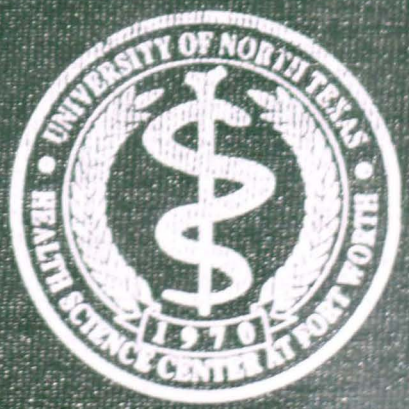
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Smith, Scott A. , Interaction of the exercise pressor reflex with central command in the regulation of blood pressure during dynamic exercise. Master of Science (Biomedical Sciences, Integrative Physiology), October, 1996, 73 pp., 7 tables, 8 figures, references.

Ten subjects, aged 26.5 ± 3.7 years, performed incremental workload cycling exercise to investigate the interaction of skeletal muscle mechano- and metaboreceptors in the regulation of blood pressure. Each subject performed four bouts of exercise: control (exercise with no intervention); exercise with thigh cuff inflation to 90 mmHg (to reduce venous outflow stimulating metaboreceptors); exercise with application of lower body positive pressure (LBPP) to 45 mmHg (to enhance mechanoreceptor activation); and exercise with the application of both LBPP and thigh cuff inflation. Measurements of mean arterial pressure (MAP), heart rate (HR), electromyographic activity (EMG), rate of oxygen uptake ($\dot{V}O_2$), cardiac output ($\dot{Q}$), and rating of perceived exertion for both the body ($RPE_B$) and the legs ($RPE_L$) were monitored. Significant mean data is presented:

| | Control | | Cuffs | | LBPP | | Cuffs + LBPP | |
|---|---|---|---|---|---|---|---|---|
| | MAP (mmHg) | $RPE_L$ (units) | MAP (mmHg) | $RPE_L$ (units) | MAP (mmHg) | $RPE_L$ (units) | MAP (mmHg) | $RPE_L$ (units) |
| **Rest** | 78.3±3.0 | ---------- | 78.1±3.7 | ---------- | 79.4±2.7 | ---------- | 80.9±1.1 | ---------- |
| **50W** | 86.6±3.6 | 7.6±0.5 | 92.9±4.5 | 10.6±0.4* | 103.3±2.3† | 10.6±0.5* | 107.0±2.2† | 11.4±0.4* |
| **100W** | 93.4±3.5 | 10.3±0.6 | 100.3±4.8 | 12.9±0.6* | 110.2±2.7† | 12.6±0.5* | 113.6±2.6† | 14.1±0.4* |
| **150W** | 101.1±4.3 | 12.6±0.7 | 106.9±4.3 | 15.7±0.7* | 117.9±3.4† | 15.0±0.7* | 122.5±3.7† | 16.7±0.5* |
| **200W** | 108.9±5.4 | 15.1±0.7 | 113.5±4.1 | 17.6±0.5* | 124.1±2.7* | 16.7±0.5* | 128.1±4.5† | 18.4±0.5* |

(*Indicates significance from control only. †Indicates significance from both control and cuffs conditions. $p<0.05$)

Indices of central command (HR, EMG, and $\dot{V}O_2$) were not significantly different between the four bouts of exercise indicating that the blood pressure response to central command activity was not altered by the interventions. Significant changes in $RPE_L$ from control during inflation of thigh cuffs, application of LBPP, and their combination indicate these stimuli successfully enhanced mechano- and metaboreceptor activation. Results indicate that MAP was significantly elevated from control only with the application of LBPP or the combination of LBPP and thigh cuff inflation. These data suggest that mechanoreceptors are the primary exercise pressor mediator of arterial blood pressure during submaximal dynamic exercise.

INTERACTION OF THE EXERCISE PRESSOR REFLEX WITH CENTRAL

COMMAND IN THE REGULATION OF BLOOD PRESSURE

DURING DYNAMIC EXERCISE

Scott Alan Smith, B.A.

APPROVED:

Major Professor

Committee Member

Committee Member

Chair, Department of Integrative Physiology

Dean, Graduate School of Biomedical Sciences

# INTERACTION OF THE EXERCISE PRESSOR REFLEX WITH CENTRAL COMMAND IN THE REGULATION OF BLOOD PRESSURE DURING DYNAMIC EXERCISE

THESIS

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Scott Alan Smith, B.A.

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## ABSTRACT PRESENTATIONS AND AWARDS

**Smith, S.A.**, K.M. Gallagher, K.H. Bryant, R.G. Querry, and P.B. Raven, FACSM. Interaction of muscle ergoreceptors with central command during progressive workload dynamic exercise to maximum. *Texas Chapter of the American College of Sports Medicine*, 1996. Third place poster competition.

**Smith, S.A.**, K.M. Gallagher, K.H. Bryant, R.G. Querry, and P.B. Raven. Role of metabolic and mechanically sensitive ergoreceptors in the blood pressure response to dynamic exercise in humans. *Society for Experimental Biology and Medicine: Southwest Section*, 1996. First place poster competition.

**Smith, S.A.**, K.M. Gallagher, K.H. Bryant, R.G. Querry, and P.B. Raven. Electromyographic activity during dynamic exercise in humans: influence of muscle chemo- and mechano-reflexes. *Society for Experimental Biology and Medicine: Southwest Section*, 1995. Third place poster competition.

PUBLISHED ABSTRACTS

Gallagher, K.M., **S.A. Smith**, K.H. Bryant, R.G. Querry, V.M. Burgos, X. Shi, and P.B. Raven. Interaction of muscle mechano- and metaboreceptors in regulating blood pressure during dynamic exercise. *The Physiologist.* 39 (5): Abst. # 8.2, A-16, 1996.

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## LIST OF ABBREVIATIONS

| | |
|---|---|
| ANOVA | Analysis of Variance |
| C/L | Cuffs + Lower Body Positive Pressure |
| cm | Centimeters |
| $CO_2$ | Carbon Dioxide |
| ECG | Electrocardiogram |
| EMG | Electromyography |
| GXT | Graded Exercise Test |
| HR | Heart Rate |
| $HR_{MAX}$ | Maximal Heart Rate |
| kg | Kilograms |
| L | Liters |
| LBPP | Lower Body Positive Pressure |
| MAP | Mean Arterial Pressure |
| min | Minute |
| ml | Milliliters |
| mmHg | Millimeters of Mercury |
| MSNA | Muscle Sympathetic Nerve Activity |

| | |
|---|---|
| MVC | Maximal Voluntary Contraction |
| μvolts | Microvolts |
| n | Sampled Population |
| $N_2$ | Nitrogen |
| $O_2$ | Oxygen |
| $PCO_2$ | Partial Pressure of Carbon Dioxide |
| $PO_2$ | Partial Pressure of Oxygen |
| PW | Peak Workload |
| $\dot{Q}_c$ | Cardiac Output |
| R | Respiratory Exchange Ratio |
| RPE | Rating of Perceived Exertion |
| $RPE_B$ | Rating of Perceived Exertion for Body |
| $RPE_L$ | Rating of Perceived Exertion for Legs |
| rpm | Revolutions Per Minute |
| SEM | Standard Error of the Mean |
| SV | Stroke Volume |
| SVR | Systemic Vascular Resistance |
| TX | Texas |

| | |
|---|---|
| $\dot{V}CO_2$ | Rate of Carbon Dioxide Elimination |
| $\dot{V}_E$ | Expired Minute Ventilation |
| VMM | Ventilation Measurement Module |
| $\dot{V}O_2$ | Rate of Oxygen Uptake |
| $\dot{V}O_{2MAX}$ | Maximal Rate of Oxygen Uptake |
| $\dot{V}O_{2PEAK}$ | Peak Rate of Oxygen Uptake |
| W | Watts |
| $WL_{MAX}$ | Maximum Workload |

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# CHAPTER I

# INTRODUCTION

The purpose of this section is to introduce the research related to the integrative function of central command and the exercise pressor reflex in eliciting cardiovascular changes during dynamic exercise. The problem addressed by this investigation is stated along with the purpose and objectives of the study. Furthermore, the hypothesis, definition of terms, delimitations, and limitations are also presented.

One of the acute cardiovascular adaptations to exercise in humans is a sharp and rapid increase in arterial blood pressure at the onset of exercise. Furthermore, an increase in the intensity of physical activity is closely matched by a continual increase in mean arterial pressure (29,47). Additionally, there is a cardiac accelerator response, an increase in ventricular contractility of the heart, and a vasoconstrictor response in resistance vessels of nonactive muscle and tissue (especially the splanchnic region and kidneys) which redirects the bulk of an increased cardiac output to the working skeletal muscle (6). It is known that the responses mediating the redistribution of the cardiac output are primarily a result of sympathetic nervous system activation. Cardiac acceleration essentially occurs because of the withdrawal of parasympathetic neural control of the heart up to a heart rate of 100 beats•min$^{-1}$. Subsequent increases in heart rate that occur in response to

progressive increases in workload are a result of continued withdrawal of parasympathetic neural control and increasing sympathetic neural control. However, it remains unclear as to the underlying neural mechanism that affect the changes in the autonomic nervous system's regulation of the cardiovascular system during exercise. Three principal mechanisms have been proposed which may be responsible for the activation of the sympathetic nervous system and the decreased activity of the parasympathetic nervous system that occurs during exercise. These proposed mechanisms are: (i) the centrally generated response (central command), (ii) the ergoreceptor response (exercise pressor reflex), and (iii) the baroreceptor response.

Experimentation has suggested that control of blood pressure by baroreflexes is as effective during exercise as it is at rest. It is believed that this is due to a central resetting of the arterial baroreflexes to a higher operating level as the intensity of exercise is increased (40). This mechanism, however, is not thought to be the dominating cause for the rise in blood pressure during severe exercise (45). Rather, the central command response and exercise pressor reflex are believed to play a more active role in blood pressure regulation during exercise. Central command, first termed "cortical irradiation" (22) serves as a feedforward mechanism which elicits changes in the autonomic nervous system activity that are thought to be a result of increased activity in the central area of the brain's subthalamic locomotor region (9,10,21,58). The signals arising in this central region activate the motor cortex as well as the medullary cardiovascular control areas (29). This central mechanism initiates the cardiovascular response to exercise determining

the level of sympathetic efferent activity to the heart and blood vessels (24,29) and the withdrawal of parasympathetic neural control of the heart. Furthermore, it is related in parallel to the neural activity responsible for the recruitment of motor units (33,46), i.e. as the intensity of exercise increases reflected by an increase in electromyographic activity (EMG) of the working muscle, the sympathetic neural outflow increases and the parasympathetic neural outflow is withdrawn (29). Therefore, it is believed that central command sets the basic pattern of cardiovascular effector activity. This basic pattern is thought to be modulated by the exercise pressor reflex which involves ergoreceptor stimulation (42) located within the skeletal muscle. These ergoreceptors respond to mechanical stimuli (mechanoreceptors) and metabolic stimuli (metaboreceptor) (20). This reflex neural mechanism, which serves as feedback control, is thought to change autonomic nervous system activity by sending afferent information from the contracting skeletal muscle to the same medullary cardiovascular center (localized to the lateral reticular nucleus) that receives input from central command (16,18,29). The afferent nervous tissue responsible for eliciting such signals have been shown to be confined to group III and IV afferent nerves from within the muscle (21,28,29). The group III nerves are thought to be associated with collagen structures and respond to mechanical events (mechanoreceptors), while the group IV afferents are associated with the walls of blood and lymphatic vessels and respond to chemical changes that occur within exercising skeletal muscle (metaboreceptors). It should be noted, however, that some group III nerves behave similarly to group IV nerves and vice versa. This is only of slight

consequence since the majority of nerves associated with group III and IV afferents behave in a manner consistent with their associated characteristics (29,57).

Most of the research conducted in this area of cardiovascular physiology has attempted to isolate the influence of either central command or the exercise pressor reflex during both static and dynamic exercise. Partial neuromuscular blockade is one model that has been used to isolate the central neural mechanism and results in a reduction of muscle strength (29). This method is believed to increase the contribution of the central command response to exercise in relation to the actual force developed. It has been found that when partial neuromuscular blockade is induced with tubocurarine , the heart rate and blood pressure responses to the same absolute force as in control conditions (10% of the control maximal voluntary contraction) are increased whereas when the same relative force is produced, the heart rate and blood pressure responses are the same as control. This suggests that, when isolated, central command increases its activity and its influence on the cardiovascular response that is increasing when the perception of work is increased (29). The exercise pressor reflex has been isolated utilizing both circulatory occlusion and lower body positive pressure (LBPP). Two-legged circulatory arrest achieved by inflation of pressure cuffs around the upper thighs has been used to isolate the vasoconstricting mechanism of the exercise pressor reflex (49). By measuring the peak forearm vascular conductance response to dynamic leg exercise, it was found that leg circulatory arrest after exercise, which isolated the skeletal muscle metaboreceptor, reduced forearm conductance by approximately 20% below the normal values recorded for leg exercise alone (49). This

suggests that stimulation of the metaboreceptor reflex , one component of the exercise pressor reflex, augments the vasoconstrictor response of nonworking tissue blood vessels and hence increases arterial blood pressure. Stimulation of ergoreceptors by LBPP has been found to elevate intramuscular pressure which activates mechanoreceptors (60) and to induce flow restriction to the areas of the body where the pressure is applied stimulating metaboreceptors (7,60). Experimentation has found that 45 Torr LBPP is sufficient to activate the metaboreceptor reflex only at work rates above 85% maximal aerobic capacity (i.e. 85 % $\dot{V}O_2$ max) eliciting a greater blood pressure increase during exercise than at rest (60). Furthermore, heart rate has been found to be increased from control during flow restriction incremental-load exercise even though it reduced exercise performance by 36% and peak heart rate by 13% (7). These findings suggest that activation of mechanoreceptors and metaboreceptors concurrently (exercise pressor reflex) augments the normal cardiovascular responses to exercise.

In summary, experimental research suggests an appropriate cardiovascular response occurs in the absence of either the influence of central command or the exercise pressor reflex, supporting the concept that these systems may be redundant and simple neural occlusion may be operative (23,32). In contrast, other experimentation reveals that enhancement or attenuation of the two neural pathways does not lead to normal cardiovascular responses suggesting that the mechanisms are additive in establishing the adaptations that take place during exercise (21). It is apparent the current research has

been unable to conclusively elucidate the contribution of central command and the exercise pressor reflex and its two components (mechanoreceptors and metaboreceptors) to the cardiovascular response to exercise. This project should provide more insight into the relative contributions of central command and the exercise pressor reflex, specifically the role of mechanoreceptors and metaboreceptors, in the regulation of arterial blood pressure during dynamic exercise.

## Statement of the Problem

The problem of this study was to determine if stimulation of muscle ergoreceptors (mechanoreceptors and metaboreceptors) augmented the cardiovascular response of increasing mean arterial pressure (MAP) during dynamic ramped workload exercise and if so to determine whether these receptors act in concert or individually to elicit such a response.

## Purpose and Objectives of the Study

The purpose of this investigation was to determine the integrative function of central command and the exercise pressor reflex in increasing MAP during dynamic exercise of increasing workload. To accomplish this goal, the following objectives were proposed: (i) To measure significant increases during graded bicycle exercise testing to maximum (GXT) in heart rate (HR), electromyographic activity (EMG), ratings of perceived exertion (RPE), cardiac output ($\dot{Q}_c$), and MAP during semi-recumbent cycle

ergometry in men and women. (ii) To measure significant metabolic differences between different exercise conditions (control, stimulation of ergoreceptors individually, and stimulation of ergoreceptors concurrently) via rate of oxygen uptake ($\dot{V}O_2$) (iii) To establish if stimulating ergoreceptors changed factors related to exercise performance (i.e. peak work rate-PW) including HR, EMG, $\dot{V}O_2$, RPE, $\dot{Q}_c$, and MAP during dynamic ramped bicycle exercise.

## Hypothesis

The following two-part hypothesis was proposed: (i) An activated exercise pressor reflex augments the normal integrated central command and exercise pressor reflex blood pressure response to ramped increases in dynamic exercise; and (ii) of the two populations of muscle ergoreceptors (mechanoreceptors and metaboreceptors), the mechanoreceptors predominate in eliciting the normal blood pressure response to dynamic exercise.

## Definition of Terms

1. Blood Pressure Response to Exercise- At the onset of dynamic exercise vagal stimulation by the parasympathetic nervous system is withdrawn which allows sympathetic outflow to increase cardiovascular variables such as cardiac output and regional peripheral vasoconstriction which increases mean arterial pressure in an attempt to increase the perfusion pressure to the working skeletal muscle.

2. Central Command- conceptual feedforward control mechanism of autonomic nerve activity to the cardiovascular system arising in a central area of the brain that activates the motor cortex and in a parallel fashion the cardiovascular control areas in the medulla.

3. Electromyographic Activity (EMG)- a fully rectified and integrated measurement of electrical activity in skeletal muscle indicative of the number of motor units recruited for exercise or the intensity of discharge of active motor units.

4. Ergoreceptors- Term used to collectively refer to the afferent sensory fibers involved in the exercise pressor reflex which respond to work (i.e.mechanoreceptors and metaboreceptors).

5. Exercise Pressor Reflex- Feedback control mechanism arising from afferent sensory fibers in working skeletal muscle which send information to the cardiovascular center of the medulla to reflexively activate sympathetic neural control of the cardiovascular center.

6. Fitness- Level of exercise fitness was based on peak work load achieved during a screening cycle ergometer graded exercise test and responses to standardized medical history and nutrition questionnaire.

7. Graded Exercise Test (GXT)- Testing protocol in which the subject exercised in a semi-recumbent position on a cycle ergometer placed in customized pressure box at 60 revolutions per minute (rpm) with a 25 Watt per minute increase in workload until volitional fatigue was reached.

8. Maximal Oxygen Uptake ($\dot{V}O_{2MAX}$)- The maximal volume of oxygen an individual can utilize during strenuous exercise. In a GXT test with an increase in workload, the $\dot{V}O_{2MAX}$ is determined by the plateau of $\dot{V}O_2$ that generally precedes the end of the exercise bout.

9. Mechanoreceptors- Group III (Paciniform corpuscles and unencapsulated nerve endings) sensory afferent fibers located in skeletal muscle. These receptors are associated with collagen structures and are stimulated by deformation changes occurring in active skeletal muscle.

10. Metaboreceptors- Group IV (unencapsulated nerve endings) sensory afferent fibers located in skeletal muscle. These receptors are associated with blood and lymphatic vessels and are stimulated by metabolic changes occurring in active skeletal muscle.

11. Peak Oxygen Uptake ($\dot{V}O_{2PEAK}$)- The greatest value of oxygen consumption obtained utilizing this experiment's GXT protocol in a semi-recumbent position on a cycle ergometer. This cycling protocol will not usually allow the individual to reach a true absolute maximal oxygen uptake not because of cardiorespiratory limitations but rather due to the onset of acute leg fatigue.

12. Peak Work Load (PW)- Level of work in watts achieved by subject in each experimental condition upon termination of the cycle ergometer GXT test.

13. Power Test for Sampled Population (n)- The term power refers to the probability of rejecting a false null hypothesis. The probability of making a type I error (rejection of the null hypothesis when it is true) is determined by the level of significance, $\alpha$ , specified. For

example if $\alpha$ is specified as 0.05, the probability of making a type I error is 0.05.The probability of making a type II error, (failure to reject the null hypothesis when it is false) is denoted by $\beta$, and the probability of making a correct rejection, is denoted by 1- $\beta$. The latter determination is the power of a statistical test.

14. Ratings of Perceived Exertion (RPE)- rating scale of perceived effort of work from 6 to 20, 6 being very,very light work and 20 being very, very hard work.

15. Volitional Fatigue- Point in GXT test when the subject can no longer maintain 60 rpms even when encouraged verbally. Used as marker for the termination of the cycle ergometer test.

## Delimitations

Factors will be incorporated into the experimental protocol to reduce the number of uncontrolled variables in an attempt to maintain feasibility and reliability of the data collected and thus obtain meaningful results:

1. Ten healthy subjects (4 women and 6 men) between the ages of 18 and 35 years were asked to volunteer for the study and were screened for fitness levels prior to being accepted.

2. Subjects completed two of four exercise bouts on two separate days. The testing occurred on the same piece of exercise equipment each trial in the same semi-recumbent position at approximately the same time of day.

3. The subject rested for a minimum of one hour in a supine position after instrumentation prior to the beginning of the experimental testing.

4. The subject rested for a minimum of one hour in a supine position between each bout of exercise.

5. The subject was allowed to consume one glass of water immediately after each exercise bout was completed in an attempt to reach normotensive levels of blood pressure for that subject.

6. The room temperature was held at approximately 22° C during all experimental trials and recovery periods.

7. The test trials that were conducted on any given day were assigned randomly in order to eliminate any learned adaptations to the exercise protocol.

8. The subjects were asked to abstain from the consumption of any stimulants on the day of testing (i.e. caffeine, nicotine) and to eat a low-fat meal on the morning of that day. Furthermore, the subject was asked to abstain from alcohol consumption or strenuous physical activity for 24 hours prior to testing.

## Limitations

1. It was possible that subjects did not heed suggestions made about substance consumption and physical activity prior to the experimental protocol which could have effected the reliability of the data collected.

2. The subjects peak work load was determined when the subject had reached volitional fatigue. This variable may have been dependent on the subjects desire to exercise under strenuous conditions and could have varied depending on psychological (i.e. mood, etc.) and physiological (i.e. nutrition, level of rest, etc.) factors.

# CHAPTER II

# REVIEW OF RELATED LITERATURE

Chapter II presents a comprehensive review of previous research in the areas cardiovascular and respiratory regulation during exercise by central command and the exercise pressor reflex. A review of such work was essential in creating the design and formulating the goals of this investigation. Furthermore, an exhaustive review of related literature insured that earlier experimentation was not duplicated unknowingly. The physiological adaptations to dynamic exercise before and after augmentation of either central command or the exercise pressor reflex are discussed within the context of this chapter. Furthermore, the significance of these earlier findings were also vital to the interpretation of the results discussed in Chapter V.

During exercise, the primary goal of the cardiovascular system is to supply oxygen and nutrients to the working skeletal muscle for energy reconstitution and to remove the metabolic waste produced from energy consumption. As a result, delivery and removal of these substances is tightly regulated by monitoring the adequacy of perfusion pressure in these working skeletal muscle beds. The basic pattern of sympathetic and parasympathetic autonomic effector activity which increases mean arterial pressure (MAP), heart rate (HR), cardiac contractility, and vasoconstriction in nonactive muscle and tissue beds

during exercise has been proposed to be set by central command (29,47). Central command relays efferent communication from its proposed location in the subthalamic locomotor region (9,10,21,58) to the medullary cardiovascular center found in the lateral reticular nucleus (16,18,29). The resultant increase in perfusion pressure and hence, energy substrate delivery and waste removal is monitored by the exercise pressor reflex within the working skeletal muscle. The mechano- and metabo-ergoreceptors, group III and IV muscle afferents respectively, provide the medullary cardiovascular center with information regarding the adequacy of this system (42).

## Central Command Studies in Human Subjects

### Dynamic Exercise

Several studies incorporating dynamic exercise have reported that increases in rate of oxygen uptake ($\dot{V}O_2$), HR, and MAP are attributable to the feedforward effector mechanisms of central command (15,55,59). Furthermore, electromyographic activity (EMG) and ratings of perceived exertion (RPE) have also been shown to increase with increasing central command activity and as such have been used as indices of central command (35). In contrast, one study has indicated that an increase in MAP during dynamic exercise is due not to central command but rather to an increase in venous return or a mechanoreceptor evoked increase in myocardial contractility and that central

command determines the HR response to exercise (35). However, Secher and colleagues (48) have reported that the HR response to exercise is not due to central command as evidenced by the fact that partial neuromuscular blockade by tubocurarine, which they assumed would block afferent feedback and accentuate the central command influence of this cardiovascular variable, did not change the HR response to the onset of exercise when subjects exercising with and without tubocurarine were compared (48).

In contrast to the findings of Secher's group, Innes et al. (15) using cycle ergometry in subjects that experienced unilateral leg weakness, were able to show that exercise with a weak leg caused an increase in ventilation, HR, and MAP when compared to exercise with a normal leg. In this study, the researchers assumed that exercise with the weak leg would require a larger contribution from central command than would exercise with the normal leg and as such provided evidence that a neurological feedforward mechanism existed that could elicit such increases in effector activity on the cardiovascular and respiratory responses to exercise (15).

It has been postulated that generalized, uniform activation of sympathetic vasoconstrictor outflow as well as tachycardia is produced at the onset of dynamic exercise (43) and that this mass sympathetic discharge may be a result of central command or the exercise pressor reflex activation, as these two systems appear to be redundant (32). Utilizing ischemic and nonischemic rhythmic handgrip in tandem with mild exercise, Victor et al. (55) found that muscle sympathetic nerve activity (MSNA) did not increase with nonischemic exercise while both HR and MAP did increase. In ischemic exercise,

MSNA did increase and remained elevated at the conclusion of exercise when the ischemia was maintained and the HR response had receded to baseline levels. This challenged the mass sympathetic discharge theory at exercise onset previously proposed. It was concluded that central command causes autonomic parasympathetic withdrawal allowing increases in HR and MAP during the early stages of exercise and that mass sympathetic discharge was mediated through metaboreceptor activation later in the exercise period when metabolites had had time to be produced and accumulated in the exercising muscle (55).

## Static Exercise

The most common models used in the research conducted to delineate the contribution of central command and the exercise pressor reflex in mediating effector activity during static exercise involves handgrip or involuntary exercise. These models of exercise are most often conducted using afferent blocking agents, e.g. curare, to eliminate contributions from the exercise pressor reflex or through electrically induced exercise which abolishes or at least diminishes the influence of central command. This research has produced several findings that support the current understanding of how central command and the exercise pressor reflex affect the autonomic nervous system during static exercise as well as cardiovascular and respiratory function.

It has been deduced that central command can increase sympathetic outflow to nonworking tissue beds during static exercise (54,56). However, the role of central

command in eliciting increased sympathetic nervous activity to active skeletal muscle is currently controversial (53,54,56). Vissing et al. (56) have suggested that neurophysiological evidence exists linking central command to a potent mass sympathetic outflow to the skin of nonworking muscle but attribute increases in muscle sympathetic activity (MSNA) in working muscle to afferent reflexes mediated through metaboreceptors. Other studies have implied that central command does not effect increases in MSNA until high levels of effort have been attained, e.g. 75% of maximal voluntary contraction (MVC) (53). Using curare to block exercise pressor reflex afferent activity, Victor and colleagues (54) found that central command caused an increase in MSNA as well as HR and MAP but that this could be blocked by atropine (acetylcholine receptor antagonist) but not by propranolol (β-receptor blocker). From this information, it was suggested that central command governs vagally mediated increases in MSNA and HR and plays a major role in regulation of parasympathetic activity. Contradicting the findings of Vissing, this study reported only a minor role of central command in the activation of sympathetic outflow to nonexercising tissue (54).

As was the case with dynamic exercise, evidence exists that central command mediates increases in HR and MAP during static exercise (3,12,13,14,54). Furthermore, it has been postulated that the blood pressure response depends upon the degree of effort and not the actual force produced by statically contracting muscle (25). In addition, Goodwin et al. (13,14) have reported isometric contraction at constant muscle tension increases HR, MAP, and ventilation in direct proportion to changes in the level of central

command effector activity. However, the integrative function of central command and the exercise pressor reflex is still controversial. Friedman et al. (12) measured cardiovascular responses during voluntary and nonvoluntary (electrically induced) one-leg static exercise and reported that HR, MAP, and cardiac output increased in both forms of exercise. These findings suggest that changes in HR, MAP, and cardiac output can be elicited without any contribution from central command since electrically induced static exercise dampens its contribution to effector activity (12). A similar study using voluntary and nonvoluntary (electrically induced) exercise under circulatory arrest to the exercising limb has found that HR and MAP could be significantly elevated by both exercise conditions. However, HR elevations dissipated at the conclusion of exercise even in the presence of circulatory arrest but blood pressure remained elevated. This supports the findings of Friedman in that central command may not be necessary for the initial increases in HR and MAP and the maintenance of blood pressure may be due to the trapping of chemical substances within the muscle interstitium (i.e. activation of metaboreceptors)(3).

## Exercise Pressor Reflex Studies in Human Subjects

### Dynamic Exercise

Dynamic incremental workload exercise is often used to assess reflex regulation of cardiovascular and respiratory function (7,8,34,60). Using this methodology it has been reported that mechanoreceptor activation can elicit an increase in HR (36) and MAP (60).

Additionally, stimulation of metaboreceptors has also been found to increase the HR response to exercise (7,41) as well as the MAP response (7,8,41). These findings have led to the evolution of an obvious question. Is one of these branches of the exercise pressor reflex more important in the regulation of HR and MAP during exercise or are they simply redundant systems which perform concurrently to evoke the desired reflex function? Nobrega and colleagues (36) found that when central command was eliminated, by having a subject cycle on a tandem bicycle while a staff member provided the power for vehicular movement, stimulation of mechanoreceptors by passive motion of a subject's legs resulted in similar HR responses to exercise as found when the subject cycled alone. This suggested that mechanoreceptors must have a functional role in HR regulation during dynamic exercise. In a second study utilizing graded muscle blood-flow restriction (accomplished by applying a supra-atmospheric pressure of 50 mmHg to the working legs during incremental load exercise) metaboreceptor function was isolated by trapping metabolites in the active skeletal muscle. Results indicated that metaboreceptor activation augmented HR and MAP responses from control conditions in which the blood flow was not restricted (7). It appears that metaboreceptors may also play a role in HR and MAP regulation during dynamic exercise.

Epidural anesthesia has been used to isolate the contribution of the exercise pressor reflex in essence by blocking its function as an afferent communicating system during dynamic exercise. Fernandez et al. (11) induced epidural anesthesia at lumbar segments 3 and 4 of the spinal column and had subjects cycle at 57% of their $\dot{V}O_{2MAX}$.

They found that the anesthesia had diminutive effects on MAP but did not change the ventilation and HR responses to exercise when compared to control conditions in which no intervention was present. It was concluded that afferent neural feedback was important for the control of MAP during dynamic exercise but not for ventilation and HR control. Supporting these findings, it has been reported by Strange and colleagues (51) that electrically induced exercise (effective elimination of central command input) results in normal or enhanced cardiovascular, metabolic, and ventilatory responses that can be abolished when electrically induced exercise and epidural anesthesia (elimination of afferent feedback from exercise pressor reflex) are incorporated simultaneously. Both of these studies conform to the idea that the exercise pressor reflex has some influence on the normal cardiovascular responses to dynamic exercise.

Another model that is often used to deduce exercise pressor reflex function is the utilization of lower body positive pressure (LBPP) during dynamic exercise (8,41,60). This mode of research has provided several indications of the true function of mechano- and metaboreceptors in reflex regulation. Incremental dynamic exercise on a cycle ergometer in the presence of 50 mmHg of LBPP has produced increases in MAP ,at any given workload, from responses seen when LBPP was not implemented (8). From these findings, it has been suggested that LBPP at 50 mmHg can reduce the driving pressure for blood flow in the vasculature sufficiently enough to activate metaboreceptors assumingly by the accumulation of metabolic end products in the working muscle. Support for these conclusions have been found in other research where varying levels of LBPP (25,35,45,

and 50-60 mmHg) have produced increases in MAP and HR that increase with the level of LBPP induced (41). From these results it has been postulated that the pressor response will tend to reduce local flow error (as that produced with LBPP) in working muscles (8). In terms of LBPP intervention, it has been proposed that small reductions in muscle perfusion will cause a greater rise in MAP than can be attributed to the mechanical effects of LBPP on MAP (41). In direct conflict with this philosophy are the findings of Williamson et al. (60). Using LBPP of 15, 30, and 45 mmHg it has been reported that LBPP does not alter $\dot{V}O_2$, HR, stroke volume (SV), or cardiac output responses to exercise but does evoke increases in MAP from baseline levels at rest. It was proposed that these changes in MAP induced by application of LBPP were representative of mechanoreceptor activation (by external compression of the lower extremities). Furthermore, these absolute changes in MAP elicited by varying levels of LBPP at rest remained throughout all stages of incremental workload dynamic exercise with the exception of the late stages of work during the 45mmHg LBPP condition where the blood pressure response was further augmented from the control exercise condition (no LBPP implementation). This late increase in MAP was attributed to metaboreceptor reflex activation. In the opinion of the experimenters, this puts into question whether the muscle metaboreceptor reflex is a primary stimulus for blood pressure control under normal physiological conditions since it required 45 mmHg of LBPP to elicit such a response (60). In a follow up investigation, Williamson et al. (61) increased continual pressure on

the lower limbs of humans to 30, 60, and 90 mmHg with and without epidural anesthesia under resting conditions. In the presence of anesthesia, the subsequent increase in MAP produced during the control condition (pressure without anesthesia) was eliminated further confirming that mechanoreceptor activation may mediate the MAP response. Utilizing a derivation of the aforementioned LBPP technique, Joyner (19) applied positive pressure of 10, 20, 30, 40, and 50 mmHg during rhythmic forearm contractions to the forearm enclosed in a Plexiglas box. It was found that blood flow was reduced to the exercising forearm and MAP elevated during moderate and heavy exercise beginning at positive pressure levels of 10 to 20 mmHg. Joyner concluded that an increase in sympathetic outflow mediated by metaboreceptor afferent activity constricts resistance vessels in contracting muscles sufficiently to prevent the elevated MAP and local vasodilating metabolites from restoring blood flow to the working muscles. This would seem to be in conflict with the hypothesis proposed by Williamson and colleagues (60, 61), however, Joyner (19) concedes that this systemic pressor response may also include contributions from sympathoexcitatory mechanoreceptor afferents activated in the forearm muscles by the rhythmic contractions.

## Static Exercise

As eluded to earlier in this review, it has been established that central command and the exercise pressor reflex set a basic pattern of sympathoadrenal activity that, in exercise, is relative to workload (6,24,29,42). In turn, this autonomic nervous system

(ANS) activity is of major significance for cardiovascular, hormonal, and metabolic responses to exercise (6). As a result, much research has been conducted to elucidate the integrative function of central command and the exercise pressor reflex in influencing the sympathetic and parasympathetic branches of the ANS during static exercise. It has been reported that when skeletal muscle metaboreceptors are impaired (as has been found to be the case in some forms of heart failure) muscle sympathetic nerve activity (MSNA) responses to static exercise are still intact leading to the conclusion that other mechanisms must be important in increasing MSNA under these conditions (50). Using microneurography to record foot volar skin sympathetic activity and leg skeletal muscle MSNA during isometric handgrip exercise, Saito et al. (44) found that sympathetic outflow to nonworking muscle and tissue may be mediated by central command and mechanoreceptors but not by metaboreceptors. In contrast to these findings, other studies have attributed an increase in MSNA to nonworking tissues during static exercise exclusively to metaboreceptor activation (26,39) and in fact Ray et al. (39) have proposed that mechanosensitive muscle afferents can attenuate the metaboreceptor mediated increase in MSNA.

These studies have only complicated the global picture of autonomic nervous system activity during static exercise that regulates cardiovascular and respiratory responses. It is apparent that the model of experimentation used and the method of analysis employed influences the interpretation of the true function of the ANS during static exercise. Iwamoto et al. (17), have presented a possible explanation to such findings.

This group has proposed that processes in active muscles elicit an increase in HR and MAP during static exercise that is directly related to the intensity of muscle contraction developed. However, the immediate cardiovascular responses at the onset of static exercise must be attributed to some other effector system (i.e. central command). Mitchell et al. (31) , by utilizing epidural anesthesia to block afferent feedback, have reported that central command does not determine the cardiovascular response to static exercise. However, Mitchell concedes that this is in direct conflict with his and Leonard's (23) previous findings in which the use of partial neuromuscular blockade delineated the importance of central command in determining the cardiovascular response to exercise. As a result, a new theory of autonomic function during static exercise has been proposed introducing the concept that both central and reflex neural mechanisms play a role in regulation MAP and HR during static exercise and as such the systems may be viewed as redundant (e.g. if one system is absent the other can sufficiently compensate to elicit a normal cardiovascular response to exercise) (23,31). However, further research has amended this theory by suggesting that greater redundancy may be present in regulating MAP during static exercise than in the vagal control of HR associated with central command (30).

Accepting this current philosophy of physiological redundancy in central command and exercise pressor reflex function still does not diminish the importance of elucidating which skeletal muscle receptor system (mechanoreceptor or metaboreceptor) is more important in regulating the normal cardiovascular response to exercise. Recent research in

which subjects were fitted with anti-shock trouser garments and subjected to three levels of pressure (30, 60, and 90 mmHg) during resting conditions has provided further insight as to the role of mechanoreceptors in cardiovascular regulation. In this study it was assumed that applying pressure and blocking translocation of fluids by inflating upper thigh cuffs to 300 mmHg would only stimulate mechanoreceptors as metabolites would not build up in the compressed skeletal muscle of the legs due to the lack of exercise. It was found that pressure application increased MAP with no changes in HR, cardiac output, thoracic impedance, or central venous pressure developing. This MAP response was abolished when afferent feedback was blocked by the utilization of epidural anesthesia. It was concluded that mechanoreceptors may act independently of muscle metaboreceptors and that the magnitude of the mechanoreceptor response is related to the increase in intramuscular pressure and to the muscle mass to which pressure is applied (61). In support of these findings, McClain et al. (27), reported that MSNA and MAP are elevated from control conditions when forearm compression of 110 mmHg is applied during isometric handgrip static exercise (40% MVC). These researchers concluded that the responses could not be due to greater metaboreceptor stimulation since posthandgrip circulatory arrest (effective trapping of metabolic end products at conclusion of exercise) responses were unaffected by forearm compression. It was therefore postulated that forearm compression activates mechano-sensitive ergoreceptors leading to greater sympathoexcitation during exercise.

In summary, the current literature seems to indicate that sympathetic and parasympathetic autonomic nervous system activity to effector cardiovascular and respiratory systems during both dynamic and static exercise is mediated by a redundant system incorporating both central command and the exercise pressor reflex. It has been shown in many models of experimentation that isolating either the central command or the exercise pressor reflex contribution to exercise elicits normal HR, MAP, and $\dot{V}O_2$ responses. However, the individual influence of mechano- and metaboreceptors to the exercise pressor reflex modulating system has not been definitively delineated. Hopefully, the current research posed by this investigation will define more accurately the role of ergoreceptors in the regulation of cardiovascular , specifically MAP, and respiratory function during dynamic exercise.

# CHAPTER III

# PROCEDURES AND METHODS

It was the goal of this investigation to determine the interaction of central command and the exercise pressor reflex on the blood pressure response to dynamic exercise by stimulating muscle ergoreceptors. In order to gain admittance into the study all subjects were required to perform a baseline graded exercise test (GXT) as part of their initial screening process. Upon admittance, all subjects were asked to perform four GXTs to maximum: (i) control-exercise with no intervention; (ii) exercise with thigh cuff inflation to 90 mmHg; (iii) exercise with application of lower body positive pressure (LBPP) to 45 mmHg; (iv) exercise with combined thigh cuff inflation and LBPP. The control GXT was compared to the three experimental GXTs to determine the effects of ergoreceptor stimulation on exercise performance and blood pressure response to dynamic exercise. This section examines the experimental protocol that was executed in acquiring and analyzing the data obtained during this investigation.

## Experimental Design and Data Analysis

The matrix of this experiment required a 4 x 10 two-factor ANOVA format with repeated measures taken across workload (Table I). Each subject performed a GXT

under the four experimental conditions and measurements were averaged over the following work rates: 0 watts (rest), 25 watts, 50 watts, 75 watts, 100 watts, 125 watts, 150 watts, 175 watts, 200 watts, and maximum watts (peak workload-PW). This experimental strategy allowed for comparison of changes in exercise performance and blood pressure response between groups during the different experimental conditions. The dependent variables that were measured in order to elucidate the effect of ergoreceptor stimulation and test the hypothesis were mean arterial pressure (MAP) and PW for each exercise condition.

TABLE I. EXERCISE TESTING DESIGN

| 4X10 TWO-FACTOR ANOVA MATRIX | | | | |
|---|---|---|---|---|
| **Peak** | $RPE_{B\&L}$, $\dot{Q}_c$ | $RPE_{B\&L}$, $\dot{Q}_c$ | $RPE_{B\&L}$, $\dot{Q}_c$ | $RPE_{B\&L}$, $\dot{Q}_c$ |
| **200 Watts** | $RPE_{B\&L}$ | $RPE_{B\&L}$ | $RPE_{B\&L}$ | $RPE_{B\&L}$ |
| **175 Watts** | | | | |
| **150 Watts** | $RPE_{B\&L}$, $\dot{Q}_c$ | $RPE_{B\&L}$, $\dot{Q}_c$ | $RPE_{B\&L}$, $\dot{Q}_c$ | $RPE_{B\&L}$, $\dot{Q}_c$ |
| **125 Watts** | | | | |
| **100 Watts** | $RPE_{B\&L}$ | $RPE_{B\&L}$ | $RPE_{B\&L}$ | $RPE_{B\&L}$ |
| **75 Watts** | $\dot{Q}_c$ | $\dot{Q}_c$ | $\dot{Q}_c$ | $\dot{Q}_c$ |
| **50 Watts** | $RPE_{B\&L}$ | $RPE_{B\&L}$ | $RPE_{B\&L}$ | $RPE_{B\&L}$ |
| **25 Watts** | | | | |
| **Rest** | $\dot{Q}_c$ | $\dot{Q}_c$ | $\dot{Q}_c$ | $\dot{Q}_c$ |
| | **Control** | **Cuffs** | **LBPP** | **Cuffs + LBPP** |

MAP, HR, $VO_2$, and EMG were taken at rest and at each workload including peak workload. RPE for both the body and legs ($RPE_{B\&L}$) were assessed at 50W, 100W, 150W, 200W, and peak workload. $\dot{Q}_c$ was taken at rest, 75W, 150W, and peak workload.

Other variables were measured in order to define differences between exercise conditions and substantiate MAP and PW findings. These variables included heart rate (HR), electromyographic activity (EMG), ratings of perceived exertion for both the legs ($RPE_L$) and the body ($RPE_B$), cardiac output ($\dot{Q}_c$), and rate of oxygen uptake ($\dot{V}O_2$).

Measurements of MAP, HR, and $\dot{V}O_2$ were monitored continuously throughout each exercise trial with the mean calculated at rest and during each workload for comparison between exercise conditions within workload levels. EMG was taken at rest and during each workload for ten seconds (between time 10-20 seconds of the particular workload stage) and the mean taken for comparison between exercise conditions. RPE was assessed every 50 watts beginning with 50 watts and continuing through the end of the exercise protocol. Cardiac output was obtained at rest, and at every 75 watts thereafter (beginning with 75 watts). At the conclusion of each exercise trial PW was recorded for each subject. Figure I exhibits the experimental strategy and time course for taking these various measurements. Differences between the control and the various exercise conditions were assessed using an analysis of variance (ANOVA) with a repeated measures design. Data was presented as exercise condition means plus or minus any standard error of the mean (SEM). Differences in dependent variables within and between exercise conditions were accepted as significant at $p<0.05$.

**FIGURE I.- EXPERIMENTAL DESIGN**

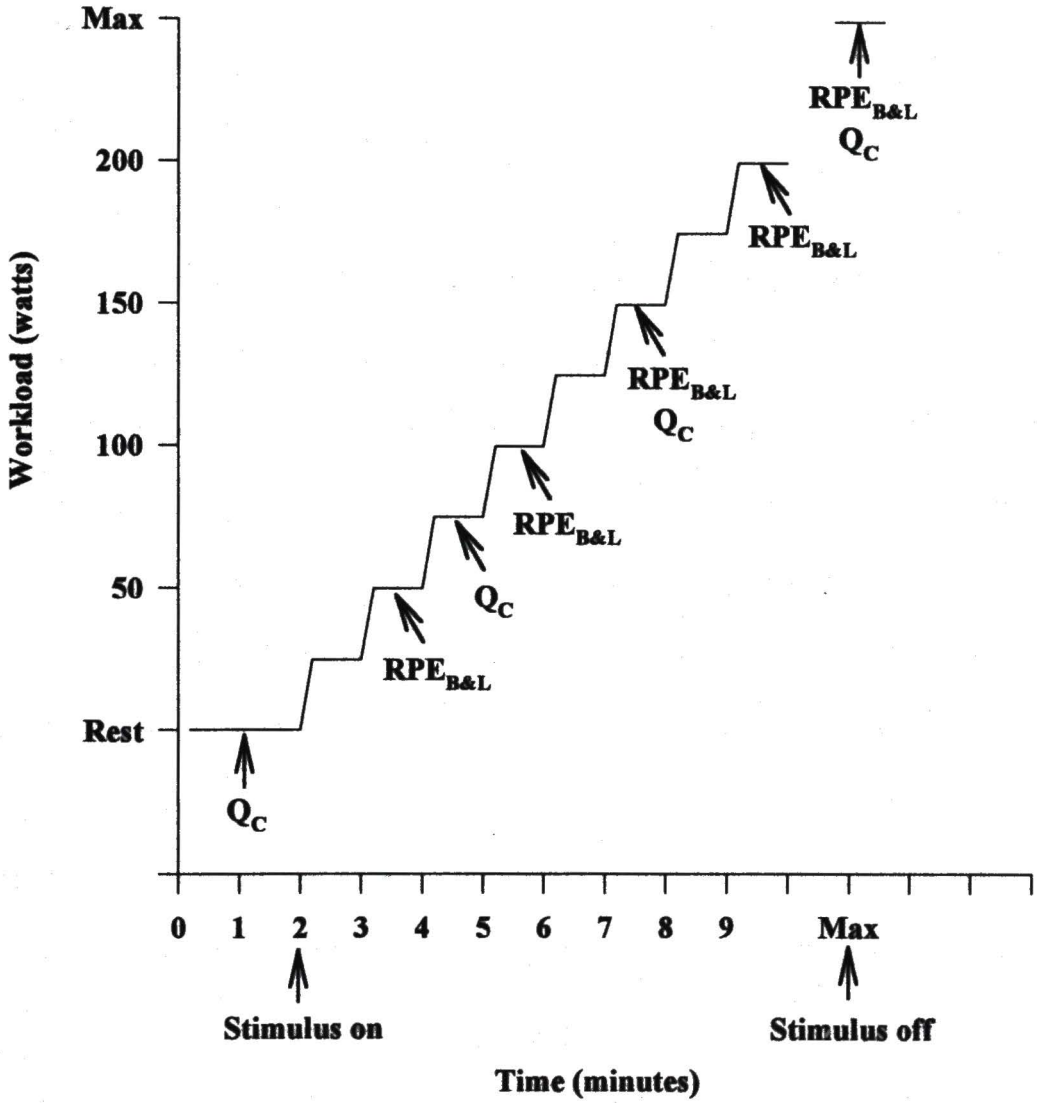


Figure I.- The experimental protocol included measurements of cardiac output and rating of perceived exertion at the time intervals shown. Additionally, MAP, HR, EMG, and $VO_2$ were measured at rest, at each workload, and at maximum workload.

## Subjects

Subjects were screened prior to admittance into this investigation following guidelines established by the American College of Sports Medicine. Any potential subject that did not meet these requirements were excluded from the study. Subjects were advised of the goals of the study, its protocol, and any negative side effects that could occur as a result of their participation. They were required to sign an informed consent before participation in any testing approved by the Institutional Review Board for the Use of Human Subjects at the University of North Texas Health Science Center. The criterion for selection was based on the subjects initial GXT performance and medical history-diet questionnaire. Four women and six men volunteers between the ages of 18 and 35 years from the general Fort Worth area were recruited. A preliminary power test for determining sample size, n, predicted that this was sufficient for the needs of the research proposed. Subjects were accepted if they could complete a minimum of 200 watt (W) workload cycle dynamic exercise, had normal heart rhythms at rest and during exercise, were asymptomatic for disease, and were non-smokers. Subjects were asked to abstain from caffeinated beverages and medications on the day they were scheduled for testing as well as from physical activity and alcohol the eve before testing. Upon acceptance into the investigation, the subjects were asked to complete four GXTs under various conditions on two separate days. Anthropometric and physiological descriptions of the subject groups initial GXT screen testing is presented in Table II.

TABLE II
DESCRIPTIVE STATISTICS FOR SUBJECT GROUP

| **Age** (Yrs.) | **Height** (cm) | **Weight** (kg) | **$HR_{MAX}$** (beats•min$^{-1}$) | **$\dot{V}O_{2MAX}$** (ml•kg$^{-1}$•min$^{-1}$) | **$WL_{MAX}$** (watts) |
|---|---|---|---|---|---|
| 26.5±1.3 | 173.7±3.2 | 73.5±4.2 | 174.9±2.3 | 40.3±13.4 | 365.0±30.0 |

Mean ± SEM. Data obtained during initial screening GXT testing.

Graded Exercise Testing Protocol

The subjects were seated in a semi-recumbent (70° back supported) position in the lower body positive pressure (LBPP) chamber which was equipped with a computerized, electronically-braked cycle ergometer (Intellifit, Inc., Houston, TX). Before the GXT tests began, data collection was taken for two minutes to quantify baseline levels of the variables being tested. Once exercise began, the workload increased every minute by 25 watts until the subject could no longer maintain a 60 r.p.m. cadence or reached volitional fatigue. The subjects were encouraged verbally to complete each stage until unable to do so and cardiovascular data and subject appearance were monitored to qualitatively determine a maximal effort. PW was determined as the highest workload level achieved before pedal cadence could no longer be maintained by the subject during each test. Cadence was verified by a visual speedometer displayed on the computer monitor of the exercise chamber. Upon termination of exercise, data was collected for an additional five minutes of the recovery period but was not used in the analysis of this experiment.

Ergoreceptor Stimulation Protocol

On the day of testing, the subjects height and weight was taken prior to instrumentation and the subject familiarized with the testing protocol. One EMG recording electrode and one reference electrode was placed on the belly of the *m. rectus femoris* of the right leg with a ground electrode placed on a bone of the knee. A five-lead electrocardiogram was positioned on the upper body of the subject in order to monitor HR. Finally, a plethysmographic blood pressure cuff (Finapress, model 2300, Omheda, Inc.) was placed on the second finger of the left hand in order to monitor MAP. After instrumentation was complete the subject rested for one hour in a supine position in order to allow baseline levels of all variables to be reached. At this time, a mouthpiece attached to a saliva trap and turbine volume transducer was placed in the subjects oral cavity for the collection of $\dot{V}O_2$ data. The subject completed two of four exercise conditions on each day of testing with a minimum one hour resting period between each trial to allow the return to baseline levels of all examined variables. On each test day the subject was allowed to have one glass of water at the completion of the first GXT. The GXTs to be executed on each day of testing were assigned randomly in order to eliminate any learned adaptations to the exercise protocol.

The subjects completed four different exercise tests. The control condition (Con) simply consisted of a GXT with no additional stimulus. In the second GXT procedure (Cuffs) pressure cuffs were placed on the upper thigh of both the right and left legs. After

two minutes of rest, the subject was instructed to begin exercising and the cuffs were inflated to 90 mmHg and remained as such until the completion of the exercise trial. The third testing procedure (LBPP) consisted of the application of LBPP to 45 mmHg after two minutes of rest.. The subjects lower body was sealed at the iliac crest in the air-tight wooden box in which the cycle ergometer was housed. The LBPP continued to be applied until the termination of exercise. The final testing condition (C/L) consisted of the application of LBPP to 45mmHg and inflation of the thigh cuffs to 90 mmHg after a two minute resting period and until completion of the exercise protocol. A five minute recovery period succeeded each testing trial.

A resting period of two minutes preceded the beginning of all GXTs in which baseline data of all variables were collected. After exercise had been initiated, HR, $\dot{V}O_2$, and MAP were monitored continuously, EMG was taken for 10 seconds every workload increase, RPE for both the body and the legs was assessed every 50 watt increase, and $\dot{Q}_c$ was taken every 75 watt increase.

## Physiological Measurements

### Metabolic Measurements During Exercise

In order to assess oxygen uptake ($\dot{V}O_2$) during each exercise test, the subject was required to breathe through a ventilation recording apparatus. This apparatus consisted of

a mouthpiece attached to a saliva trap and a turbine volume transducer. The saliva trap was equipped with a sampling port which allowed the collection of respired oxygen ($O_2$) and carbon dioxide ($CO_2$) partial pressures ($PO_2$ and $PCO_2$) which were then analyzed by a mass spectrometer (Perkin-Elmer MGA-1100A). The subject was also required to wear a noseclip in order to prevent respiration through their nasal passages. Before the utilization of this equipment during each test the mass spectrometer was calibrated with known gas concentrations of $CO_2$, $O_2$, and nitrogen ($N_2$). A turbine transducer was utilized to measure the expired and inspired air flow which transmitted this information via a voltage output to the ventilation measurement module (VMM; Alpha Technologies, Inc.).The signals were analyzed using analog-to-digital conversion using a laboratory computer (Dell Computers) equipped with a customized $\dot{V}O_2$ program (Dufis) for on-line, breath-by-breath computation of $\dot{V}O_2$, carbon dioxide output ($\dot{V}CO_2$), respiratory exchange ratio (R), and minute ventilation ($\dot{V}_E$).

## Cardiovascular Measurements

Mean arterial pressure (MAP) was non-invasively measured on a continuous basis by indirect photoplethysmographic method (Finapres, Ohmeda Inc.). A small finger pressure cuff was placed on the second finger of the left hand with the hand supported at the horizontal level of the heart in order to eliminate any hydrostatic effects on blood pressure readings. Using a light source and photoelectric cell placed in the lining of an

inflatable digit cuff, this plethysmographic system measured instantaneous changes in digit volume which was directly related to the changes in vascular volume afforded by arterial pulse wave pressure. The pressure cuff was interfaced with a pressure monitor and continuously recorded MAP on a computer (Gateway 2000) equipped with a customized cardiovascular assessment program. HR was continuously monitored using a 5-lead electrocardiogram interfaced with a pressure monitor (Hewlett-Packard 78342A) and was also recorded on the Gateway 2000 computer with customized cardiovascular assessment program (CVMON3). Previous research in our laboratory has proven that this non-invasive measure of MAP is a reliable substitute for arterial lines as a means of obtaining blood pressure data. When we compared arterial pressures measured non-invasively with the Finapres with invasive radial artery cannula during progressive exercise to maximum, we found that the correlations between the change in Finapres pressures and the change in radial artery pressures were $r = 0.93$, 0.89 and 0.95 for systolic, diastolic, and mean pressures, respectively. In addition, a t-test statistical comparison was made between averaged pressures at rest, 100 watts, 200 watts, and 300 watts between the Finapres and radial artery pressures and no significant differences in systolic, diastolic, and mean arterial pressures were found at any level of exercise.

## Electromyographic Activity Measurements

EMG activity was recorded noninvasively by placing a reading surface electrode and a reference surface electrode on the belly of the *m.rectus femoris* of the right leg with

a ground electrode placed on a bone of the right knee. The electrical activity conducted through the active motor units of the skeletal muscle was sensed by the electrodes and transmitted to a monitoring computer system (Mespec 4001 EMG system, Kuopio, Finland). The computer was equipped with an EMG recording program which fully rectified and integrated the signal emitted by the muscle.

## Measurement of Cardiac Output

Cardiac output ($\dot{Q}_c$) was determined during rest and dynamic cycle exercise by using a non-invasive acetylene rebreathing technique (52). Acetylene gas uptake from the alveoli is proportional to pulmonary capillary blood flow and therefore can be used to accurately estimate $\dot{Q}_c$. Concentrations of acetylene, carbon dioxide, and oxygen were analyzed using a mass spectrometer (Peking-Elmer MGA-1100A) with a sample flow rate of 60 ml min. During experimental collection of $\dot{Q}_c$ , a nose-clip was utilized to prevent the subject from inhalation through the nasal passages. A rebreathing apparatus equipped with a mouthpiece, turbine flowmeter, and rebreathing bag was placed in the subjects mouth. A customized cardiac output analysis program (Dufis) triggered the release of acetylene into the rebreathing bag at the subjects end exhalation. The subject was instructed to take a deep inhalation once the bag had been filled with acetylene and rebreathe into the bag for a minimum of five breaths. The computer program then recorded the mixed expiratory

fractions from the mass spectrometer of acetylene, carbon dioxide, and oxygen during the rebreathing period as well as the flow rate in order to elucidate the final cardiac output reading.

## Measurement of Perceived Exertion

Rating of perceived exertion (1) was measured using the Borg scale which began with a numerical grade of 6 (very, very light work) and continued to a numerical grade of 20 (very, very hard work).This scale has been validated against HR and is used as a cognitive assessment of the perception of workload. The subject was asked to identify their level of work by responding to a technician holding a chart with the ratings displayed. The technician called out the numbers on the chart and the subject was asked to respond by nodding his/her head. The subjects perception of the level of work done by their legs and their body were assessed using this technique.

# CHAPTER IV

# RESULTS

Chapter IV introduces the results obtained during this investigation. The presentation of the data includes the mean values of the group in each of the four experimental conditions as well as the standard error of the mean (± SEM) associated with each value. Comparisons were made within the group between each exercise protocol executed during this experiment. The analysis concentrated on delineating the cardiovascular adaptations that may occur during dynamic exercise for any given stimuli. Special emphasis was given to those cardiovascular variables associated with the contribution of "central command" and the "exercise pressor reflex" in controlling or regulating the blood pressure response to the exercise.

## Descriptive Characteristics of Subject Group

Physical characteristics of the subject group as well as the results from the initial graded exercise test to maximum (GXT) which includes the maximum heart rate ($HR_{MAX}$), maximum rate of oxygen uptake ($\dot{V}O_{2MAX}$), and maximum workload ($WL_{MAX}$) are

presented in Table II of Chapter III, p.32. The mean age and $\dot{V}O_{2MAX}$, which is a traditionally used parameter to evaluate individual fitness, adhered to the guidelines set forth in the design of this study. All subjects were able to successfully execute the initial exercise protocol past the minimum of 200 watts (W) which had been set as an essential criterion for inclusion in the study.

The mean peak workloads (PW) ± SEM attained by the subject group during each of the exercise trials is presented in Table III. Although no significant difference was found between exercise conditions for PW at the set significance level of $p<0.05$, there was a strong trend for a decrease in PW from control attained in each of the exercise conditions that involved some form of stimulus. This finding was most pronounced in the cuffs + lower body positive pressure (LBPP) condition in which a p value of 0.07 was produced. This trend for a decrease in PW when stimuli were implemented during the exercise trials suggests that LBPP, inflation of thigh cuffs, and utilization of both LBPP and thigh cuff inflation may decrease exercise tolerance to these stresses. The tests were terminated when the subject could not maintain pedal cadence or requested the session end. Most subjects reported leg fatigue as the primary reason for cessation of exercise rather than cardiorespiratory limitations.

TABLE III. PEAK WORKLOADS (MEAN ± SEM) ACHIEVED DURING VARIOUS EXERCISE CONDITIONS

| Control | Cuffs | LBPP | Cuffs + LBPP |
|---|---|---|---|
| **$Workload_{PEAK}$ (watts)** | **$Workload_{PEAK}$ (watts)** | **$Workload_{PEAK}$ (watts)** | **$Workload_{PEAK}$ (watts)** |
| 352.5±32.0 | 287.5±31.5* | 277.5±22.0† | 252.5±26.8‡ |

*Indicates p=0.10 for cuffs vs. control. †Indicates p=0.09 for LBPP vs. control. ‡Indicates p=0.07 for cuffs + LBPP vs. control.

Indices of Central Command

Table IV presents the mean data ± standard error of the mean elucidated during each exercise condition for the variables associated with central command's influence on effector systems during dynamic exercise. The variables which can be taken as indices of central command during the testing trials consisted of HR, electromyographic activity (EMG), $\dot{V}O_2$, and rating of perceived exertion of the body ($RPE_B$).

After conclusion of a minimum of one hour of rest in the supine position (after instrumentation or between exercise trials on a given day), measurements of HR, EMG activity, and $\dot{V}O_2$ were evaluated at rest and subsequently taken continually throughout the incremental stages of exercise. These values were then averaged over the one minute at each stage of workload until the trial concluded. During the incremental exercise, the application of LBPP to +45 mmHg and the inflation of thigh cuffs to +90 mmHg or the combination of both stimuli did not significantly alter the response of HR (Figure II, p.43), EMG activity (Figure III, p.44), or $\dot{V}O_2$ (Figure IV, p.45) from control during the

TABLE IV. INDICES OF CENTRAL COMMAND

| | | Rest | 25W | 50W | 75W | 100W | 125W | 150W | 175W | 200W | Peak |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **HR** (beats•min$^{-1}$) | **Con** | 63.8 ±2.6 | 78.3 ±2.7 | 82.8 ±3.1 | 88.9 ±3.7 | 96.1 ±3.7 | 103.0 ±5.1 | 108.6 ±5.4 | 116.7 ±6.3 | 125.3 ±7.2 | 167.8 ±4.3 |
| | **Cuff** | 67.4 ±2.8 | 85.1 ±2.9 | 89.4 ±3.7 | 95.1 ±3.9 | 102.6 ±4.3 | 109.5 ±5.2 | 116.6 ±6.3 | 124.2 ±7.1 | 132.6 ±8.1 | 155.0 ±6.7 |
| | **LBPP** | 66.1 ±3.0 | 87.3 ±3.8 | 92.3 ±3.6 | 97.4 ±4.0 | 104.0 ±4.7 | 110.5 ±5.3 | 115.7 ±5.5 | 124.8 ±6.4 | 132.7 ±6.8 | 152.3 ±4.6 |
| | **C/L** | 59.0 ±3.4 | 80.7 ±4.3 | 84.8 ±3.0 | 91.2 ±2.9 | 98.8 ±3.8 | 105.6 ±5.2 | 113.8 ±5.9 | 122.6 ±6.6 | 130.3 ±7.4 | 147.4 ±6.5 |
| **EMG** (µvolts) | **Con** | 8.7 ±0.6 | 27.3 ±2.6 | 35.4 ±3.9 | 44.8 ±5.3 | 49.1 ±5.7 | 52.5 ±5.2 | 61.9 ±5.7 | 72.7 ±5.5 | 76.6 ±6.4 | 112.9 ±2.8 |
| | **Cuff** | 10.2 ±1.2 | 41.0 ±7.5 | 46.4 ±7.1 | 50.5 ±7.5 | 55.4 ±8.1 | 62.5 ±8.2 | 65.2 ±9.2 | 72.0 ±11.3 | 77.0 ±12.0 | 89.6 ±10.7 |
| | **LBPP** | 8.6 ±1.0 | 38.2 ±4.4 | 43.2 ±4.4 | 51.8 ±4.4 | 58.3 ±3.4 | 63.9 ±4.8 | 74.5 ±5.9 | 85.3 ±6.3 | 88.0 ±5.5 | 99.9 ±8.9 |
| | **C/L** | 6.8 ±0.6 | 33.3 ±3.0 | 35.5 ±3.2 | 37.9 ±4.2 | 43.1 ±4.3 | 50.2 ±5.3 | 58.9 ±6.6 | 67.2 ±8.3 | 74.5 ±9.3 | 96.9 ±8.0 |
| **$\dot{V}O_2$** (ml•kg$^{-1}$•min$^{-1}$) | **Con** | 5.5 ±0.3 | 10.6 ±0.5 | 11.5 ±0.6 | 14.0 ±0.7 | 15.9 ±1.0 | 17.8 ±1.2 | 19.9 ±1.0 | 21.5 ±1.6 | 23.7 ±1.8 | 43.6 ±4.9 |
| | **Cuff** | 5.6 ±0.2 | 10.0 ±0.8 | 11.0 ±0.6 | 13.7 ±1.2 | 14.9 ±1.2 | 16.2 ±1.7 | 18.8 ±1.9 | 19.9 ±1.4 | 21.7 ±1.8 | 33.6 ±2.5* |
| | **LBPP** | 5.6 ±0.3 | 12.0 ±0.6 | 12.6 ±0.7 | 15.0 ±0.5 | 16.4 ±1.0 | 18.9 ±1.3 | 21.3 ±1.4 | 22.0 ±1.6 | 24.6 ±1.7 | 32.3 ±2.1* |
| | **C/L** | 5.8 ±0.3 | 11.1 ±0.4 | 12.4 ±0.6 | 15.2 ±0.8 | 16.3 ±0.7 | 17.5 ±0.8 | 19.5 ±0.9 | 21.2 ±1.3 | 22.6 ±1.4 | 30.1 ±2.9* |
| **$RPE_B$** (units) | **Con** | ------- | ------- | 7.2 ±0.4 | ------- | 8.8 ±0.4 | ------- | 11.2 ±0.7 | ------- | 13.3 ±0.9 | 16.8 ±0.8 |
| | **Cuff** | ------- | ------- | 7.6 ±0.2 | ------- | 9.7 ±0.4 | ------- | 11.9 ±0.5 | ------- | 13.7 ±0.4 | 15.1 ±0.8 |
| | **LBPP** | ------- | ------- | 8.6 ±0.4* | ------- | 10.3 ±0.3* | ------- | 12.6 ±0.6 | ------- | 14.2 ±0.7 | 16.3 ±0.6 |
| | **C/L** | ------- | ------- | 8.1 ±0.3* | ------- | 10.4 ±0.6* | ------- | 13.1 ±0.6 | ------- | 14.2 ±0.6 | 16.1 ±0.6 |

Mean ± SEM. *Indicates significance from control condition.

**FIGURE II.- HEART RATE RESPONSES TO EXERCISE**

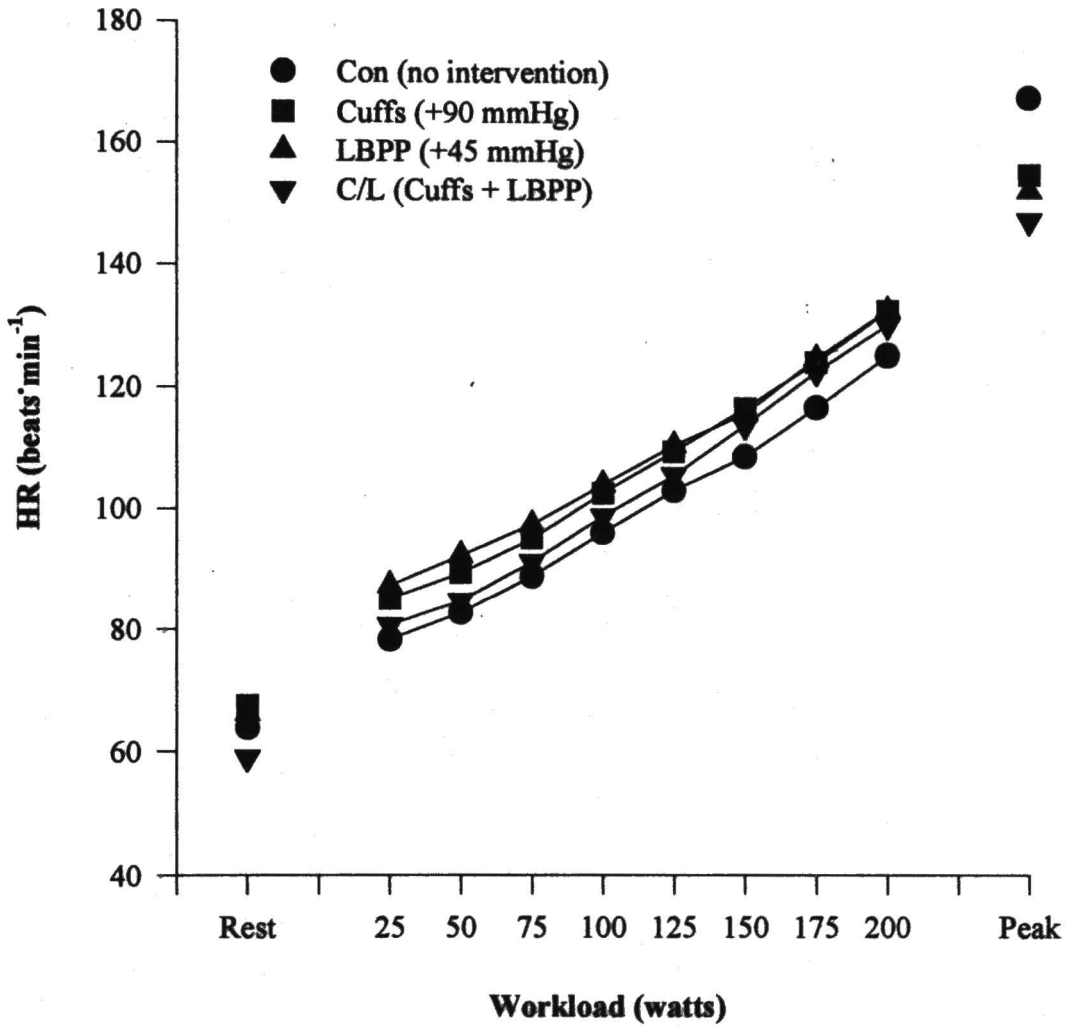


Figure II.- Mean HR data obtained from four exercise conditions. No significant difference was found in HR between the various types of exercise. Standard errors for HR data are presented in Table IV.

**FIGURE III.- ELECTROMYOGRAPHIC ACTIVITY IN RESPONSE TO EXERCISE**

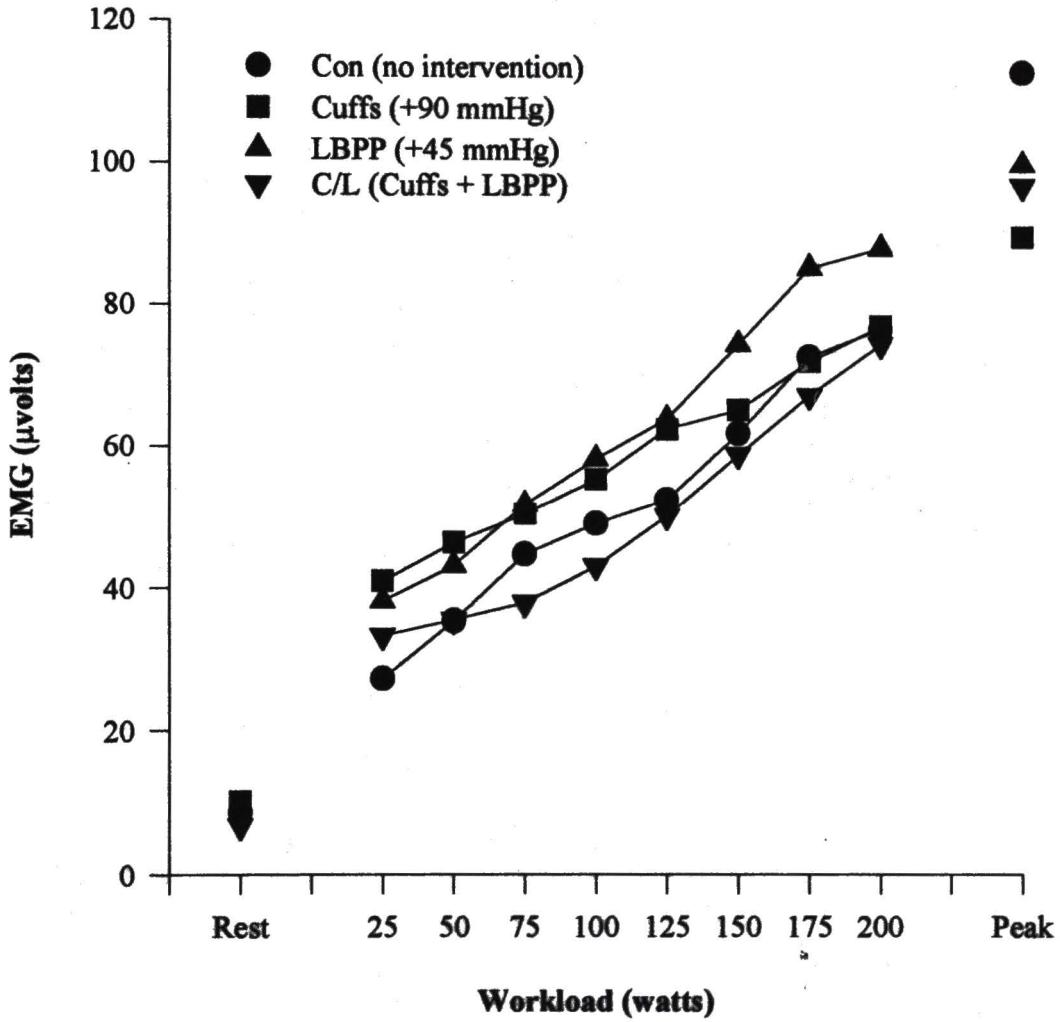


Figure III.- Mean EMG data obtained from four exercise conditions. No significant difference was found in EMG activity between the various exercise types. Standard errors for EMG data are presented in Table IV.

**FIGURE IV.- MEASURES OF THE RATE OF OXYGEN UPTAKE DURING EXERCISE**

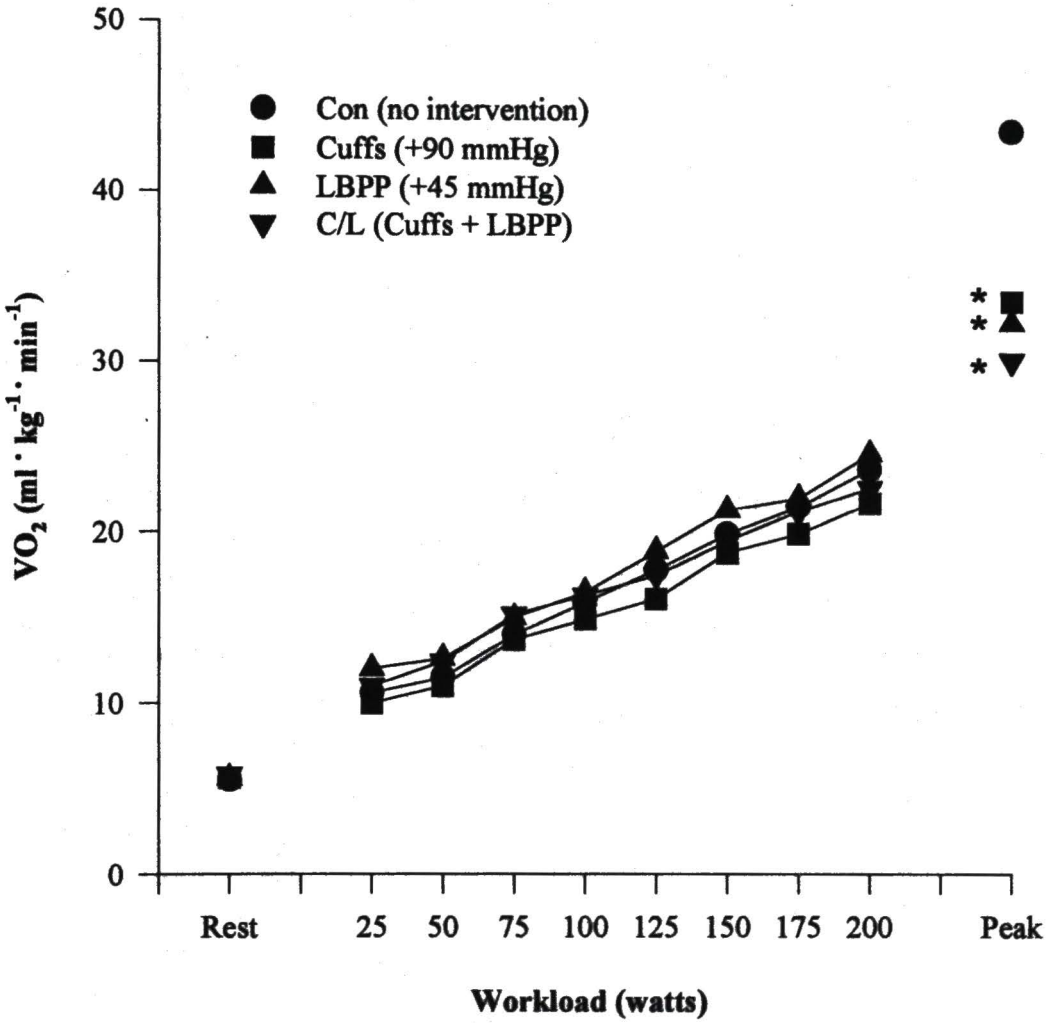


Figure IV.- Mean $VO_2$ data obtained from four exercise conditions. * Indicates significant differences from the control condition at a level of $p<0.05$. Standard errors for $VO_2$ data are presented in Table IV.

exercise to 200 W. However, at PW employment of LBPP, inflation of the thigh cuffs, and the combination thereof significantly reduced the $\dot{V}O_{2PEAK}$ from control (Figure IV). It is interesting to note that the greatest value gathered for all three variables presented here was during the control condition at PW when stimuli intervention was absent during the experimental trial. However, the value obtained during control PW was not significantly increased in HR and EMG measures.

The rating of perceived exertion for the whole body effort ($RPE_B$, Figure V) was assessed at 50W, 100W, 150W, 200W, and PW for each of the incremental exercise maneuvers. The $RPE_B$ reported by the subjects was significantly increased with the utilization of LBPP and the use of LBPP in conjunction with the thigh cuff inflation during the early stages of the exercise protocol at 50W and 100W (Figure V). The elevated $RPE_B$ found in these early stages dissipated as the work continued to increase so that at 150W, 200W, and PW were not found to be significantly different from control. Furthermore, although not significantly higher, the greatest value obtained for $RPE_B$ was found during the control condition at PW.

## Determinants of Exercise Pressor Reflex Activation

An average of the subjects mean arterial pressure (MAP) and rating of perceived exertion of the legs ($RPE_L$) responses to the four exercise conditions undertaken in this experimental exercise as well as the associated SEM's are found in Table V, p.48. MAP

**FIGURE V.- RATING OF PERCEIVED EXERTION FOR THE BODY DURING EXERCISE**

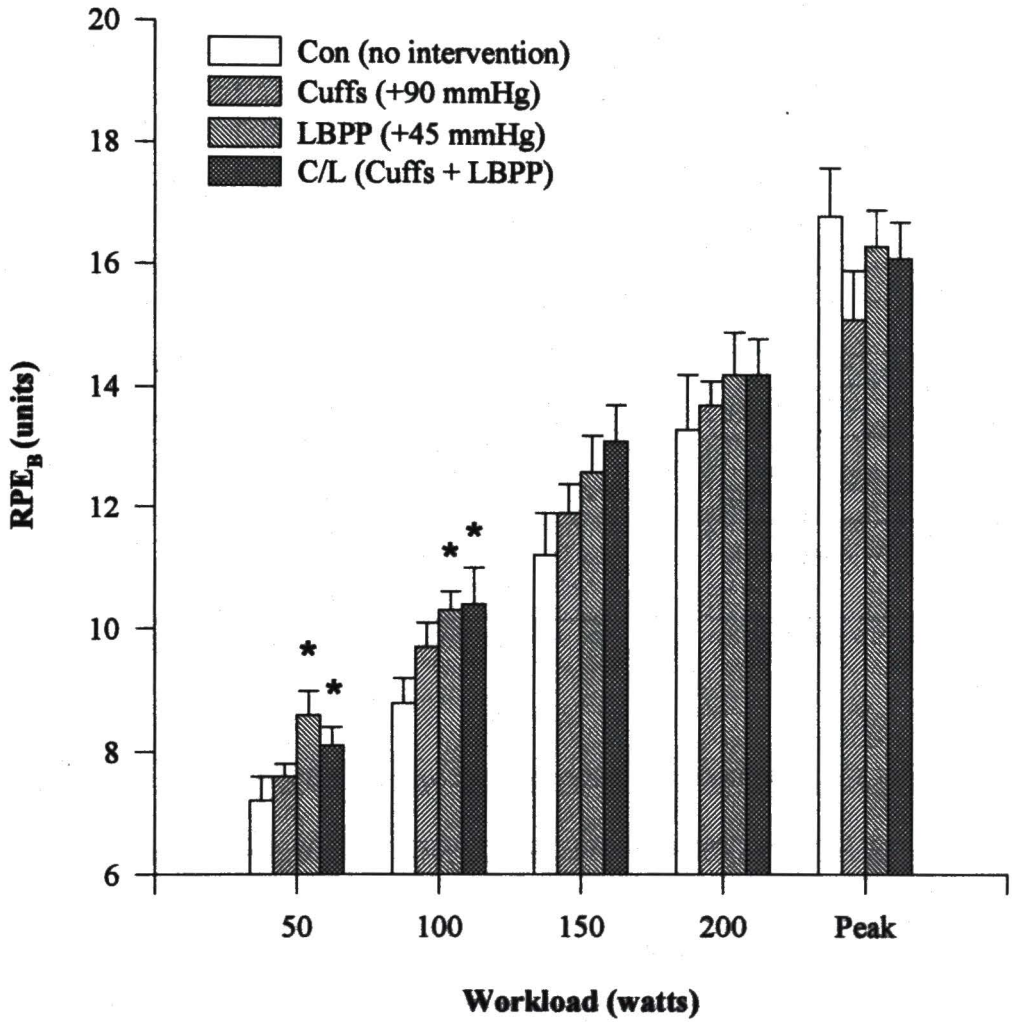


Figure V.- Mean $RPE_B$ data obtained from four exercise conditions. * Indicates significant differences from the control condition at a level of $p<0.05$.

TABLE V. INDICES OF EXERCISE PRESSOR REFLEX ACTIVATION

| | | Rest | 25W | 50W | 75W | 100W | 125W | 150W | 175W | 200W | Peak |
|---|---|---|---|---|---|---|---|---|---|---|---|
| **MAP** (mmHg) | **Con** | 78.3 ±3.0 | 85.1 ±3.5 | 86.6 ±3.6 | 88.8 ±3.5 | 93.4 ±3.5 | 97.6 ±3.5 | 101.1 ±4.3 | 104.1 ±4.8 | 108.9 ±5.4 | 127.6 ±5.3 |
| | **Cuffs** | 78.1 ±3.7 | 90.1 ±4.2 | 92.9 ±4.5 | 95.5 ±4.9 | 100.3 ±4.8 | 104.0 ±4.5 | 106.9 ±4.3 | 109.9 ±4.0 | 113.5 ±4.1 | 122.1 ±4.0 |
| | **LBPP** | 79.4 ±2.7 | 99.5 ±2.4† | 103.3 ±2.3† | 105.7 ±3.1† | 110.2 ±2.7† | 114.6 ±3.5† | 117.9 ±3.4† | 122.0 ±3.0† | 124.1 ±2.7* | 134.5 ±2.4 |
| | **C/L** | 80.9 ±1.1 | 103.7 ±2.7† | 107.0 ±2.2† | 110.9 ±2.4† | 113.6 ±2.6† | 117.7 ±3.6† | 122.5 ±3.7† | 125.6 ±4.0† | 128.1 ±4.5† | 141.3 ±6.7† |
| **$RPE_L$** (units) | **Con** | ------- | ------- | 7.6 ±0.5 | ------- | 10.3 ±0.6 | ------- | 12.6 ±0.7 | ------- | 15.1 ±0.7 | 19.6 ±0.2 |
| | **Cuffs** | ------- | ------- | 10.6 ±0.4* | ------- | 12.9 ±0.6* | ------- | 15.7 ±0.7* | ------- | 17.6 ±0.5* | 19.3 ±0.3 |
| | **LBPP** | ------- | ------- | 10.6 ±0.5* | ------- | 12.6 ±0.5* | ------- | 15.0 ±0.7* | ------- | 16.9 ±0.5* | 19.4 ±0.2 |
| | **C/L** | ------- | ------- | 11.4 ±0.4* | ------- | 14.1 ±0.4* | ------- | 16.7 ±0.5* | ------- | 18.4 ±0.5* | 19.8 ±0.1 |

Mean ± SEM. *Indicates significance from control condition only. †Indicates significance from both the control condition and cuffs condition.

was measured continuously throughout the experimental procedure and a mean calculated for rest, 25W, 50W, 75W, 100W, 125W, 150W, 175W, 200W, and PW. MAP was not found to be significantly different at rest (no stimuli intervention) in any of the exercise conditions establishing that all trials commenced at the same baseline value for MAP. However, employment of LBPP +45 mmHg significantly augmented the MAP response from control as well as the cuffs condition until a workload of 200W was achieved at which time the MAP was significant only from the control exercise condition. This response was initiated at the earliest level of work (25W) and was preserved throughout

the incremental exercise session. The LBPP induced increase in MAP did not disappear until the PW was achieved at which time significance from the control exercise condition was absent. In addition, the concurrent activation of LBPP and thigh cuffs elucidated a further increase in MAP that was significantly elevated not only from control values but also MAP values obtained for the condition in which the only stimulus was inflation of the thigh cuffs. MAP was consistently elevated throughout the exercise, again beginning at 25W of work, until the cessation of exercise. MAP elicited from inflation of the thigh cuffs exhibited a trend for an increase in pressure but not to the same magnitude or significance level of the LBPP or the cuffs + LBPP conditions as it was not significantly different from control. This trend presented at the beginning workload, 25W, and continued through 200W but tapered by PW and in fact was lower than control pressures at this level of work. These relationships are seen in Figure VI.

Peripheral RPEs were assessed for the legs ($RPE_L$) at 50W, 100W, 150W, 200W, and PW. The subjects reported significantly increased levels of perceived exertion from control at all workloads that were assessed except for PW for the three exercise bouts in which stimuli was implemented in the trial (Figure VII, p.51). Not surprisingly, this finding coincides with those found for PW (Table III, p.41) where LBPP, thigh cuff inflation, and LBPP + thigh cuff inflation reduced exercise performance albeit not significantly. Peak workload $RPE_L$ values were very similar and were not significantly different from each other.

**FIGURE VI.- MEAN ARTERIAL PRESSURE RESPONSES TO EXERCISE**

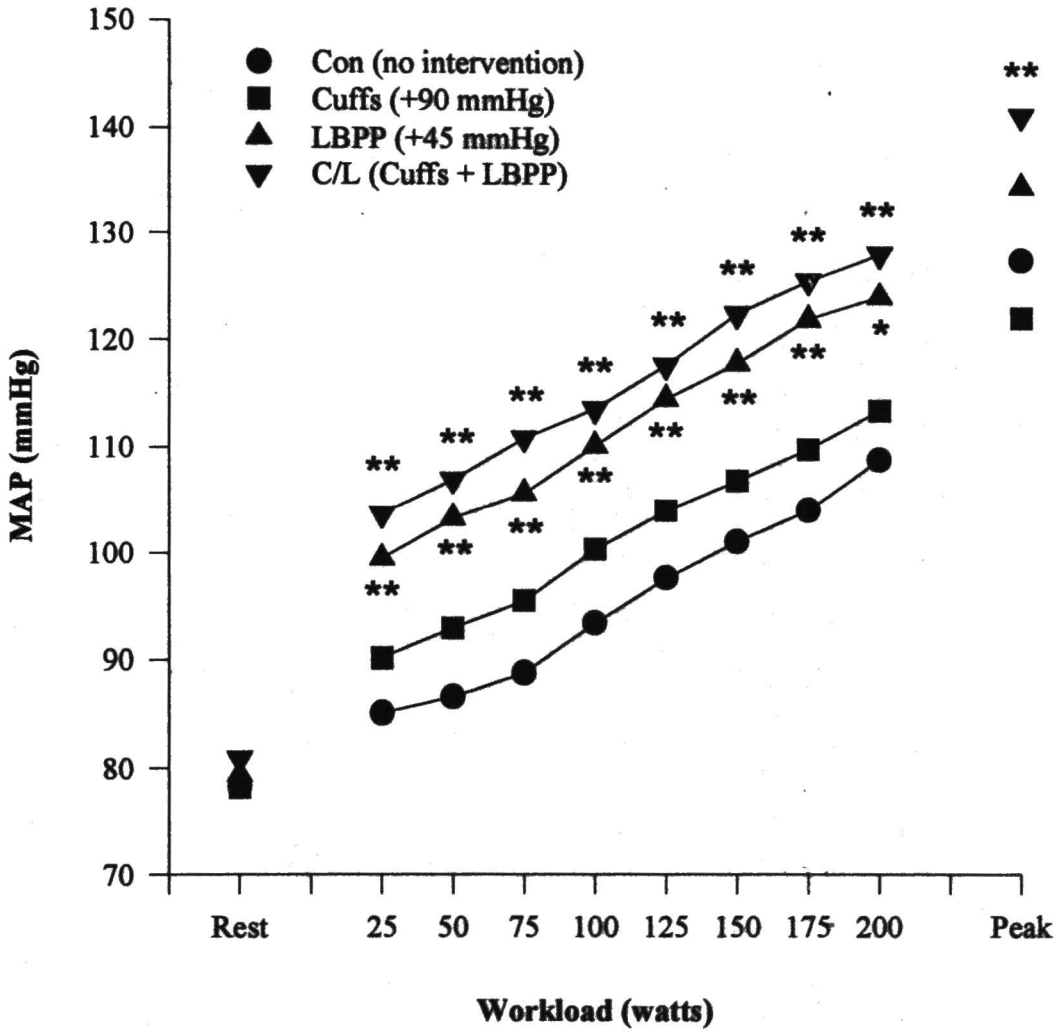


Figure VI.- Mean MAP data obtained from four exercise conditions. * Indicates significant differences from the control condition only. ** Indicates significance from the control and cuff conditions. The level of significance was set at $p<0.05$. Standard error for MAP data are presented in Table V.

**FIGURE VII.- RATING OF PERCEIVED EXERTION FOR THE LEGS DURING EXERCISE**

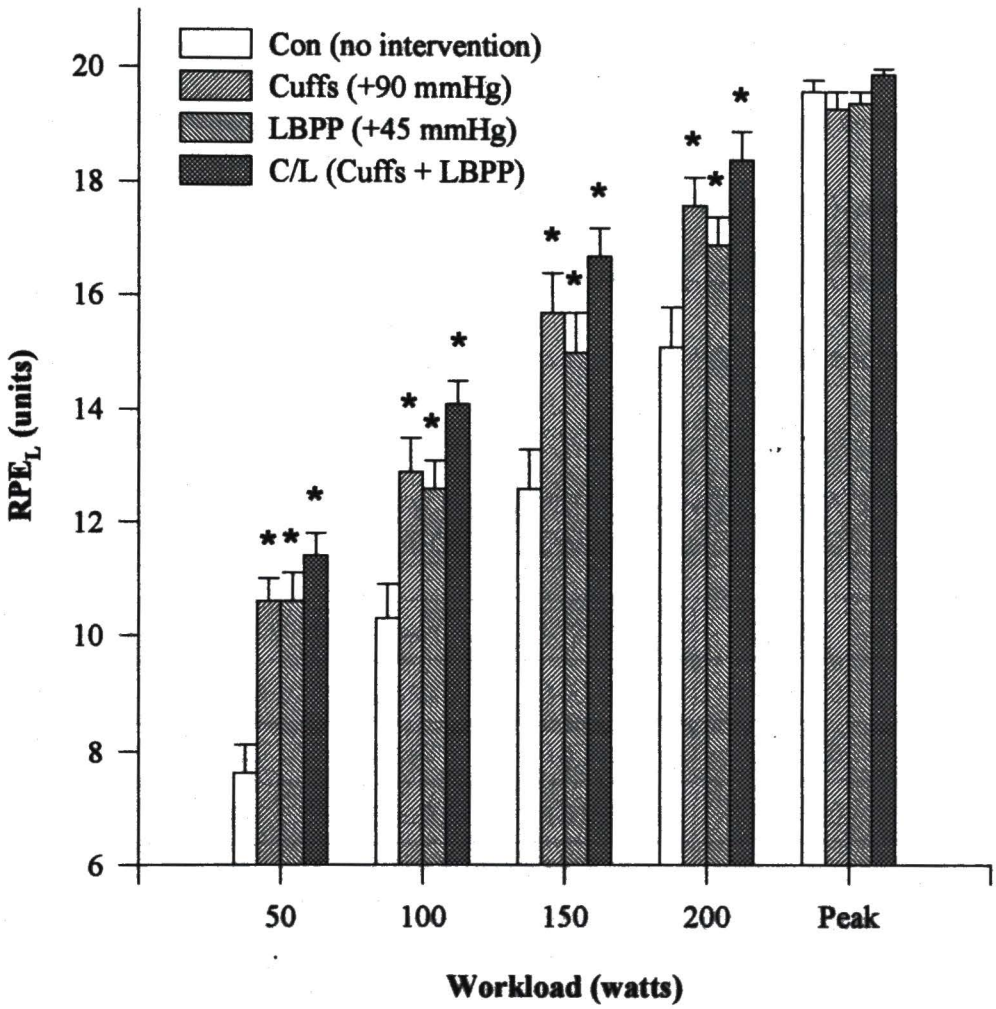


Figure VII.- Mean RPE$_L$ data obtained from four exercise conditions.
* Indicates significance from the control condition at a level of $p<0.05$.

Determinants of Increased MAP: Cardiac Output

Cardiac output means ± standard error of the mean are presented in Table VI. Cardiac output ($\dot{Q}_c$) is valuable to the analysis of the current findings of this research because it can be used to propose the cardiovascular adaptations that are responsible for the previously mentioned increases in MAP found during the LBPP and cuffs +LBPP conditions. Systemic vascular resistance (SVR) can be calculated using $\dot{Q}_c$ and MAP. However, an extensive investigation of SVR will not be incorporated in this analysis, rather a sample calculation will suffice and will be reported in the Discussion portion of this work in Chapter V, p. 61.

TABLE VI. CARDIAC OUTPUTS ACHIEVED DURING VARIOUS EXERCISE CONDITIONS

| | | Rest | 75W | 150W | Peak |
|---|---|---|---|---|---|
| $\dot{Q}_c$ ($L \cdot min^{-1}$) | Control | 6.0±0.3 | 10.3±0.6 | 12.0±1.0 | 17.7±1.3‡ |
| | Cuffs | 5.2±0.4 | 10.3±0.7 | 10.7±0.6 | 13.7±0.9‡ |
| | LBPP | 5.8±0.5 | 10.0±0.9 | 11.8±1.0 | 14.7±1.3‡ |
| | C/L | 5.0±0.5 | 10.6±0.9 | 12.3±1.1 | 14.8±1.6‡ |

Mean ± SEM.. ‡ Peak cardiac outputs were not necessarily taken at peak workload but rather represent the peak level at which the subject was able to successfully execute the cardiac output procedure.

Cardiac outputs were assessed at rest, 75W, 150W, and a peak $\dot{Q}_c$ was obtained. Peak $\dot{Q}_c$ was not necessarily obtained at PW due to limitations of the $\dot{Q}_c$ assessment procedure. As a result of the subject having to endure a rebreathing technique, often $\dot{Q}_c$

assessment at PW was unobtainable due to the lack of required oxygen that the body demands at high levels of cardiovascular stress that the rebreathing apparatus could not provide. Therefore, the last obtainable $\dot{Q}_c$ was used in this analysis. During incremental exercise, cardiac output was not found to be significantly different between any of the experimental conditions incorporated in this study (Figure VIII). However, $\dot{Q}_c$ was significantly different across workloads exhibiting an increase as the level of work increased.

**FIGURE VIII.- CARDIAC OUTPUT MEASURES DURING EXERCISE**

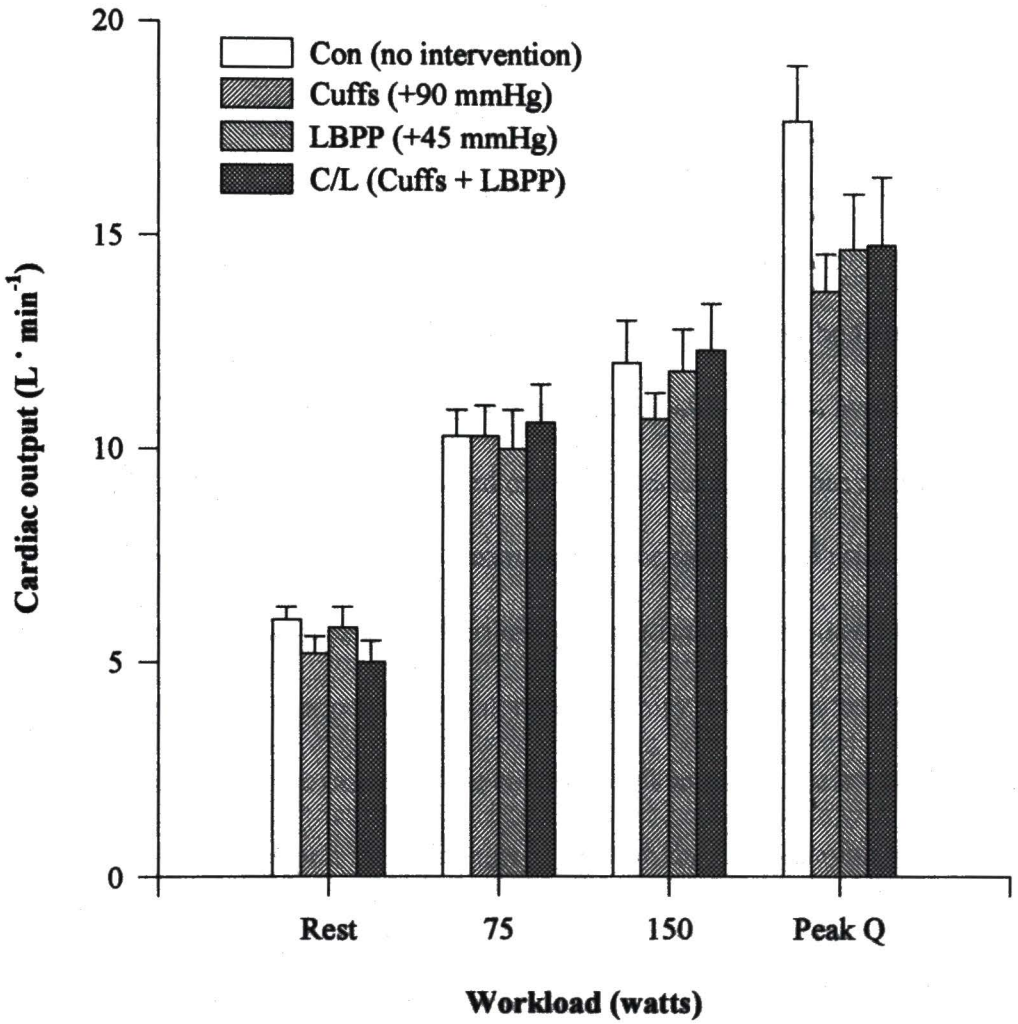


Figure VIII.- Mean cardiac outputs obtained during four exercise conditions. No significant difference was found in cardiac output between the various exercise types. Peak cardiac outputs represent the peak workload at which the subject was able to execute the cardiac output procedure successfully.

# CHAPTER V

# DISCUSSION AND SUMMARY

The purpose of Chapter V is to review the relevant findings elicited from this investigation and to determine their importance in relation to previous research. The major finding from this investigation was a significant augmentation in the blood pressure response to dynamic exercise subsequent to the application of lower body positive pressure (LBPP) to 45 mmHg. This finding is consistent with the first hypothesis presented in Chapter I p.7 that an activated exercise pressor reflex does augment the normal integrated central command and exercise pressor reflex blood pressure response to ramped increases in dynamic exercise. Furthermore, the second hypothesis presented on p.7 was also accepted as it appears mechanoreceptors may predominate in eliciting the pressor response to dynamic exercise. The results of this investigation are explained and conclusions drawn based upon these findings along with the extrapolation of results from other studies of relevance to this research. Additionally, recommendation for further investigation into the current problem are presented.

## Subject Group Analysis

Based on the results of the initial graded cycle ergometer exercise test, all subjects met the criteria for inclusion in this study. This was essential as physical fitness levels below the standard set forth by this experimentation could have negatively effected the analysis and conclusions of the research. The reductions in both peak rate of oxygen uptake ($\dot{V}O_{2PEAK}$) and exercise performance with application of cuffs, LBPP, and the combination thereof are in accordance with previous findings (7,8,60). The earlier termination of exercise in these conditions can be attributed to the accumulation of exercise-related by-products that promote premature fatigue in the working muscles (8).

## Cardiovascular and Respiratory Responses to Central Command During Exercise

It has been previously reported that increases in rate of oxygen uptake ($\dot{V}O_2$) and heart rate (HR) (15,55,59) as well as electromyographic activity (EMG) and rating of perceived exertion (RPE) (35) are related to increases in central command activity. Therefore, these variables were taken as indices of central command activity during the present investigation. Furthermore, the blood pressure response to dynamic exercise has been shown to be in part regulated by signals emanating from central command (15,55,59). As a result, it became imperative during this investigation to maintain a constant amount of influence from central command during all exercise conditions. This is not to be confused with abolishing or dampening the effect of central command during

dynamic exercise which has been a technique utilized by previous investigators (35,36,51). On the contrary, central command influences were left intact and invariably could have affected the MAP response to dynamic exercise found in each exercise protocol. The finding that HR, EMG, and $\dot{V}O_2$ were not significantly different across exercise conditions is of great importance suggesting that the assessment of mean arterial pressure (MAP) during the experiment was not confounded by variable influences of central command. This agrees with the previous findings of Williamson et al. (60) when they applied increasing levels of LBPP during dynamic exercise. The influence of central command on MAP during all dynamic exercise trials was maintained, increasing similarly with increasing exercise in all experimental conditions. Therefore, it was concluded that an augmentation in MAP during dynamic exercise was due to some other factor, but not to increased central command effector activity.

The subject group did exhibit increases from control in rating of perceived exertion of the body ($RPE_B$) during the early stages of work (50W and 100W) with the application of LBPP and cuffs + LBPP. However, previous studies have reported that HR and $\dot{V}O_2$ are central factors highly correlated to perceived effort (5). Since neither of these two factors was found to be significantly different between exercise conditions, the increase in $RPE_B$ observed at 50W and 100W may be indicative of some other factor rather than an increase in central command activity. These findings may have resulted from unfamiliarity with the exercising conditions employed that falsely elevated subjective responses from the

group during the initial stages of work. This seems to be a plausible explanation when considering that at the later and more strenuous levels of exercise (150W and 200W) significant increases in $RPE_B$ from control subsided.

Cardiovascular Responses to the Exercise Pressor Reflex During Exercise

It has been suggested that differential ratings of perceived exertion should be utilized, in order to provide a more accurate examination of a subject's perceived level of effort (37). Local muscular ratings of the legs ($RPE_L$) were assessed in addition to the more generalized central rating ($RPE_B$) for perceived exertion. If one assumes that perceived effort is correlated with metabolite accumulation and muscle fatigue as has previously been accepted (60), the elevations from control in reported $RPE_L$ in all experimental conditions (cuffs, LBPP, and cuffs + LBPP) provide a definitive example that ergoreceptor stimulation was augmented during these interventions. Previous investigations propose that local input predominates over central factors in the perception of effort during exercise (4,38) and, therefore, may be a more sensitive assessment for fatigue onset than $RPE_B$. It is therefore concluded that the elevations in $RPE_L$ are indicative of increases in pressure or metabolite concentrations in the working skeletal muscle and as such promoted premature muscle fatigue and termination of the exercise session.

The blood pressure increases during 45 mmHg of LBPP agree with the findings of Williamson et al. (60), who documented a parallel increase from control values in MAP

during progressive incremental workload dynamic exercise when LBPP of 45 mmHg was applied. Similarly, Rowell et al. (41) and Eiken and Bjurstedt (8) have also successfully produced an increase in MAP with the application of LBPP at 45 mmHg and 50 mmHg respectively. These researchers accredited the blood pressure response to metaboreceptor activation which they assumed were stimulated by the accumulation of metabolic end-products in the working muscle. The premise for this conclusion is that LBPP effectively reduces the driving pressure for blood flow in the vasculature resulting in a small reduction in muscle perfusion producing a local flow error sensed by the metaboreceptors; an event that Rowell et al. (41) states cannot be attributed to the mechanical effects of LBPP (i.e. a rise in intramuscular pressure that could activate mechanoreceptors). In this investigation, we tested the validity of these conclusions by selectively activating the metaboreceptors using thigh cuff inflation to 90 mmHg (to reduce venous outflow from the working tissue) and compared the MAP response produced to the MAP response seen with the application of LBPP of 45 mmHg. We did not find that inflation of thigh cuffs to 90 mmHg had a significant effect on the MAP response to exercise (see Figure VI, p.50). It is unlikely that this is a result of utilization of an insufficient method for trapping metabolites in the muscle interstitium as the $RPE_L$ was significantly elevated during this condition. Furthermore, Sinoway and Prophet (49) have shown that two-legged circulatory arrest achieved by inflation of pressure cuffs around the upper thighs can be

used to effectively trap metabolites in the working muscle interstitium. Rather a more likely explanation is that metaboreceptor activation at this level of exercise does not augment the arterial pressure response significantly.

For comparative analysis, we tested the hypothesis that mechanoreceptors may be involved in the pressor response to dynamic exercise as had been suggested previously by Williamson et al. (60). It has been reported that LBPP of 45 mmHg raises intramuscular pressure significantly from control conditions (no LBPP intervention) as well as effectively increasing the metabolite concentration in the muscle interstitium by reducing the gradient for capillary blood flow (60). Given that the MAP response was markedly elevated during LBPP application during the present investigation when compared to control and cuffs conditions, see Figure VI, p.50, it seems unlikely that this pressor response can be attributed to metaboreceptor afferent activity, especially when compared to the previously mentioned response noted with the inflation of thigh cuffs only. A more logical interpretation is that the MAP response seen during dynamic exercise is mediated by mechanoreceptor activation due to a rise in intramuscular pressure. Furthermore, when both cuffs and LBPP were applied concurrently, the MAP response was further increased above control and cuffs conditions MAP values. This supports the findings of Williamson et al. (60) and gives credibility to their conclusion that the muscle metaboreceptors may not be tonically active during dynamic exercise under normal conditions. This should not be erroneously interpreted as a discountenance of metaboreceptor involvement in the blood pressure response to dynamic exercise but rather a validation of Rowell's (41)

hypothesis that metaboreceptor function requires a critical reduction in muscle blood flow before becoming activated. Williamson et al. (60) has demonstrated that in the normal response to dynamic exercise the threshold for metaboreceptor activation does not occur until near maximal workloads.

In agreement with the findings of Williamson and colleagues (60) blood pressure was elevated with the application of LBPP and cuffs + LBPP although there were no observed changes in cardiac output between conditions. This MAP increase appeared to be mediated primarily through increases in systemic vascular resistance (SVR). Utilizing actual changes in cardiac output and MAP we were able to calculate SVR during exercise employing the hemodynamic equation: SVR = MAP/$\dot{Q}_c$ (Table VII, p.62). Using this information, we calculated the relative contributions of $\dot{Q}_c$ and SVR toward the change in MAP by using methods previously introduced by Rowell et al. (41) and Williamson et al. (60). The increases in MAP that could be attributed exclusively to changes in $\dot{Q}_c$ were estimated by calculating the expected changes in MAP with the SVR held constant at control values. For example, using data from Table VII at 75W, if the control SVR (8.6 mmHg•L$^{-1}$•min$^{-1}$) were to remain constant, the expected change in MAP with a difference in $\dot{Q}_c$ from a control value of 10.3 to 10.0 L•min$^{-1}$ during LBPP would be approximately 2.8 mmHg (from 88.8 to 86.0). The measured change in MAP, however, was from 88.8 to 105.7 mmHg, or 16.9 mmHg. Thus, none of the increase in MAP could be attributed to a change in cardiac output but rather 100% of the observed change was a result of an

TABLE VII. CALCULATED SYSTEMIC VASCULAR RESISTANCE DURING EXERCISE FROM MEASURED MEAN ARTERIAL PRESSURES AND CARDIAC OUTPUTS

| | Rest* | | | 75W | | | 150W | | |
|---|---|---|---|---|---|---|---|---|---|
| | $\dot{Q}_c$ ($L \cdot min^{-1}$) | MAP (mmHg) | SVR ($mmHg \cdot L^{-1} \cdot min^{-1}$) | $\dot{Q}_c$ ($L \cdot min^{-1}$) | MAP (mmHg) | SVR ($mmHg \cdot L^{-1} \cdot min^{-1}$) | $\dot{Q}_c$ ($L \cdot min^{-1}$) | MAP (mmHg) | SVR ($mmHg \cdot L^{-1} \cdot min^{-1}$) |
| **Control** | 6.0 | 78.3 | 13.1 | 10.3 | 88.8 | 8.6 | 12.0 | 101.1 | 8.4 |
| **Cuffs** | 5.2 | 78.1 | 15.0 | 10.3 | 95.5 | 9.3 | 10.7 | 106.9 | 10.0 |
| **LBPP** | 5.8 | 79.4 | 13.7 | 10.0 | 105.7 | 10.6 | 11.8 | 117.9 | 10.0 |
| **C/L** | 5.0 | 80.9 | 16.2 | 10.6 | 110.9 | 10.5 | 12.3 | 122.5 | 10.0 |

SVR was calculated from the following hemodynamic relationship: SVR = MAP/$\dot{Q}_c$. *No interventions were implemented during rest.

increase in SVR. During the utilization of cuffs + LBPP at 75W this same method of analysis was employed predicting the difference in $\dot{Q}_c$ from a control value of 10.3 to 10.6 $L \cdot min^{-1}$ would produce an approximately 2.4 mmHg (from 88.8 to 91.2) change in MAP. The measured change in MAP was from 88.8 to 110.9 mmHg, or 22.1 mmHg. Only a 2.4 mmHg increase in MAP could be attributed to $\dot{Q}_c$ while a 19.7 mmHg rise could be accounted for by changes in SVR. In other words, the observed blood pressure response was produced by an increase in $\dot{Q}_c$ resulting in a 10% increase in MAP while 90% of the increase in MAP was due to the increase in SVR. These same calculations were made at 150W for both the LBPP and cuffs + LBPP conditions. In the LBPP condition, MAP increases involved no change in cardiac output and, therefore, 100% of the change was attributable to increased SVR. In the cuffs + LBPP condition, the change in $\dot{Q}_c$ produced

10% of the increase in MAP while 90% of the change in MAP was attributable to an increase in SVR. Thus, we conclude that MAP is elevated primarily through increases in SVR with a flow change apparently not contributing to the pressor response. In order to validate this finding, we also calculated the increases in MAP that could be attributed exclusively to changes in SVR by holding the $\dot{Q}_c$ constant at control values employing the same methodology as previously described. For example, again using data from Table VII at 75W, if the control $\dot{Q}_c$ (10.3 $L \cdot min^{-1}$) were to remain constant, the expected change in MAP with a difference in SVR from a control value of 8.6 to 10.6 $mmHg \cdot L^{-1} \cdot min^{-1}$ during LBPP would be approximately 20.4 mmHg (from 88.8 to109.2). The measured change in MAP was from 88.8 to 105.7 mmHg, or 16.9 mmHg. Thus, 100% of the increase in MAP could be attributed to a change in SVR but none to a change in $\dot{Q}_c$. During the utilization of cuffs + LBPP at 75W the difference in SVR from a control value of 8.6 to 10.5 $mmHg \cdot L^{-1} \cdot min^{-1}$ would produce an approximately 19.4 mmHg (from 88.8 to 108.2) change in MAP. The measured change in MAP was from 88.8 to 110.9 mmHg, or 22.1 mmHg. A 19.4 mmHg increase in MAP could be attributed to changes in SVR while only a 2.7 mmHg could be accounted for by changes in $\dot{Q}_c$. This agrees with our previous calculations, in that 88% of the increase in MAP resulted from the increase in SVR while 12% of the increase was due to changes in $\dot{Q}_c$. These calculations were also made at 150W for both the LBPP and cuffs + LBPP conditions. In the LBPP condition, MAP increases involved no change in cardiac output with a 100% of the change being related to

the increase in SVR, while the cuffs + LBPP condition exhibited 91% of the increase being due to the SVR increase and only 9% of the change being a result of the increase in $\dot{Q}_c$. After examination of the findings produced from these calculations, we postulate that the pressor response to exercise is mediated primarily through mechanoreceptor activation of the sympathetic nervous system eliciting an increase in MAP through elevations in systemic vascular resistance.

## Summary

In accordance with previous findings (60), an augmented exercise pressor reflex was not found to alter the normal HR, $\dot{V}O_2$, and EMG responses to dynamic exercise when central command influence was left uninhibited. In agreement with our results, Strange (51) demonstrated that abolition of central command's involvement to dynamic exercise , by electrically induced exercise, did not alter the HR response. Previous reports that mechanoreceptor (36) and metaboreceptor (7,41) activation augment the HR response to exercise appear to be in direct conflict with our findings. This is not necessarily a viable conclusion, however, as in these studies central command influences were diminished. Rather, the current dogma that central command and the exercise pressor reflex are part of a redundant system mediating the cardiovascular and respiratory responses to dynamic exercise may present a more plausible explanation to these conflicting reports.

The augmented MAP response to LBPP of 45 mmHg supports previous findings reported by Williamson et al. (60). It appears that the response was mediated by an increase in group III mechanoreceptor afferent activity. This conclusion was derived from the finding that during thigh cuff inflation to 90 mmHg, which has been previously reported to effectively trap metabolic end- products in the working interstitium activating group IV metaboreceptor afferents (49), MAP was not significantly elevated from control values. This contradicts speculations previously made by Rowell (41) and Eiken et al. (7,8) which attribute the blood pressure response to dynamic exercise to metaboreceptor activation. As a result, we support the conclusion of Williamson et al. (60) that metaboreceptor reflex mediated increases in MAP may not be tonically active during dynamic exercise under normal conditions. The finding that MAP was further augmented with the application of thigh cuff inflation and LBPP concurrently was speculated to be a result of either: (i) thigh cuff inflation to 90 mmHg effectively sensitized mechanoreceptors due to the compressive forces transmitted to the legs transmurally, which facilitated the rise in intramuscular pressure induced by LBPP application; or (ii) a critical reduction in muscle blood flow was attained, that elicited metaboreceptor activation (60) as a result of cuffs restricting outflow of the metabolites and, in combination with LBPP, resulted in an additive effect on the mechanoreceptor mediated MAP response to dynamic exercise. In conclusion, the present data suggests that the MAP response to dynamic exercise is produced by an increase in SVR mediated primarily by afferent mechanoreceptor sympathoexcitation.

## Recommendation for Further Investigation

In order to determine if the proposed conclusions are in fact valid, a similar study should be undertaken with the goals of determining the cardiovascular responses to dynamic exercise when the central command contribution is completely abolished and kept constant at the control resting influence throughout all stages of work. This study should incorporate lower body positive pressure of 45 mmHg, thigh cuff inflation of 90 mmHg, and the combination thereof as a means of augmenting the exercise pressor reflex response. Measurements of MAP, HR, $\dot{V}O_2$, EMG, $RPE_B$, $RPE_L$, and $\dot{Q}_c$ should be incorporated into the design of the study. Furthermore, calculations of SVR should be assessed to determine the cause of any elevation in MAP obtained. In addition assessment of intramuscular pressure and blood metabolite concentrations from the working muscles would validate the success of LBPP and thigh cuff inflation interventions. Central command influence could be effectively reduced or abolished by electrical induction of exercise.

As the present investigation has indicated that the MAP response to dynamic exercise is mediated primarily by group III mechanoreceptor afferent activity, we propose that by the elimination of the central command influence during dynamic exercise, the finding would be further substantiated. We were left with two questions that remain to be investigated: (i) Why was the MAP response further elevated by the application of thigh cuffs and LBPP concurrently?; and (ii) Could our findings have been influenced by the

proposed polymorphic characteristics of the mechano- and metaboreceptors previously reported by Mitchell (29)? This polymorphism indicates that some Group III fibers respond to metabolic changes and some Group IV fibers respond to mechanical changes suggesting that responses to one or the other stimulus may be heightened or suppressed dependent upon the background metabolic activity of the muscle. Hopefully this proposed research would elucidate a more tenable conclusion.

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