79	0.99±0.03	32±2.02	33±1.04
14	1.583±0.12	50.2±1.58	1.00±0.04	32±2.36	33±1.32
15	1.597±0.06	53.7±2.36	1.00±0.03	34±2.36	34±1.65
16	1.688±0.04	57.6±3.55	1.00±0.03	34±2.78	34±1.63
17	1.650±.014	56.7±2.41	1.02±0.04	35±2.38	34±1.32
18 (n=3)	1.662±0.10	57.5±2.31	1.02±0.04	35±3.18	34±2.19
19	1.836±0.05	62.6±2.53	0.98±0.02	34±0.58	35±0.33
20	1.912±0.05	67.7±2.37	1.01±0.02	35±1.33	35±1.16
21	1.804±0.12	65.3±1.08	1.03±0.03	37±2.85	35±1.67
22	1.778±0.04	63.6±1.34	0.98±0.03	36±0.58	36±0.67
23	1.989±0.05	73.3±5.34	0.99±0.04	37±3.28	37±2.03
24	1.875±.015	71.3±6.56	1.03±0.05	39±3.84	37±2.03
25	1.990±0.02	77.3±3.63	1.01±0.01	39±2.65	38±1.33
26	2.193±0.02	83.8±6.77	0.99±0.02	38±4.58	38±3.61
27	1.979±0.13	86.6±6.24	1.08±0.05	44±5.49	41±3.22
28 (n=2)	2.155±0.05	85.2±0.47	1.01±0.84	39±1.50	39±0.00
29	2.266±0.13	88.1±4.12	0.99±0.01	39±0.00	39±0.50
30	2.235±0.14	100.9±7.12	1.06±0.01	45±0.00	43±0.50
31	2.213±0.11	101.3±5.38	1.06±0.02	47±4.5	44±3.5
32	2.269±0.08	104.6±2.42	1.03±0.05	46±0.00	44±2.00
33 (n=1)	2.427	135.3	1.09	56	51
34	2.182	134.6	1.13	62	55
35	2.479	147.1	1.08	59	55

APPENDIX B (CONT.)

Group means ± SE (Quad)

Time (min)	$\dot{V}O_2$ (L/min)	$\dot{V}E$ (L/min)	RER ($\dot{V}O_2/\dot{V}CO_2$)	$\dot{V}E/\dot{V}O_2$	$\dot{V}E/\dot{V}CO_2$
1	0.447±0.07	14.2±2.10	0.77±0.03	32±0.58	42±1.33
2	0.593±0.01	17.3±0.58	0.74±0.01	29±1.53	39±1.76
3	0.655±0.01	19.2±0.52	0.78±0.01	29±0.67	38±0.88
4	0.679±0.01	22.7±1.07	0.87±0.02	33±1.20	38±0.67
5	0.762±0.06	25.6±1.34	0.91±0.07	34±3.84	37±1.45
6	0.791±0.04	28.3±1.25	0.92±0.05	36±2.33	39±0.58
7	0.762±0.00	27.4±2.14	0.95±0.03	36±2.65	38±1.53
8	0.836±0.05	29.4±2.26	0.96±0.06	36±4.73	37±2.65
9	0.883±0.03	31.0±1.59	0.96±0.02	35±1.53	37±0.88
10	0.855±0.03	31.6±3.79	0.98±0.03	37±3.22	38±2.33
11	0.973±0.05	33.8±1.35	0.96±0.05	35±2.89	36±1.20
12	0.959±0.04	34.9±1.30	0.97±0.02	37±1.20	38±0.88
13	0.939±0.03	38.7±3.94	1.03±0.03	41±3.46	40±2.08
14	1.065±0.04	40.0±1.84	0.98±0.03	38±2.40	38±1.45
15 (n=2)	0.950±0.03	39.7±1.00	1.05±0.06	42±2.50	40±0.00
16	0.997±0.03	40.4±5.35	1.03±0.07	41±4.5	40±1.50
17	1.099±0.07	44.6±5.55	0.99±0.09	41±7.00	41±3.50
18 (n=1)	1.155	46.2	1.02	40	39
19	1.077	37.5	0.95	35	37
20	1.308	44.3	0.93	34	36
21	1.146	45.6	1.01	40	39
22	1.179	41.6	0.93	35	37
23	1.342	48.2	0.93	36	39
24	1.219	48.1	1.02	39	39
25	1.234	50.4	1.01	41	40
26	1.467	57.3	0.98	39	40
27	1.282	55.3	1.05	43	41

APPENDIX C

INDIVIDUAL SUBJECT AND GROUP CATECHOLAMINE (NE & EPI) and LACTATE (LA) DATA

Subject 1 (Quad)

Workload (Watts)	NE (ng/ml)	EPI (ng/ml)	LA (mM)
Rest	0.187	0.018	0.803
0	0.161	0.210	0.841
6	0.243	0.020	1.083
12	0.368	0.010	1.597
18	0.632	*missing data	1.766
24	0.309	0.012	2.206
30	0.223	0.014	2.084
36	0.334	0.020	2.854
42	0.391	0.030	3.482
48	0.427	0.210	3.856

Subject 2 (Quad)

Workload (Watts)	NE (ng/ml)	EPI (ng/ml)	LA (mM)
Rest	0.349	0.020	0.700
0	0.419	0.009	0.807
6	0.510	0.053	1.209
12	0.426	0.038	1.496
18	0.492	0.039	2.525
24	0.561	0.083	3.123
30	0.370	0.070	2.925

APPENDIX C (CONT.)

Subject 3 (Quad)

Workload (Watts)	NE (ng/ml)	EPI (ng/ml)	LA (mM)
Rest	0.255	0.047	0.850
0	0.115	*missing data	1.203
6	0.131	0.046	2.577
12	0.129	0.025	1.436
18	0.144	0.041	1.669
24	0.260	0.065	2.647

Subject 4 (Para)

Workload (Watts)	NE (ng/ml)	EPI (ng/ml)	LA (mM)
Rest	0.335	0.047	0.898
0	0.289	0.108	1.580
8	*missing data for NE, EPI and LA		
16	0.618	0.160	3.140
24	0.760	0.160	3.358
32	*missing data for NE and EPI		3.647
40	*missing data for NE, EPI and LA		
48	0.980	0.260	4.361
56	1.275	0.225	5.161
64	1.526	0.284	5.090
72	1.842	0.309	6.223
80	2.013	0.354	7.116
88	2.554	0.409	7.849

APPENDIX C (CONT.)

Subject 5 (Para)

Workload (Watts)	NE (ng/ml)	EPI (ng/ml)	LA (mM)
Rest	0.278	0.204	0.935
8	0.397	0.147	1.945
16	0.579	0.287	2.850
24	0.568	0.119	2.974
32	0.826	0.192	3.611
40	1.042	0.231	4.389
48	1.294	0.252	4.806
56	1.644	0.333	4.758
64	2.383	0.429	6.441
72	4.093	0.571	7.723

Subject 6 (Para)

Workload (Watts)	NE (ng/ml)	EPI (ng/ml)	LA (mM)
Rest	0.839	0.045	0.849
16	0.229	*missing data	1.863
24	1.349	0.388	2.867
32	1.189	0.135	3.345
40	1.134	0.116	4.409
48	1.461	0.221	4.019
56	1.496	0.197	4.428
64	1.699	0.229	4.932
72	2.132	0.281	5.477
80	2.865	0.580	6.819
88	4.001	0.601	6.911
96	5.232	1.000	7.396

APPENDIX C (CONT.)

Subject 7 (Para)

Workload (Watts)	NE (ng/ml)	EPI (ng/ml)	LA (mM)
Rest	0.215	0.042	0.757
0	0.258	0.097	2.869
8	0.279	0.108	3.760
16	0.375	0.117	4.288
24	0.479	0.136	4.651
32	0.650	0.142	5.562

Group means ± SE (Quads)

Workload (Watts)	NE (ng/ml)	EPI (ng/ml)	LA (mM)
Rest	0.264±0.05	0.028±0.01	0.784±0.04
0	0.232±0.10	0.015±0.01 (n=2)	0.950±0.13
6	0.295±0.11	0.040±0.01	1.623±0.48
12	0.307±0.09	0.024±0.01	1.510±0.05
18	0.423±0.15	0.040±0.00 (n=2)	1.987±0.27
24	0.484±0.11	0.033±0.02	2.659±0.27
30	0.339±0.03 (n=2)	0.042±0.03 (n=2)	2.504±0.42 (n=2)
36 (n=1)	0.334	0.020	2.854
42 (n=1)	0.391	0.030	3.482
48 (n=1)	0.427	0.021	3.856

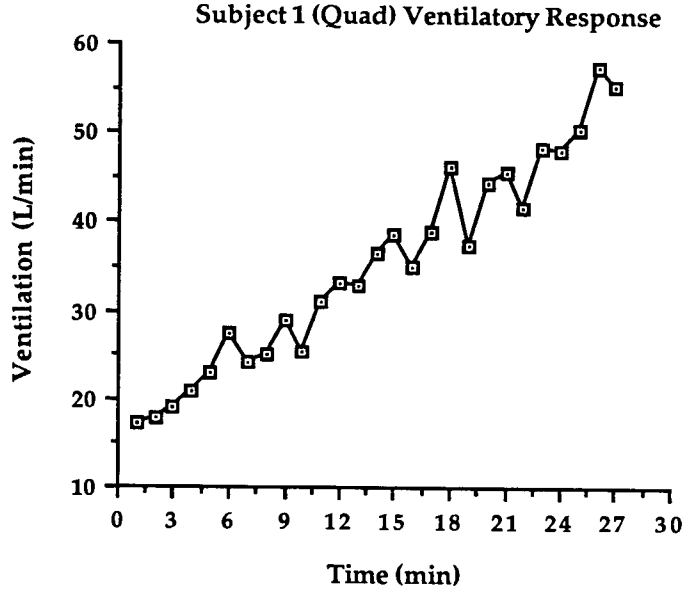
APPENDIX C (CONT.)

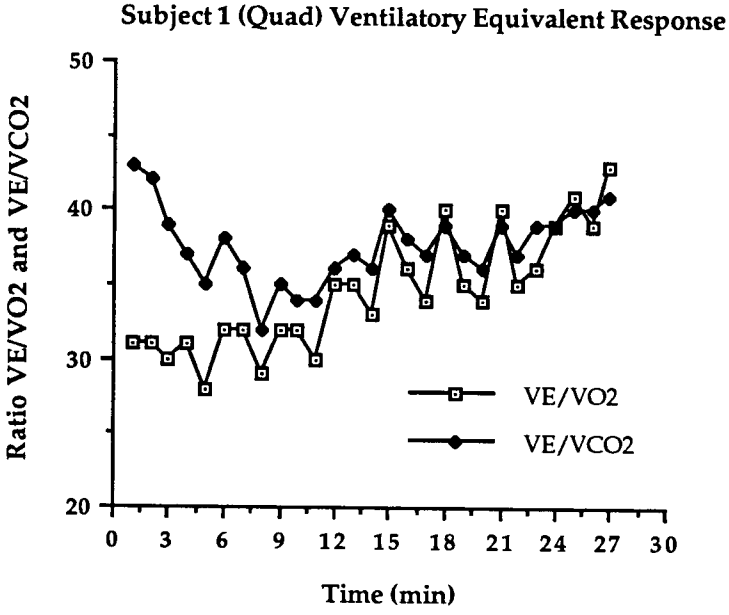
Group means ± SE (Para)

Workload (Watts)	NE (ng/ml)	EPI (ng/ml)	LA (mM)
Rest	0.417±0.14	0.084±0.04	0.860±0.04
0 (n=2)	0.273±0.012	0.103±0.01	2.225±0.65
8 (n=2)	0.338±0.06	0.128±0.02	2.852±0.91
16	0.045±0.09 (n=4)	0.188±0.05 (n=3)	3.026±0.05 (n=4)
24 (n=3)	0.799±0.28	0.214±0.09	3.497±0.58
32	0.888±0.16 (n=3)	0.156±0.02 (n=3)	4.041±0.01 (n=4)
40 (n=2)	1.088±0.05	0.173±0.06	4.399±0.01
48 (n=3)	1.245±0.14	0.244±0.01	4.395±0.23
56 (n=3)	1.468±0.12	0.252±0.04	4.516±0.12
64 (n=3)	1.869±0.25	0.314±0.06	5.488±0.48
72 (n=3)	2.689±0.71	0.387±0.09	6.097±0.82
80 (n=2)	2.439±0.43	0.467±0.11	6.968±0.15
88 (n=2)	3.277±0.72	0.505±0.10	7.380±0.47
96 (n=1)	5.232	1.000	7.369

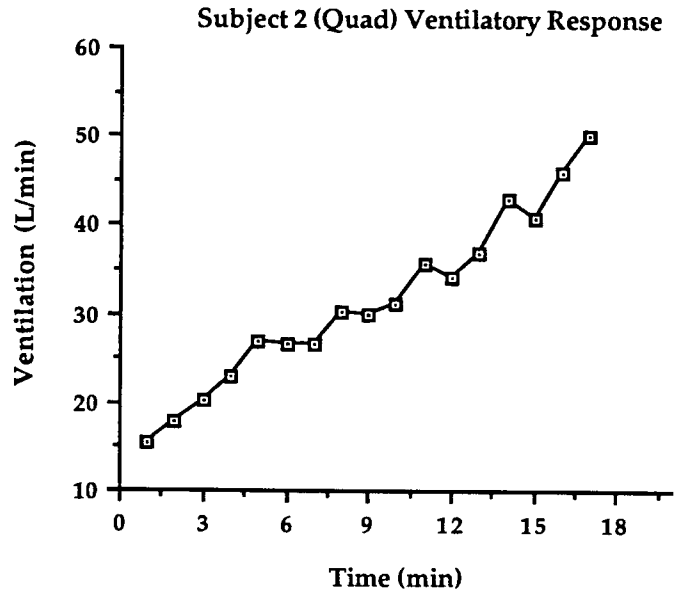
APPENDIX D

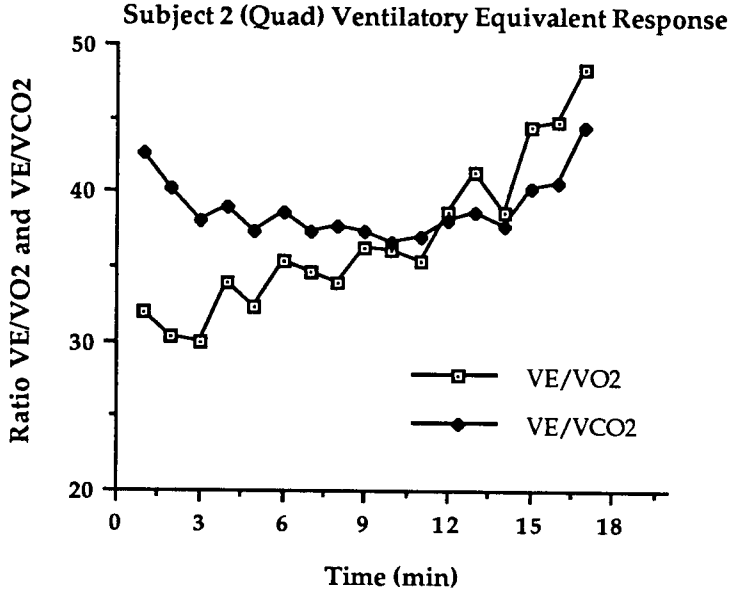
GRAPHIC DISPLAY OF INDIVIDUAL VENTILATORY RESPONSE



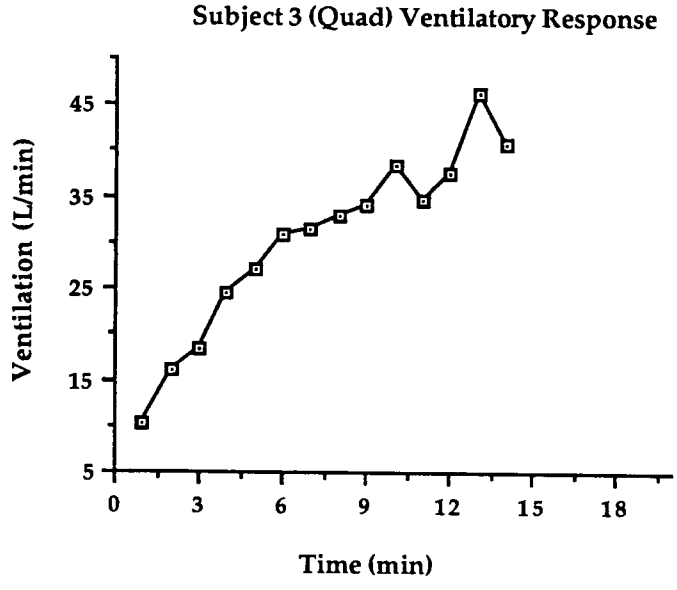


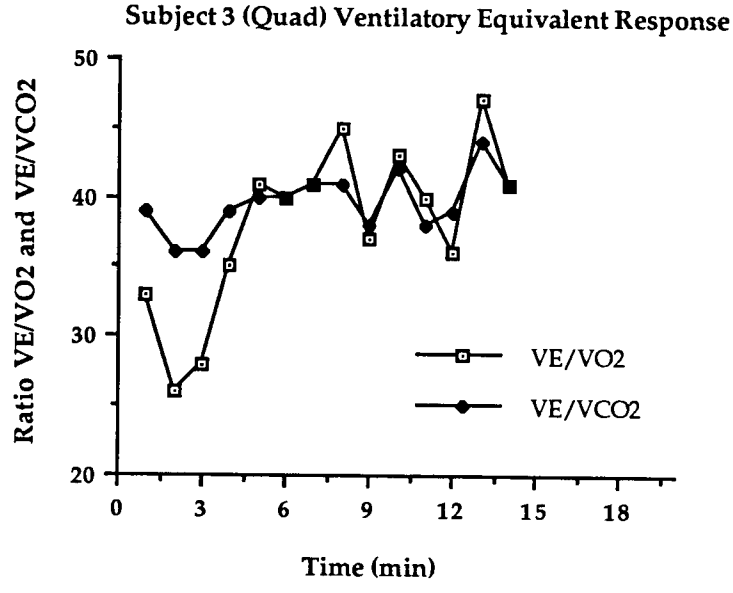
APPENDIX D (CONT.)



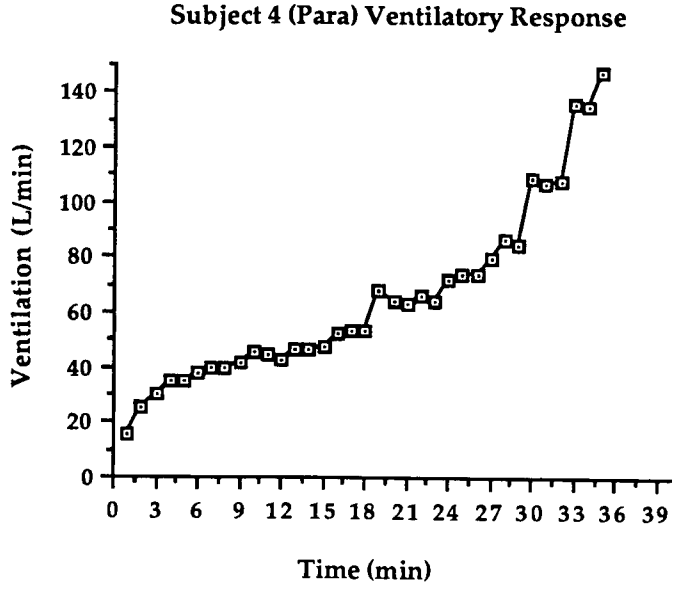


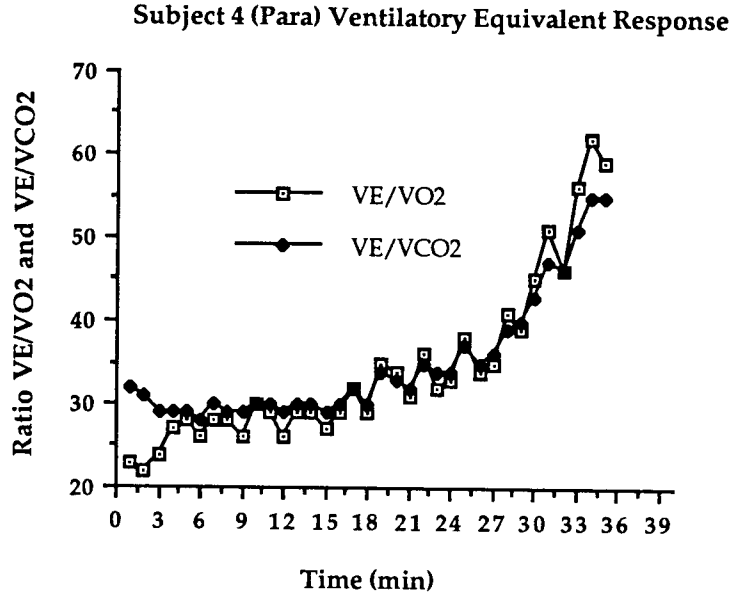
APPENDIX D (CONT.)



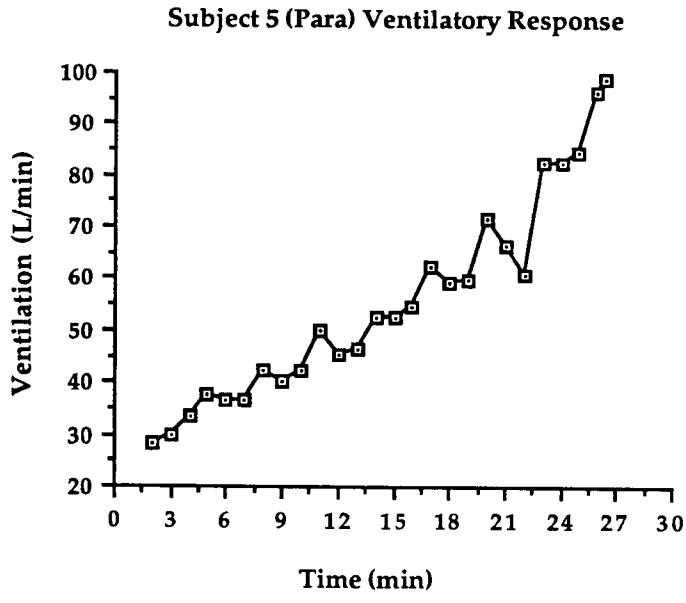


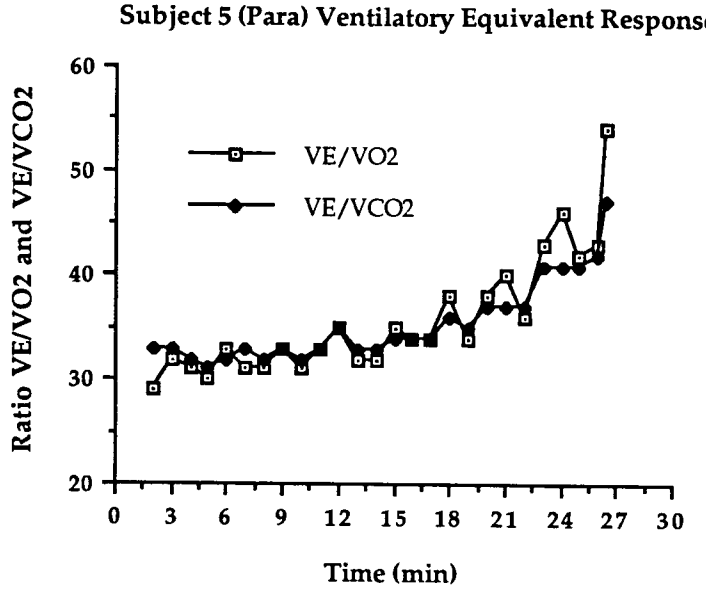
APPENDIX D (CONT.)





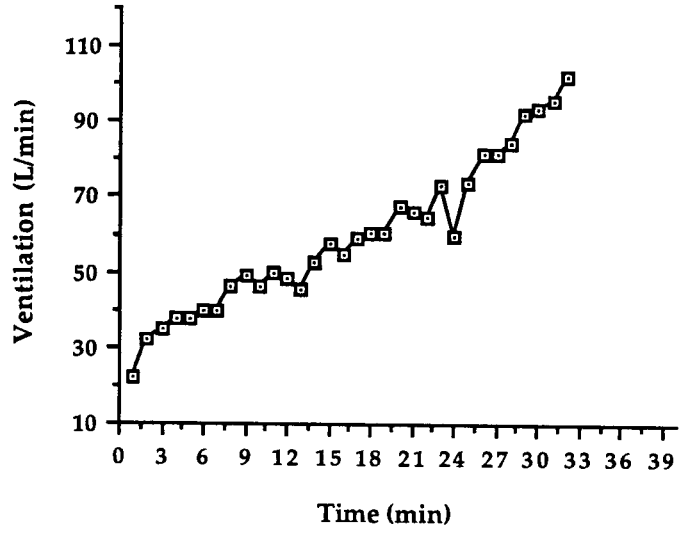
APPENDIX D (CONT.)



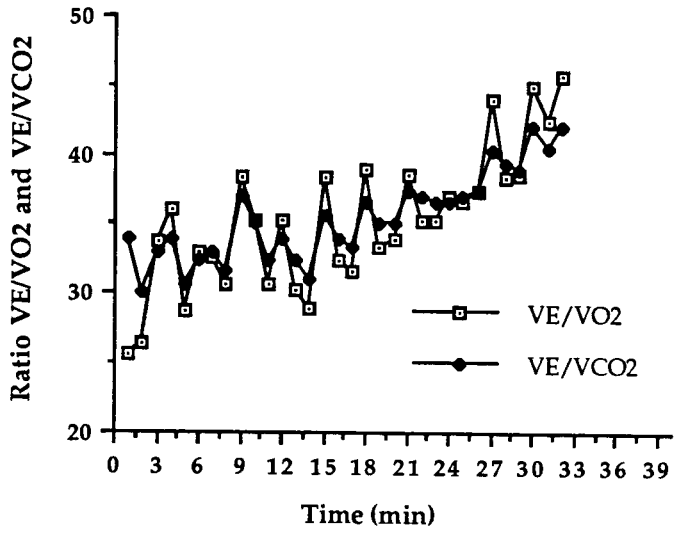


APPENDIX D (CONT.)

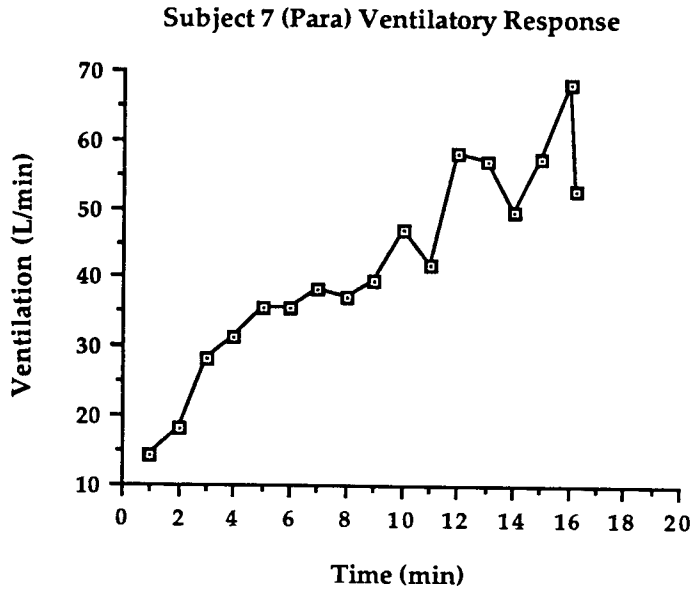
Subject 6 (Para) Ventilatory Response

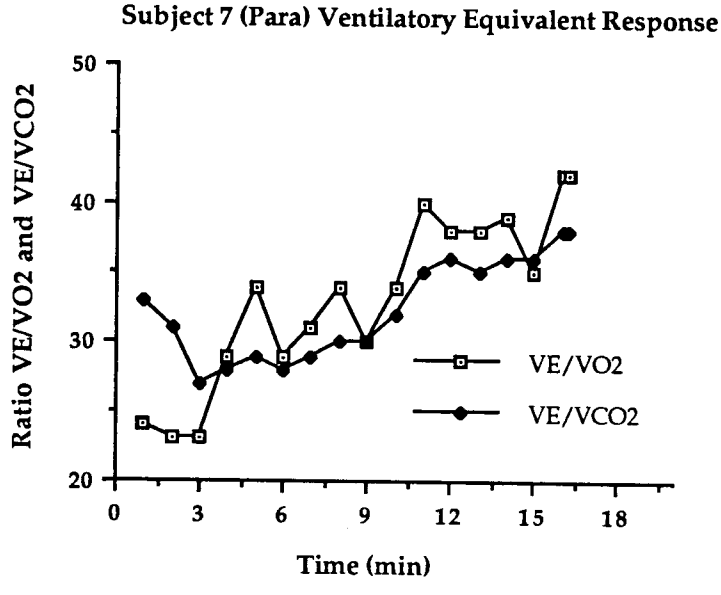


Subject 6 (Para) Ventilatory Equivalent Response



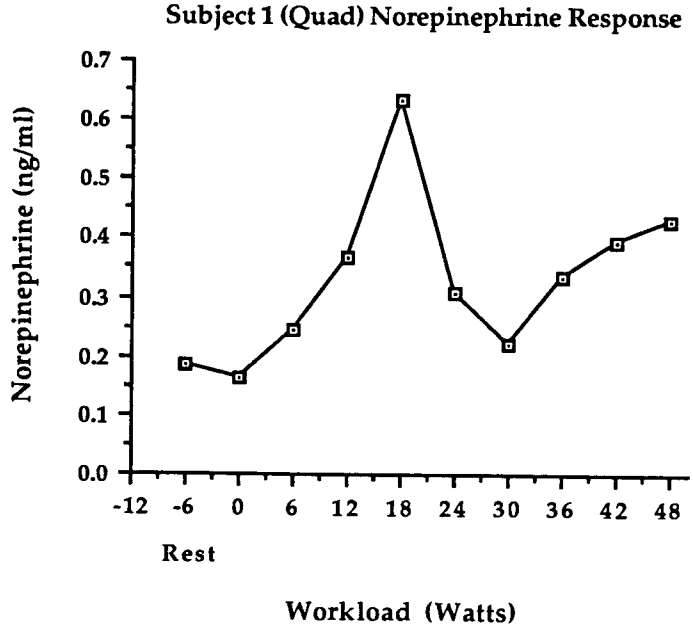
APPENDIX D (CONT.)

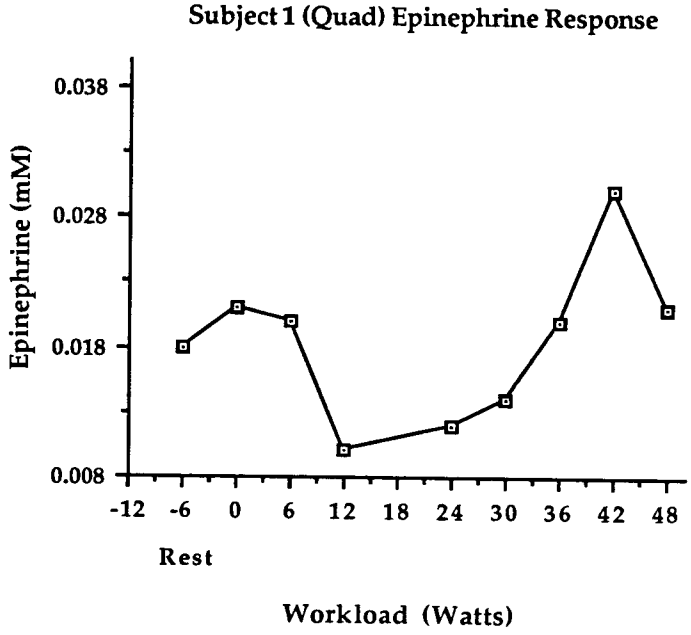




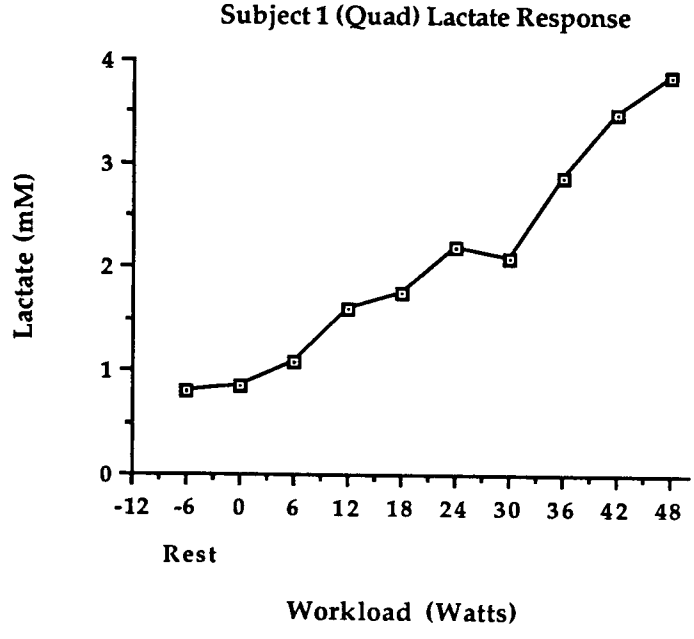
APPENDIX E

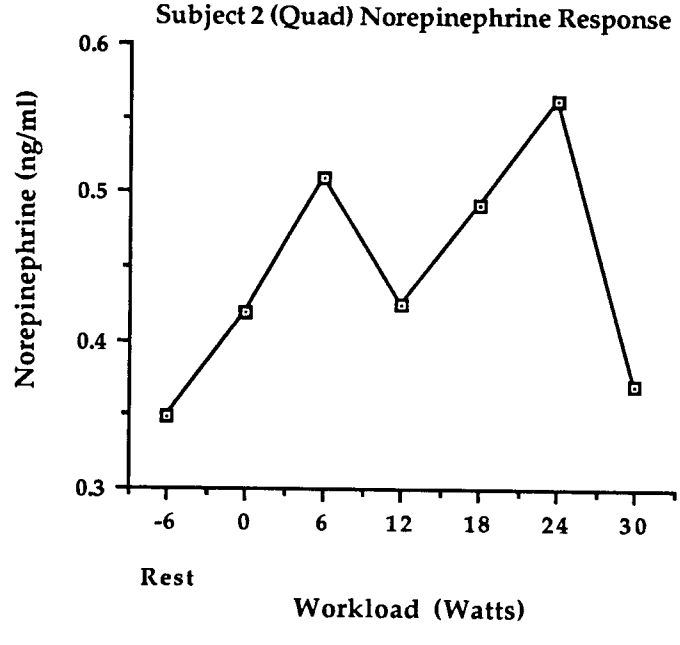
GRAPHIC DISPLAY OF INDIVIDUAL NE, EPI AND LA RESPONSE



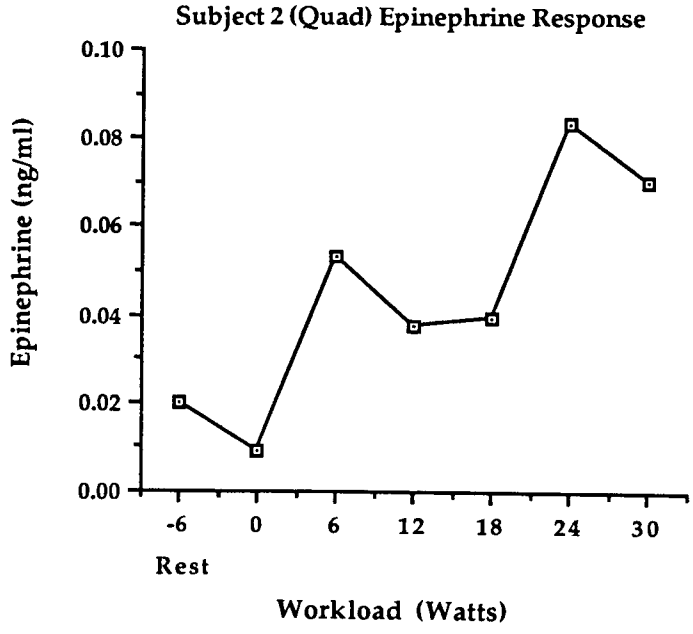


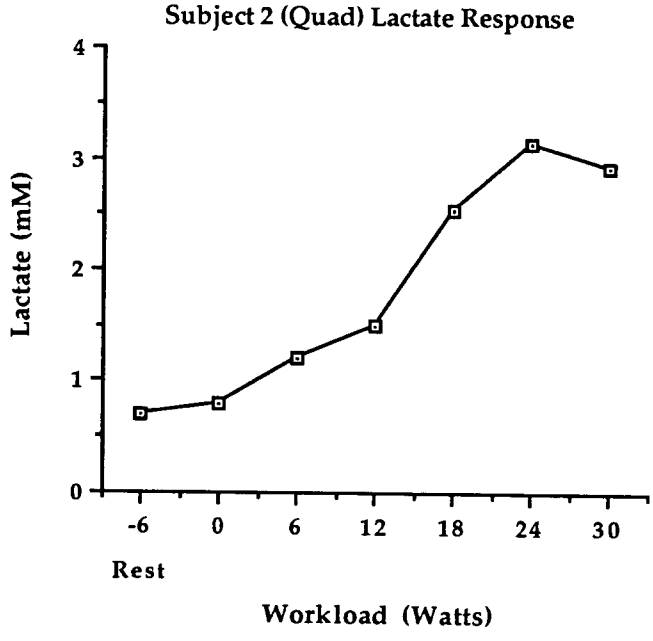
APPENDIX E (CONT.)



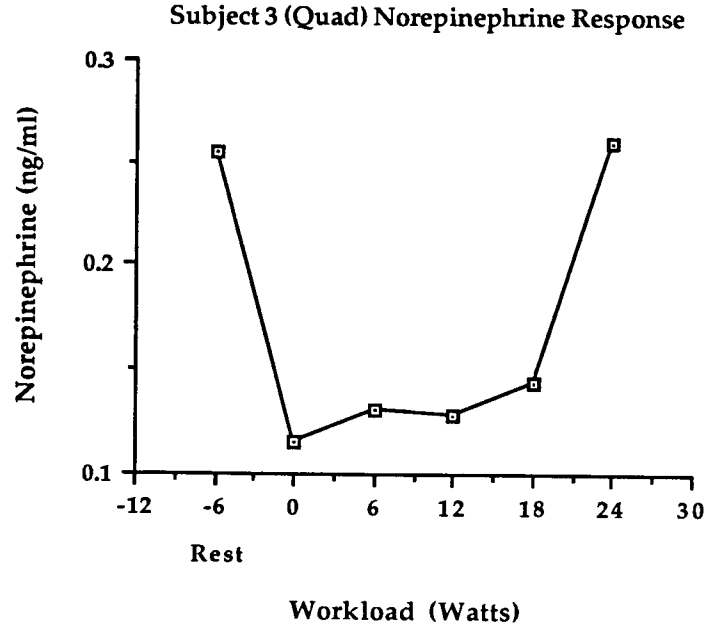


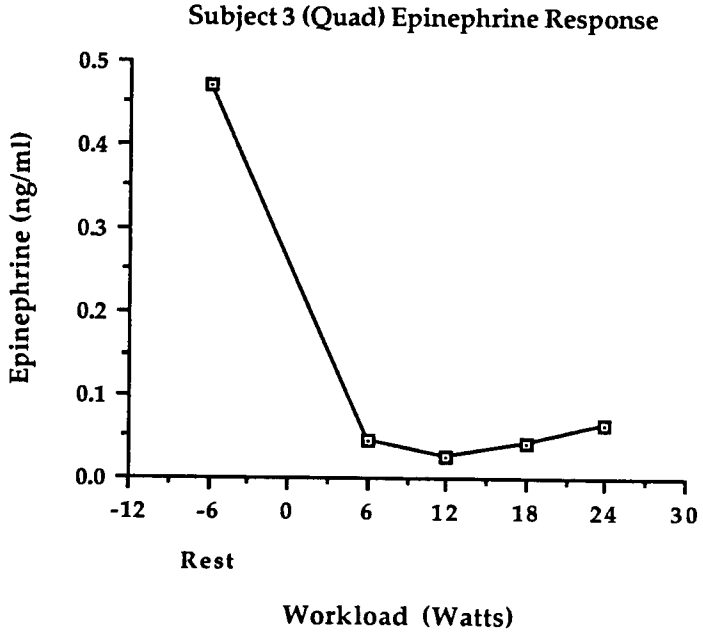
APPENDIX E (CONT.)



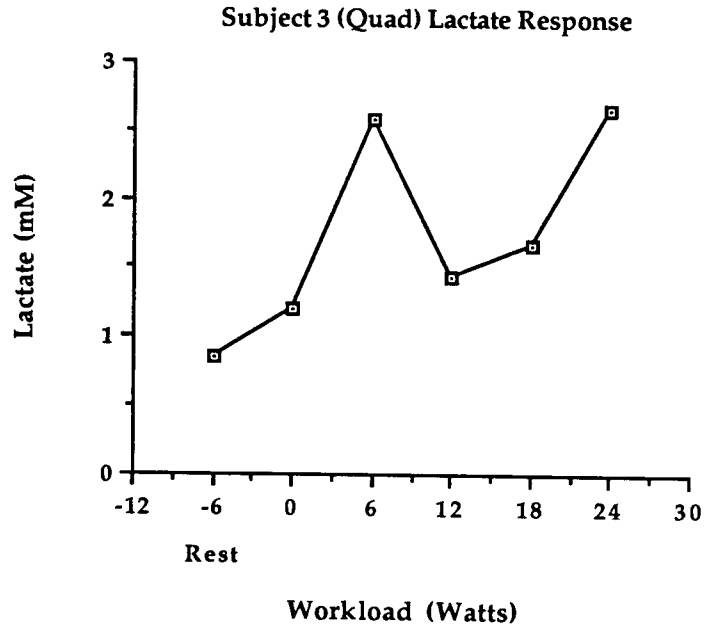


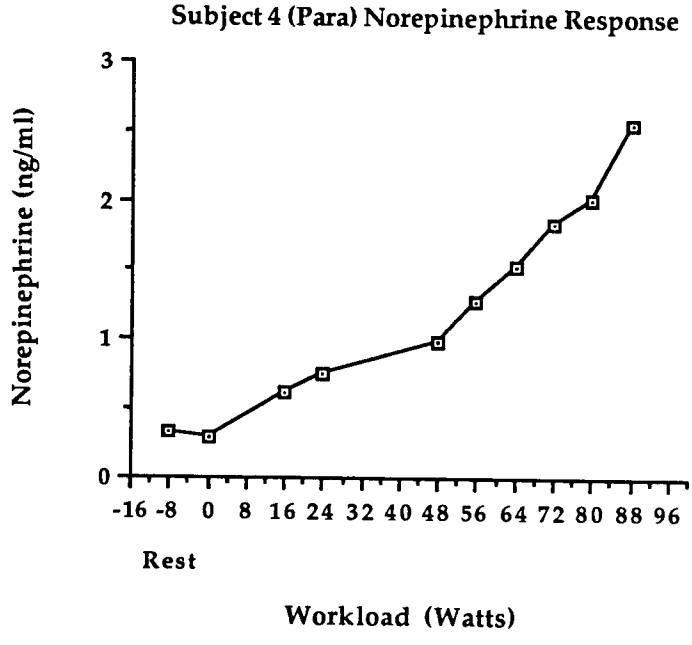
APPENDIX E (CONT.)



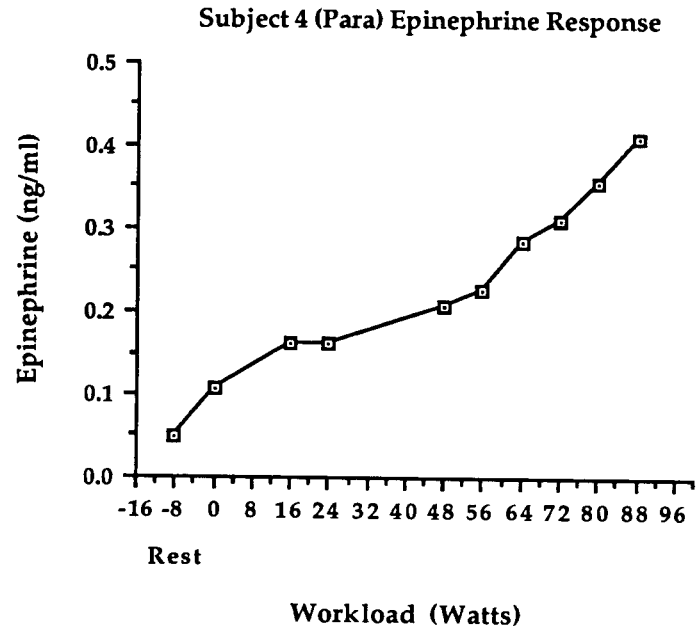


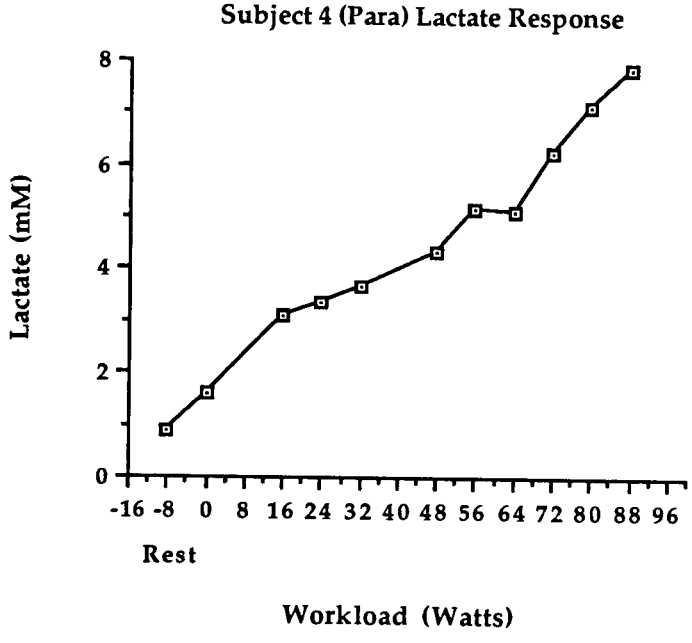
APPENDIX E (CONT.)



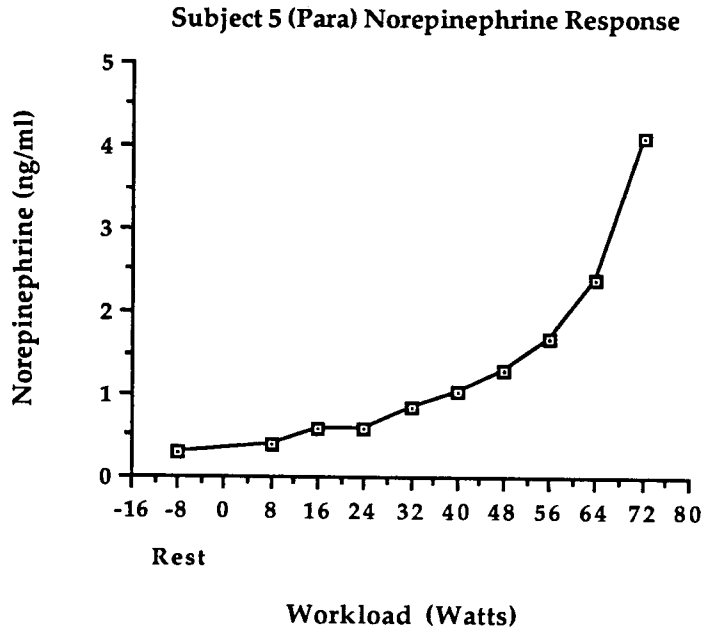


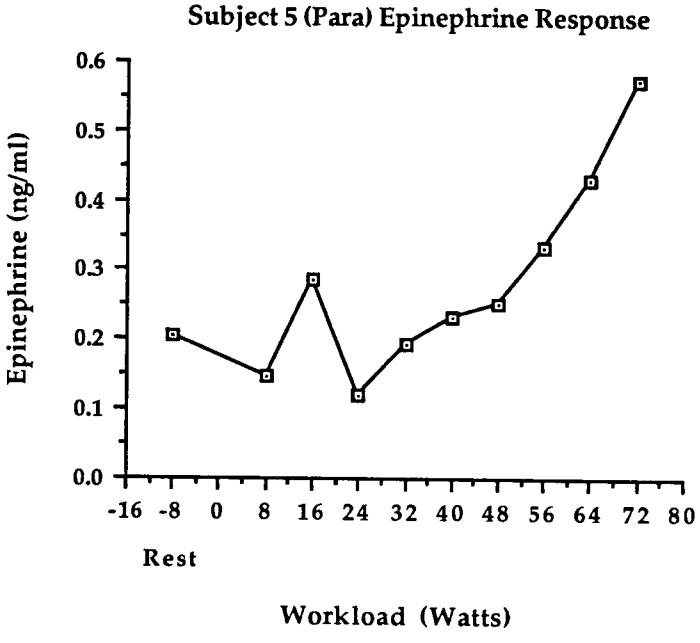
APPENDIX E (CONT.)



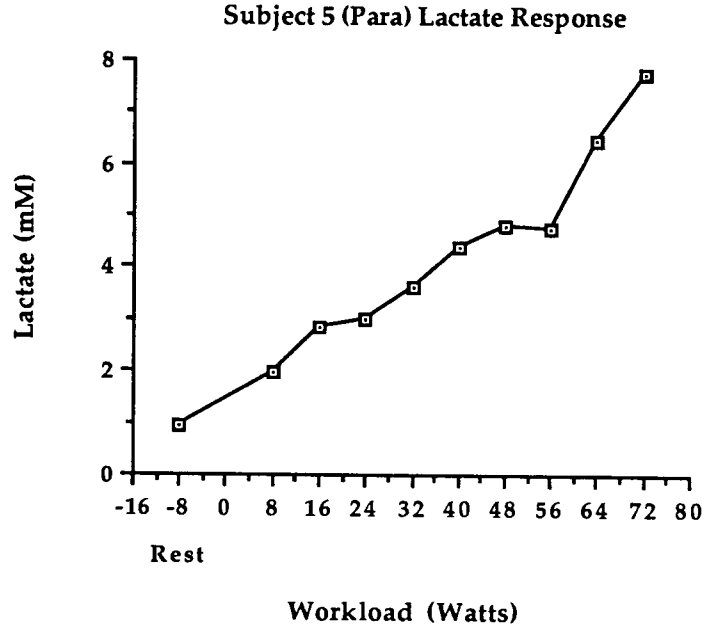


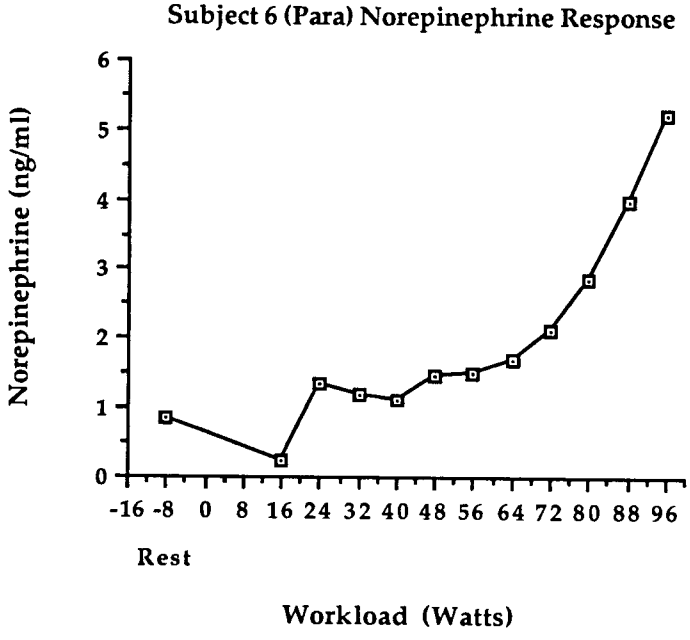
APPENDIX E (CONT.)



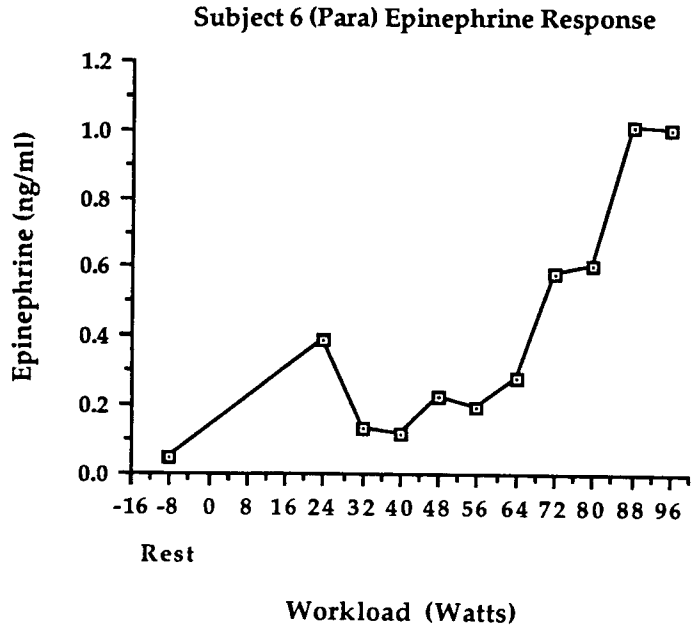


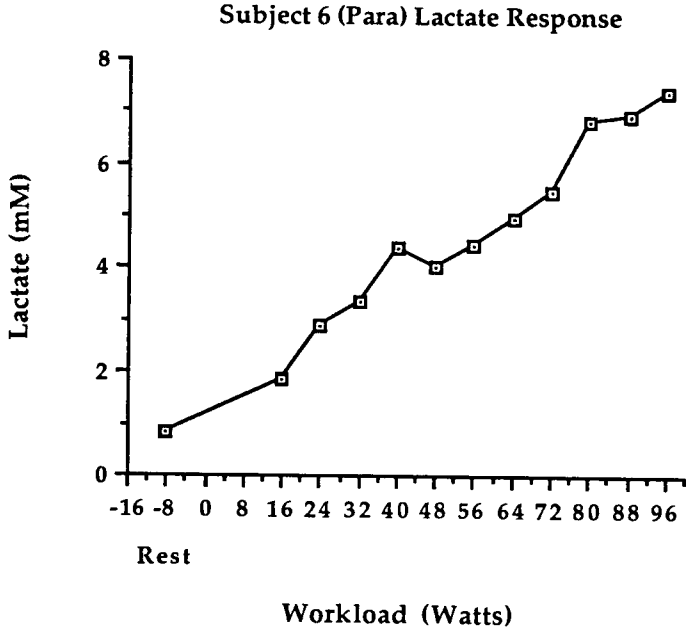
APPENDIX E (CONT.)



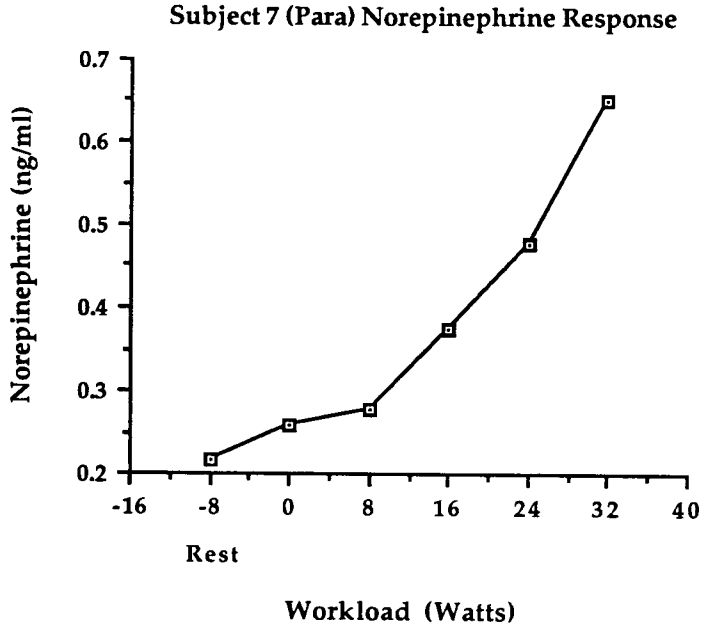


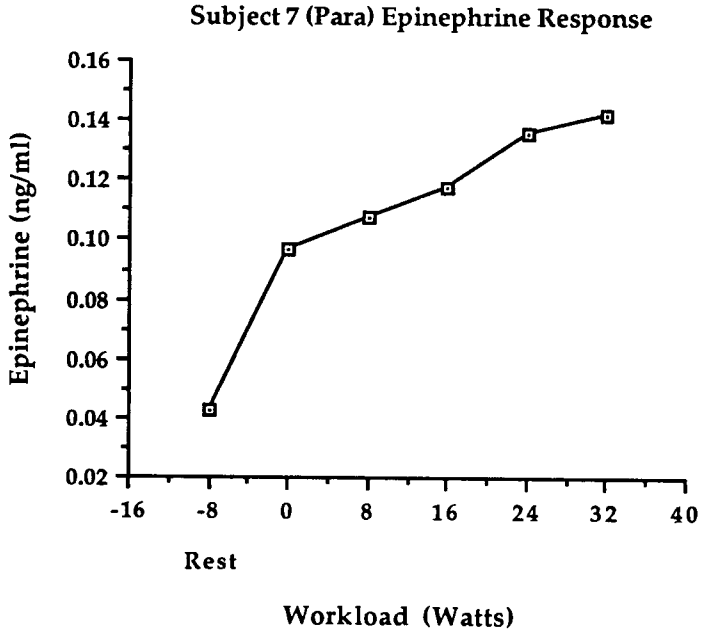
APPENDIX E (CONT.)



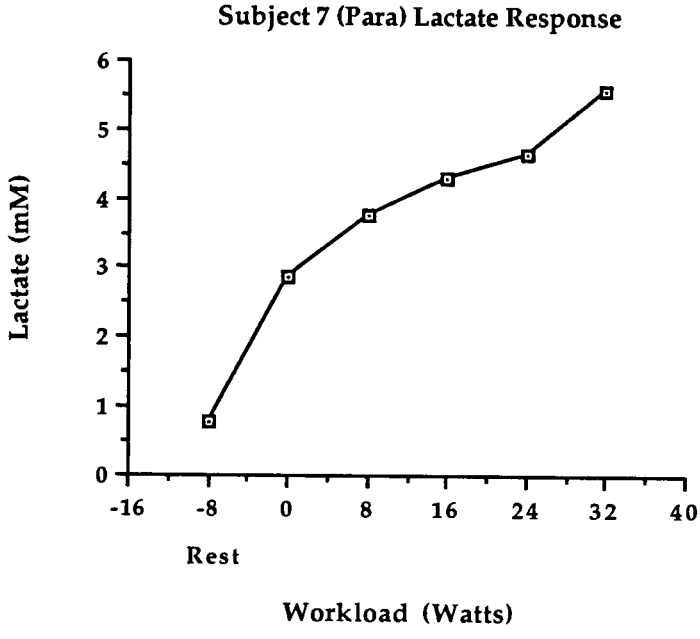


APPENDIX E (CONT.)



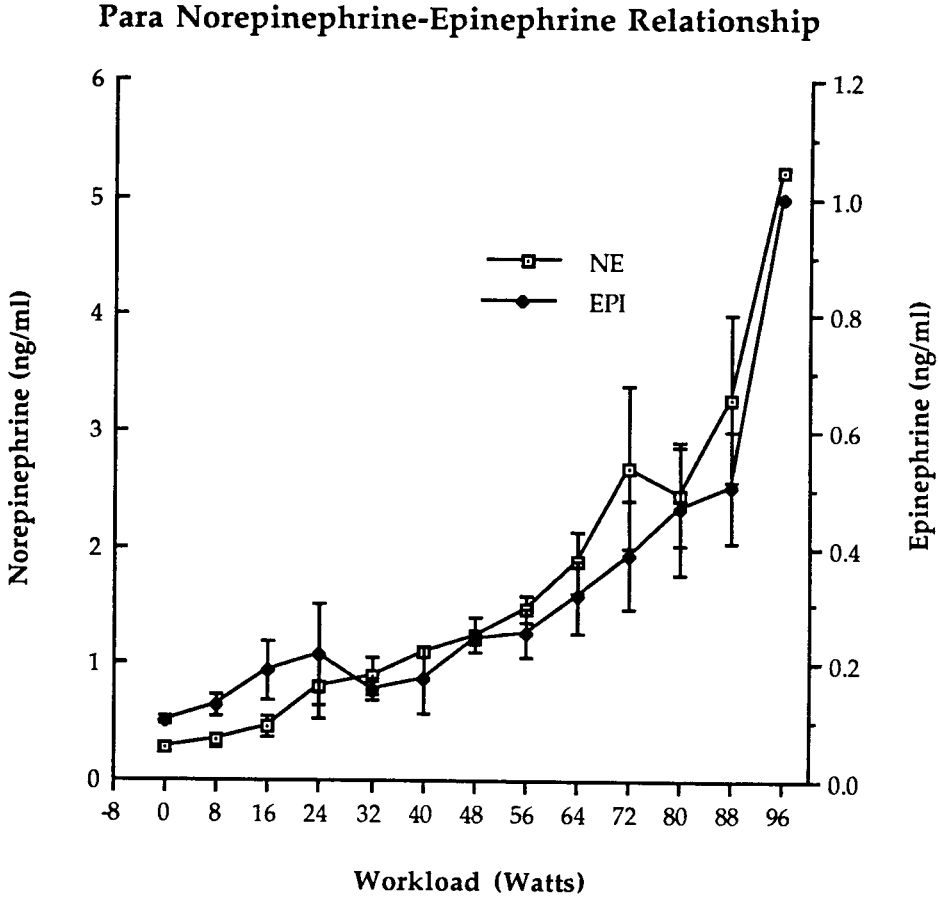


APPENDIX E (CONT.)

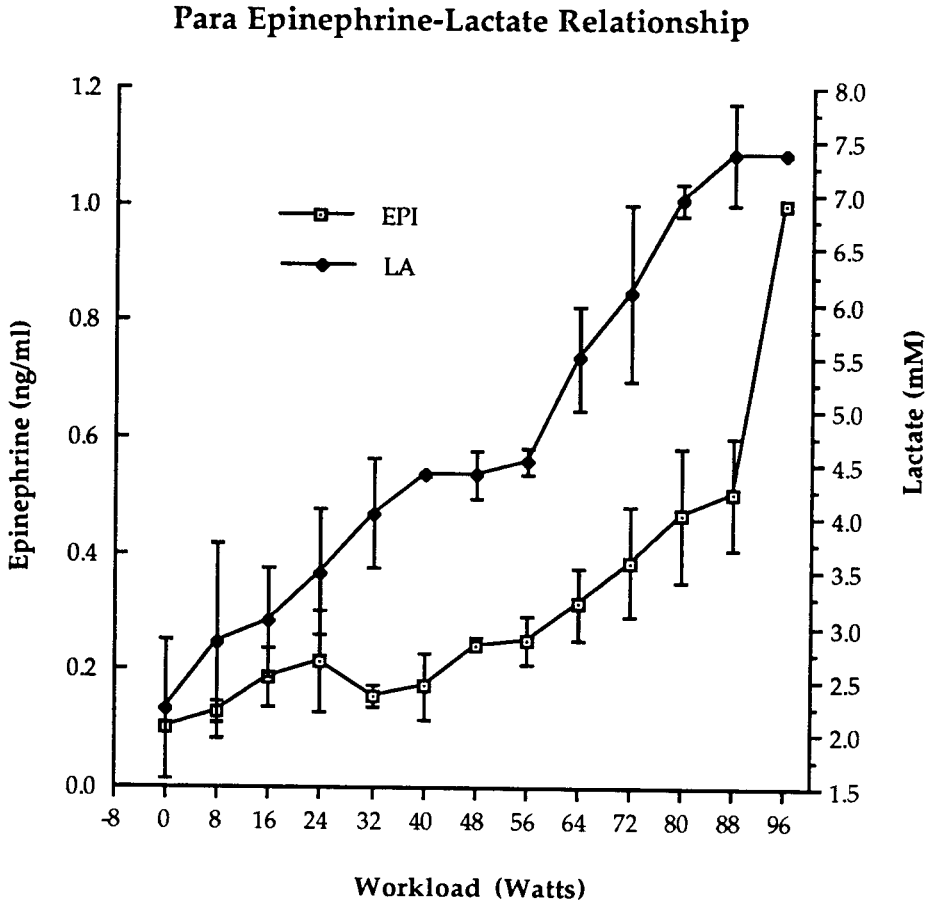


APPENDIX F

VISUAL REPRESENTATION OF CORRELATIONS BETWEEN NE-EPI, NE-LA AND EPI-LA FOR PARA and QUAD GROUPS



APPENDIX F (CONT.)



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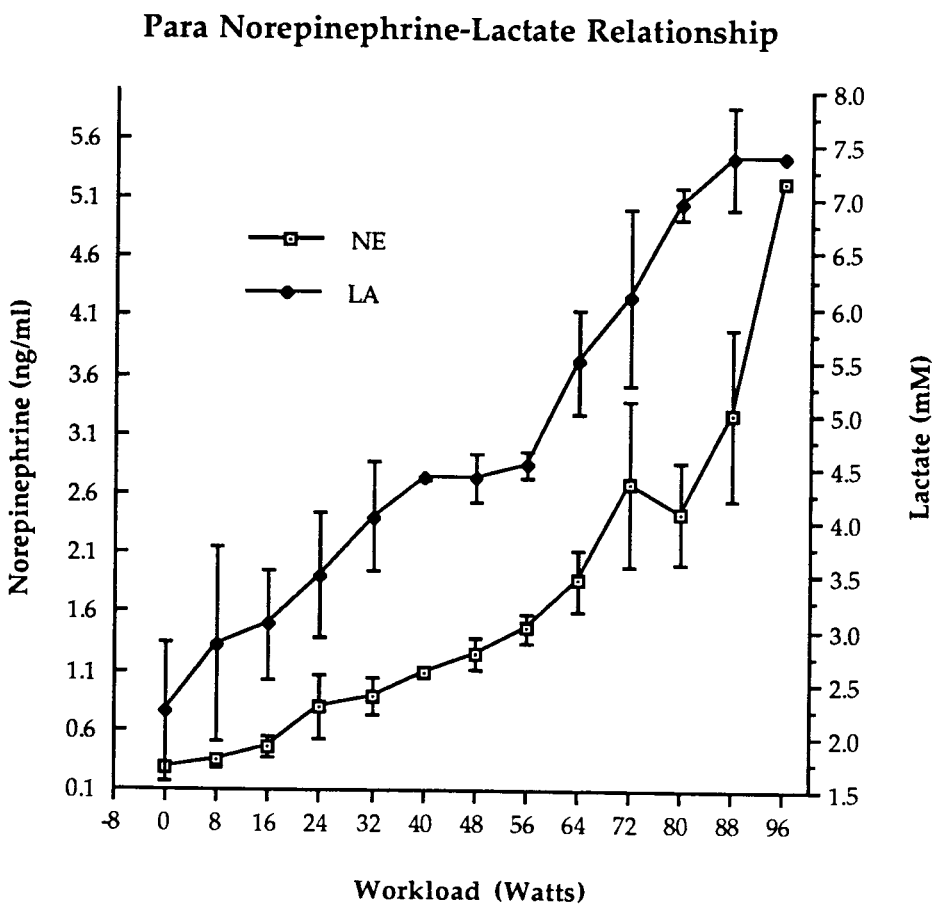

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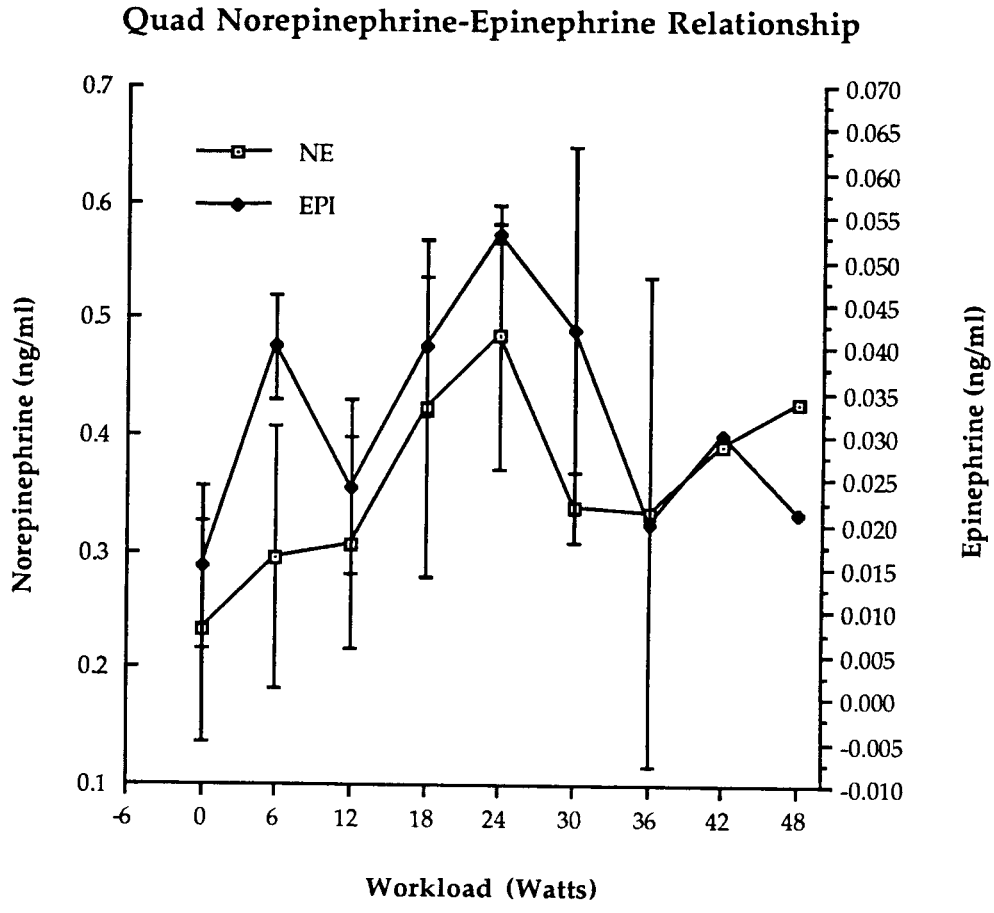
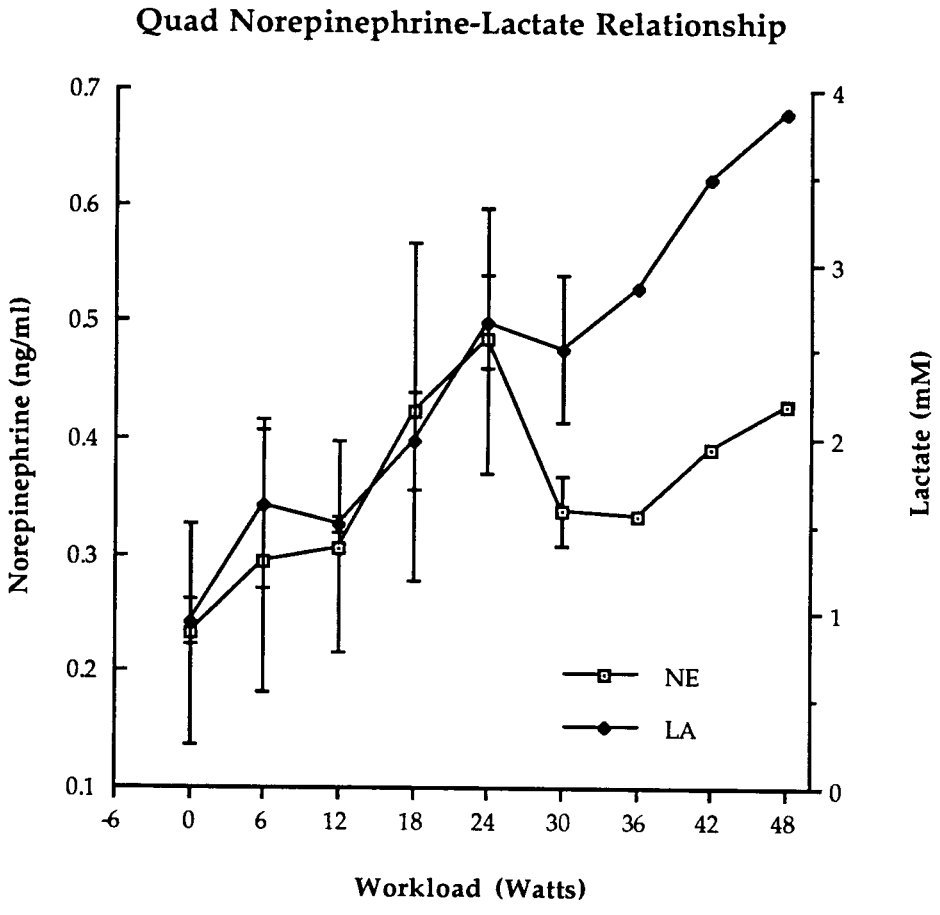


APPENDIX F (CONT.)



APPENDIX F (CONT.)