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I am submitting herewith a thesis written by Randal P. Claytor entitled "Plasma Catecholamine and Cardiovascular Responses of Trained and Untrained Men Exposed to Physical and Psychological Stressors." I have examined the final copy of this thesis for form and content and recommend that it be accepted in partial fulfillment of the requirements for the degree of Master of Science, with a major in Physical Education.

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PLASMA CATECHOLAMINE AND CARDIOVASCULAR RESPONSES OF TRAINED AND UNTRAINED MEN EXPOSED TO PHYSICAL AND PSYCHOLOGICAL STRESSORS

A Thesis

Presented for the

Master of Science

Degree

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Randal P. Claytor

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DEDICATION

To my wife Lisa, for her love, support, and ability to help me keep things in perspective.

Thanks for being on my team, for this project truly was a team effort.

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ABSTRACT

The plasma catecholamine and cardiovascular responses of trained(T) and untrained(UT) males were measured during exposure to several physical and psychological laboratory stressors. Sixteen subjects (8 T and 8 UT) were exposed to an orthostatic hypotension test, a cold-pressor test, an isometric hand grip test, a reaction time-avoidance of shock task, and a reaction time-appetitive task. Five to 10 minute rest periods separated the tasks. The Ss were randomly assigned to a test order based on a latin square design. During the experimental protocol, heart rate(HR), systolic blood pressure(SBP), diastolic blood pressure(DBP), and plasma epinephrine(E) and norepinephrine(NE) concentrations were measured at specified time intervals. Maximal oxygen uptake was 70.6 $\pm$ 0.8 and 45.5 $\pm$ 1.1 ml(kg.min)-1 $\pm$SE for the T and UT groups, respectively ($p<0.0001$). Multiple t-tests for independent means were used to test for differences between the groups.

Although there were no significant differences between groups for any of the dependent variables for any test except mean resting HR ($p<0.05$), it was interesting to note that plasma NE concentrations were consistently higher in the trained group for each task. These results suggest that a form of adaptation evidenced in a chronically trained population may involve increased secretion of NE in response

to novel stressors, or that adaptation to exercise is specific and that there is no SNS cross adaptation to these laboratory stressors.

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CHAPTER 1

INTRODUCTION

Stress can be thought of as physical, chemical, or psychological factors that may disrupt physiological equilibrium. In day to day life the human body must deal with a variety of stressors. Cannon (1911) was one of the first researchers to recognize a physiological reaction to a variety of noxious stimuli. There is considerable evidence that suggests the adrenal medulla and the sympathetic nervous system (SNS) actively participate in response to noxious stimuli, whether physical and/or psychological in nature (Cannon, 1911; Euler, 1964; Kvetnansky et al., 1970; LeBlanc, 1975; Lake et al., 1976; Sinyor et al., 1983). Research has shown that when an organism is exposed to particular stressors two catecholamines (CA), epinephrine (E) and norepinephrine (NE), are released into the system in greater quantities (Euler, 1964; Euler, 1974; LeBlanc, 1975; Lake et al., 1976; Winer and Carter,1977).

Epinephrine is released into the blood stream from the cells of the adrenal medulla and acts mainly as a hormone. The secretion of E into the blood provides a generalized mechanism for spreading sympathetic activity to distant target cells of the body that affect metabolic and cardiovascular parameters (Axelrod and Weinshulbaum, 1972; Euler, 1974). Concomitantly, norepinephrine, a

neurotransmitter substance is released from the sympathetic nerves of the peripheral and central nervous systems. It acts locally on effector cells of the vascular smooth muscle, liver, heart, and brain. Norepinephrine's primary purpose is to maintain homeostasis within the vascular system (Axelrod and Weinshulbaum, 1972; Euler, 1974; Silverberg et al., 1978). Although controversy exists concerning the specific physiological actions of the CA there is a considerable volume of evidence that suggests one function of the SNS is to maintain phsiological homeostasis within an individual via release of E and NE (Goldenberg et al., 1948; Axelrod and Weinshulbaum, 1972; Silverberg et al., 1978).

Physical training is one factor that has been shown to modify the functional capability of the SNS. Recent studies have shown that the level of fitness of an individual is an important factor with respect to the concentrations of circulating catecholamines. Several researchers have demonstrated that at equivalent absolute submaximal workloads the magnitude of increase for plasma catecholamine concentrations is significantly lower after training when compared to pre-training values (Hartley,1975; Galbo et al., 1977; Winder et al., 1979; Peronnet et al., 1982). Peronnet et al.(1982) and Hartley (1975) suggest the alterations in SNS activity are a result of neural control mechanisms, while Galbo et al.(1977) and Winder et al.(1979) implicate metabolic processes as the means for altering SNS activity. Regardless of the modifying mechanisms, physical training is

an important factor with respect to the function of SNS activity.

To date the literature provides evidence to suggest that the SNS responds with an increase in activity to a variety of stimuli: orthostatic stressors, isometric exercise, acute cold, and psychological challenge situations. However, there is confusion as to what effect repeated exposure to one stimulus (stressor) will have on that organism's SNS response to a new stressor.

Kvetnansky et al. (1970) and (1971) and Kvetnansky (1980) developed the notion that an adaptation occurs in response to repeated exposure to a stressor which involves an enhanced activity of the sympathetic-adrenomedullary system and a diminished response from the central nervous system (CNS). This enables the system to respond more intensely to new and/or different stressors. Although the SNS response to a repeated stressor will diminish across time as a result of CNS adaptation to that stressor, Kvetnansky and co-workers suggest that repeated exposure to the same stressor increases catecholamine levels in peripheral tissues, blood, and urine. He has attributed this to enhanced catecholamine synthesis and also to diminished catecholamine degradation. Consequently, the SNS can respond to new stressors with greater quantities of catecholamines.

On the other hand, Selye (1961) has theorized that adaptation to one stressor (i.e. exercise) may lower the stress response of an organism to a variety of other

stressors. He labeled this mechanism cross-resistance (Selye, 1961). Ostman and Sjostrand (1972) found that physically well trained rats developed adaptive changes in the cardiovascular system that allowed the SNS of the trained rats to operate at a lower level of activity during submaximal exercise. Using exercise and cold as the stressors to test for cross tolerance, Ostman and Sjostrand (1975) found that physical training induced cross tolerance to cold stress while cold-acclimation did not lead to cross tolerance to acute exercise in rats. They concluded that increased physical activity may lead to a better fitness to withstand cold and possibly other stressful conditions. In human studies examining cross resistance, Morgan et al. (1982) have shown a decreased cardiovascular response to leg isometric exercise but not to hand isometric exercise following a five week aerobic training program. However, more data needs to be collected to better examine the phenomenon of cross resistance in the human population.

The purpose of this study was to evaluate whether one's state of aerobic fitness produced a physiological adaptation to novel laboratory stressors. Specifically, the cardiovascular system and the sympathetic nervous system responses to physical and psychological stressors of aerobically trained and untrained young men were measured. To quantify these physiological responses, heart rate (HR), systolic blood pressure (SBP), diastolic blood pressure (DBP), and plasma E and NE concentrations were measured

during the experimental tasks. The stressors used in this study were: an orthostatic stressor (STAND), a cold-pressor test (CP), an isometric hand grip task (ISO), and psychological challenge situations involving avoidance of shock (RT-AV) and monetary reward (RT-AP).

CHAPTER II

REVIEW OF RELATED LITERATURE

The nature of this study requires a literature review of several areas related to the physiological responses to stress. The first section of this review surveys the physiological response to particular physical and psychological laboratory stressors. The second part of the literature review will focus on the physiological response to exercise training. Specifically, it will deal with the cardiovascular and the catecholamine responses at rest and during exercise and examine the effect of aerobic training. The final section focuses on the effect aerobic training has on the cardiovascular and plasma catecholamine responses to particular novel laboratory stressors.

I. PHYSIOLOGICAL RESPONSE TO PHYSICAL AND PSYCHOLOGICAL STRESSORS

Confusion exists as to the definitions of "stress" and "stressor" (Mason,1975 I, II). Selye (1961) defined stress as "the state mainfested by the specific syndrome that consists of all the nonspecifically induced changes within a biologic system" or more simply "the sum of all nonspecific changes caused by function or damage." He defined the term stressor as "that which produces stress" (Selye,1961). It is

not the intent of this investigation to measure stress, but only to use particular stressors to produce cardiovascular and sympathetic nervous system responses. The stressors selected for use in this study include: an orthostatic standing task, a cold pressor task, an isometric hand grip task, and two forms of psychological challenge tasks that involve a reaction time task to avoid shock and to gain monetary reward (appetitive).

Upright Standing

Cryer et al. (1974) described a new single isotope modification of an assay for the measurement of plasma E and NE. The plasma E and NE concentrations at rest were found to be 41±23 pg/ml and 223±92 pg/ml, respectively. After five minutes of standing plasma E and NE concentrations increased to values of 73±17 pg/ml and 425±28 pg/ml, respectively. Standing values were found to be significantly greater than rest values. Lake and coworkers (1976) reported plasma NE concentrations of 292±16 pg/ml in 74 resting, supine, normal subjects ranging in age from 10 to 70 years of age (mean 32.7). In 44 subjects who stood upright for five minutes the plasma NE concentrations increased to 538±44 pg/ml. The authors also found a positive correlation for plasma NE levels and age. As a result of this it was suggested that experimental groups should be age matched when evaluating sympathetic function. Other studies have also reported increased plasma CA levels during postural changes from

supine to standing (DeQuattro et al., 1972 and Ziegler et al., 1976).

Cold Pressor Test

In 1941 Wolf and Hardy measured the relationship between pain and the rise in blood pressure during immersion of one hand in cold water. They found that as the temperature of the water was decreased the perception of the pain increased. The authors concluded that the rise in blood pressure could be quantitatively determined by the subjects' response to the pain. Wolf (1951) conducted an experiment with patients who had cerebral vascular lesions and patients with hysterical anaesthesia to determine whether the cold pressor response was a result of a central reflex or whether it was dependent on pain perceptions. He concluded that the cold pressor response was dependent on pain perceptions and was not the result of a reflex. In contrast, Winer and Carter (1977) discussed the cold pressor response as being a reflex mechanism involving lateral afferent tracts and the efferent SNS. The authors reported consistent increases in HR,BP, and plasma NE. Heart rate increased approximatley 10 beats per minute during the three minutes of hand immersion. Mean arterial blood pressure increased approximately 25 mmHg during the last minute of the cold tasks. Plasma NE concentrations increased approximately 100 percent by the third minute of the test.

LeBlanc et al. (1975) studied the cardiovascular

responses in adaptation to cold. Essentially they found decreased BP responses to acute cold after adaptation, indicative of important changes in the activity of the autonomic nervous system. They reasoned that adaptation improves the function of the CV system during acute cold exposure, improves peripheral circulation, and alleviates some of the psychological effects of cold stress.

Lovallo and Zeiner (1975) used the cold pressor test to examine peripheral vascular responses to acute cold. They found that when the blood vessels of the hand were dilated prior to cold pressor the stress response was vaso-constriction. They reasoned that these responses in the skin were caused by alpha-adrenergic receptor stimulation. However, when the vascular state of the hand prior to cold pressor was vasoconstriction, the response was either no change or a vasodilatory response to the stressor. This was thought to occur as a result of passive dilation in the blood vessels caused by an increased cardiac output and an associated BP increase. The authors concluded that three factors interact to determine the vascular response to a cold pressor test: the stressor itself, the ongoing level of vascular compensation and sympathetic tonus, and finally the prior history of exposure to the stressor.

Cuddy et al. (1966) reported consistent rises in blood pressure and heart rate during hand immersion. However, these authors found that only about half of the subjects responded to the cold pressor test with an increase in

arterial norepinephrine. This finding may be attributed to the lack of sensitivity of the catecholamine assay. A fluoremetric technique was employed whereas a more sensitive radioenzymatic technique has become a common procedure.

Lake et al. (1976) evaluated sympathetic function by measuring plasma NE. They found that plasma NE was increased by 137% above basal levels in 12 subjects as a result of a four minute cold presor test. Also, the authors noted that the subjects levied more complaints against the cold pressor test, but elicited less NE response than to an isometric handgrip test.

Isometric Handgrip Task

Lind et al. (1964) conducted a detailed study of the circulatory effects of isometric contraction. They found the cardiovascular response to static work similar to that of dynamic exercise. But, at the same level of work there was a greater rise in HR and BP in relation to the increase in oxygen uptake. The authors postulated that the high blood pressure might have resulted from the absence of vascular dilation in the working muscles in light of an indirectly measured increase in cardiac output. The rise in blood pressure resulted from a increased cardiac output because systemic vascular resistance showed no change. Lind and coworkers thought the progressive increase in blood pressure with increasing intensity of work was a physiological compensation to overcome the mechanical resistance to blood

flow so that the blood supply to the working muscle might be maintanined. Further, the authors state that their study and an earlier experiment (Humphreys et al., 1963) demonstrate the capability of the exercising muscle to invoke compensatory circulatory reflexes to increased blood flow to the affected area. The authors also noted that, as a result of an increase in perfusion pressure and an absence of any increase in blood flow through the nonworking musculature, a vasocontriction of this musculature may have taken place.

Freyschuss, (1970) studied the cardiovascular effects of isometric handgrip exercise with autonomic blockade in ten healthy males. Varing intensities of contraction (50%-100% of maximal voluntary contraction) were exerted for 5 to 10 seconds separated by rest periods. During the pre-drug study the mean increase in HR and aortic pressure during static exercise was 19 beats/minute and 15 mmHg, respectively. Under the influence of atropine the HR response was inhibited while the pressor response was only slightly lessened.

Administration of phentolamine did not affect the HR response, but did lower the aortic pressure response to isometric contraction. Administration of both drugs inhibited the HR and the aortic pressure response to isometric hand grip. Freyschuss concluded that the HR response to static contraction was initiated by a release from vagal tone and that the pressure response was affected by HR acceleration and a change in systemic vascular resistance as a result of SNS activation.

Martin et al.(1974) studied the autonomic nervous system's role in the hemodynamic response to isometric exercise. Twenty-five young adult males held a static contraction at 30% of their maximal voluntary contraction for three minutes during a control test, and under the influence of propranolol, practolol, atropine, and a combination of atropine and propranolol. During the control session HR increased approximately 17 beats/minute, and cardiac output increased by approximately 1.5 liters/minute without a change in stroke volume. Stroke volume was derived by dividing HR into cardiac output; which was indirectly measured by a dye dilution method. Systolic, diastolic, and mean blood pressures increased by approximately 27mm Hg, 26mm Hg, and 28mm Hg, respectively. The authors concluded that the HR response to sustained handgrip may have been controlled by a dual autonomic mechanism. Vagal withdrawal was responsible for the early response while the sympathetic activation occurred later. This mechanism has also been demonstrated during severe dynamic exercise. The blood pressure response in the control phase of static work was directly related to cardiac output. However, after administration of propranolol static work did not increase cardiac output. The rise in pressure was attributed to systemic vascular resistance.

To test this explanation, practolol, a cardioselective beta-adrenergic receptor-blocking drug was used during isometric work by Martin et al.(1974). The pressure response was similar to that of propranolol. Vasoconstriction as a

result of sympathetic stimulation was mentioned as a possible machanism for raising blood pressure during isometric contraction. The importance of SNS stimulation is dependent on several factors such as: autoregulation, baroreceptor reflexes, increased cardiac output, sympathetic vaso-constriction, and/or a combination of these. The authors noted that the functional capabilities of the SNS may have been dependent on the individual variation in reactivity of the sympathetic vasoconstrictors.

Kozlowski et al.(1973) suggested that there was increased SNS activity but little increment in medullary activity during static grip work. They attributed this finding to the increase in NE with only minor changes in E. Few et al.(1975) provided further evidence for increased SNS activity. Known concentrations of NE were infused and blood pressures were measured, then they calculated a linear regression equation. The rises in BP were not correlated with plasma catecholamine changes. The authors concluded that, because circulating catecholamine concentrations during static work were insufficient to account for the increases in BP, these plasma catecholamines represented an "overspill" from the sympathetic nerve endings. The activation of the SNS was suggested to have resulted from an afferent reflex mechanism located in the working muscle. Kozlowski and coworkers (1973) noted the increase in plasma NE during isometric exercise was greater than that during heavy bicycle ergometry work. The authors reported plasma NE

concentrations of approximately 1800 pg/ml after five minutes of static work, which was equivalent to plasma NE values during bicycle ergometer work at 1200 kpm/minute. The catecholamine concentrations reported in this study should be examined with caution. Rest and treatment values reported are much higher than those reported in later studies using more sophisticated assay techniques.

Lake et al.(1976) measured plasma NE during isometric handgrip exercise, in their evaluation of sympathetic neuronal function, using a sensitive radioenzymatic technique. At the end of a five minute handgrip test the net plasma NE concentrations reported were approximately 240±80 pg/ml. When the total plasma NE values were subtracted from the upright positioning values, wich immediately preceeded the isometric test, an 89% increase above the plasma NE values for standing upright was calculated.

Psychological Challenge

Public awareness of the effects of emotionally challenging situations in daily life has helped popularize the use of laboratory stressors that are emotional in nature. These emotional stressors can be used to test for physiological pathology. The reason for using psychological stressors, though artificial in nature, is to "mimic the emotional challenges of everyday life" (Cox, personal communication, 1980). Although several sub-classifications of psychological challenge situations have been defined this

review will focus on a reaction time task to avoid shock.

Nestel (1969) compared a group of hypertensives with a group of control subjects exposed to a mental stressor. Although this was considered to be a mild stressor SBP, DBP, E, and NE values for both groups exhibited increased responses to the task. However, Esler and Nestel (1973) reported no urinary NE response to a mental task. Although BP and urinary E excretion increased, the fact that urinary NE concentrations were not affected suggested to the authors that, a visual puzzle task was a poor SNS stimulant.

Lawler, Obrist, and Lawler (1975) conducted a study to evaluate the CV changes during pre-avoidance, avoidance, and post-avoidance of shock and to determine the cardiac sympathetic influence by measuring dp/dt in dogs. Heart rate, SV, and BP were found to be elevated throughout the experiment, exhibiting the greatest values during training. Several CV changes occurred as a result of behavioral stressors. The change in carotid pressure divided by delta time (dp/dt) was associated with sympathetic activity during stressful situations. The recorded cardiac output, total peripheral resistance, and BP responses to this situation were shown to be similar to the stress of mental arithmatic in humans (Fencl et al., 1959).

Obrist et al.(1974) used a reaction time-avoidance of shock task and a monetary reward system to provoke a group of controls and a group of subjects receiving beta-adrenergic blockade (propranolol). The ability to avoid a stressor may

be important with respect to the SNS response. The authors reported a consistent and substantial sympathetic effect using indirect measures such as the slope of the carotid pulse wave and HR in the control group, but found inconsistent sympathetic effects in the propranalol treated group. Obrist suggested that sympathetic excitation influenced HR and contratility but the sympathetic influence on the HR could only be evaluated under conditions with and without pharmacological blockade.

Obrist et al. (1978) utilized stressors that offered varying degrees of control. Thus, the physiological responses to active or passive stressors could be monitored. A shock avoidance task was employed as the active stressor. The subject could maintain control during this task by reacting to a light signal within a specified time period. Control was either minimal or not possible during the passive stressors that consisted of a pornographic film and a cold pressor test.

During the active stressor heart rate, carotid dp/dt, and SBP were elevated to a greater extent. The difference in response to active and passive stressors was greatly diminished during sympathetic blockade. The authors concluded that control over a stressor was associated with SNS activity in the cardiovascular system while the passive stressors were controlled by vagal activation.

Manuck et al. (1978) manipulated the difficulty of an active and a passive experimental task to delineate the

physiological responses to active and passive stressors. Change scores for SBP were greater for the control-difficult task group. They concluded that control of a task and a specific level of difficulty are neccessary to elicit an increase in SBP.

II. PHYSIOLOGICAL RESPONSE TO EXERCISE TRAINING

Many investigators have reported consistent results concerning the cardiovascular and catecholamine responses to exercise training (see table 1). Heart rate , BP, and plasma catecholamine responses to exercise have been shown to decrease as training progresses. After training endurance times are increased while the CA response to absolute work intensities are decreased. The hormonal responses to exercise following training increase the cardiovascular and metabolic efficiency of the system (Hartley et al., 1972; Galbo et al., 1977). The development of increasingly sophisticated assay techniques has enabled researchers to more consistently and accurately measure plasma CA during dynamic exercise. Ostman, Sjostrand, and Swedin, (1972) found that as a consequence of exercise training, trained rats exhibited significantly less increases in urinary catecholamine excretion in response to an exercise bout. They interpeted this finding as an increase in SNS efficiency and as an indication of sympatho-adrenal adaptation to chronic exercise.

TABLE 1. Response of Plasma Catecholamines to Training During Exercise

			PRE-TRAINED			TRAINED	
Study	N	Train Period	Workload	E pg/ml	NE pg/ml	E pg/ml	NE pg/ml
Peronnet et al. (1981)	10	20 wk	735 kgm/min		1371±286		687±64
			158 beats/min		1371±286		1729±371
Hickson et al. (1979)	8	20 wk	1000 yd swim	770±100	3380±540	90±20	1250±150
			200 yd swim	2440±630	5580±860	630±120	4950±960
Winder et al. (1979)	6	9 wk	58% mVO2	640±40	1810±400	290±30	810±240
Winder et al. (1978)	6	7 wk	95% mVO2	530±130	2950±320	140±30	1600±90
			100% mVO2			1240±30	4040±670
Galbo et al. (1977)	51 rats C and T	12 wk	45 or 90 swim	4420-15670	2500-6100	780-2960	700-2220

Hartley et al. (1972) measured plasma E and NE and several other hormonal responses to prolonged work before and after a seven week training program. Heart rate, and plasma NE responses to absolute work and to exhaustion were decreased after training. The increased endurance with training was suggested to be at least partially a result of endocrine adjustments. These changes were thought to spare muscle glycogen and maintain glucose and free fatty acid availability. Winder et al. (1979) reported that the time course for lowered plasma CA and plasma glucagon were similar, approximately three weeks after training began. This provides further evidence for a possible metabolic adaptation to exercise mediated by the SNS.

Galbo et al. (1977) reported that the hormonal response to exercise was lowered as a result of increased glucose levels. They concluded that increased lipolysis and glycogen depletion may proceed without corresponding changes in glucagon and insulin levels in response to increased adipose tissue sensitivity to CA. Also, the trained rats exhibited decreased E and NE responses to 90 minutes of swimming.

Again, Hartley (1975) discussed the decrements in E and NE concentrations after a program of training. Norepinephrine concentrations were decreased at any absolute oxygen uptake but unchanged at particular relative workloads. Hartley suggested that sympathetic activity in response to exercise is lessoned after training. Also it was hypothesized that lessoned neuromuscular activity may have

corresponded to decreased sympathetic activity.

Winder et al. (1978) examined the plasma CA-HR relationship during a seven week training program. They found that the majority of the training induced decrease in plasma CA occurred at the end of the third week of training. The increase in NE after three weeks of training was approximately one-half of the pretraining response. The exercise HR continued to decline after the plasma CATS response had stabilized. This was attributed to increased parasympathetic tone, to reduced CA sensitivity of the heart, or to intrinsic adaptations. Also, the reduction in plasma CA and exercise HR was hypothesized to be somewhat affected by intramuscular adaptions. Hickson et al. (1979) utilized experienced swimmers to show that decreased SNS activity was in fact a result of training and not a familarity affect.

Peronnet et al. (1981) evaluated plasma NE of subjects at rest and during exercise before and after a twenty week training program. Resting HR was slightly decreased; plasma NE concentrations did not change after training. Plasma NE concentrations were not affected at the same relative workload but were decreased for a particular absolute workload. However, Winder et al. (1978) conducted a similar study, but did not report lower plasma NE concentrations at specific relative submaximal workloads after training. Peronnet and co-workers concluded that SNS activity was linked to exercise requirements. This was further eluded to by high correlation coefficients among renal and splanchnic

blood flows, HR, relative work load, and plasma NE concentrations during exercise. Because of the relationship between SNS activity and exercise requirements, the authors speculated that the sympathetic response to work was influenced by precise control mechanisms.

III. AEROBIC TRAINING INFLUENCE ON PHYSICAL AND PSYCHOLOGICAL STRESSORS

The effect physical training has on the attenuation of the SNS and cardiovascular responses to exercise is well documented. Whether aerobic training affects the CV and CA responses elicited by different and/or additional stressors has both clinical and theoretical interests. Regular physical exercise may play a role in the reduction of coronary heart disease and other cardiovascular diseases. Theoretically, the SNS and the CV system adjustment mechanisms to stressors other than exercise are of interest. Two divergent hypotheses have been formulated to explain the SNS response to different or novel stressors after adaptation to previous stressors has taken place. Hans Selye made popular the term cross resistance. He thought stressors were interchangeable so that adaptation to one stressor could be carried over to another stressor. He theorized that the response to a stressor was general and could be elicited by any number of events.

Selye (1961) treated animals with small doses of drugs

to produce a stress reaction. The doses, taken alone, were too small to produce a stress reaction but subsequent exposure to another stressor elicited massive necroses. These induced necroses failed to occur if the animals were exposed to the identical stress treatments prior to the specified treatment. This mechanism was called "simple resistance" because the animals became insensitive to a certain stressor following pretreatment with the same stressor. The phenomenom of cross resistance was illustrated when necroses were prevented by pretreatment with a different stressor from that used as an eliciter.

Ostman and Sjostrand (1975) studied the effects of physical training induced cross tolerance to acute exercise in rats. The authors suggested that training did induce cross tolerance to acute cold, but cold-acclimation did not lead to a cross tolerance to acute exercise. Adaptive changes associated with training included a greater economy of sympathetic activity. This was attributed to increased sensitivity of the tissues to the vascular and metabolic actions of NE. The trained animals developed a greater tolerance to conditions that required an increased neurotransmitter secretion for maintenance of homeostasis. The authors concluded that increased levels of physical activity in mammals led to better fitness to withstand cold and possibly other stressful conditions, but that cold-acclimation did not produce a cross resistance to acute exercise strain.

LeBlanc et al. (1978) studied the effects of physical fitness, age, and sex in response to acute cold. A partial correlation analysis revealed that the level of fitness (VO2max) affected the response to a cold hand test. The fit subjects exhibited a reduced increase in BP in response to the cold hand test and a reduced fall in skin temperature during a cold face test. These findings indicated that vasoconstriction was diminished in the fit subjects. This was considered to be the result of reduced sympathetic activity or a reduced sensitivity of the blood vessels to catecholamines. Another study by LeBlanc et al. (1977) did not substantiate the sensitivity hypothesis. The blood pressure response to infused NE was not different in trained and untrained subjects.

The previous studies have shown attenuated CA responses to secondary stressors. Kvetnansky (1980), on the other hand, holds a different view of the stress response. He states that repeated exposure to a particular stressor results in enhanced activity of the CA synthesizing enzymes (Kvetnansky et al., 1970). Continual chronic exposure to a stimulus resulted in a diminished SNS response to that stressor. He hypothesized that this was ultimately the result of a central nervous system (CNS) adaptation. However, when a new stimulus was presented to the system the CNS was dishabituated and exaggerated peripheral SNS responses were exhibited because of the enhanced CA production and storage capacity (Kvetnansky et al., 1971; Kvetnansky, 1980).

The functional importance of this phenomenom has yet to be determined. Also, the question remains as to whether increased CA levels are advantageous or harmful to the system.

Little systematic study of repeatedly stressed animals or humans has taken place. However, several studies have been published concerning the effects of aerobic conditioning and the physiological response to physical and psychological stressors. Chronic exercise can be viewed as a repeated stressor. This permits the data to be evaluated with regard for the hypotheses of Kvetnansky.

Longhurst et al. (1980) measured HR, BP, and several other indirect cardiac parameters in two groups of weight trainers, two groups of control subjects, and a group of long-distance runners during rest and isometric work. In general, they found that the aerobically trained group responded differently than controls or athletes who weight trained. The weight-trained groups and the control groups responded similarly. The results of this study suggested that there were no differences between any of the groups at rest or during isometric contraction for SBP and DBP. However, the HR at rest and during time 1/2 and time max of the work period was significantly lower in the trained group. Also, the runners' double product was lower at rest and throughout static exercise.

The interpetation of these data, offered by the authors, may be unsubstantiated. The HR change scores from rest to

exercise showed that the groups may not have responded differently. The change scores for HR were very similar in all groups. The differential HR response noted by the authors during static effort may be a function of the differences in the HR of the trained group at rest. Therefore, the trained group may not have exhibited a different response to exercise, but only at rest. Because double product is a function of HR X SBP, the lowered response exhibited by the trained group for double product can be attributed to the relative resting bradycardia exhibited by the runners.

Morgan et al. (1982) trained a group of subjects to assess the effects of aerobic exercise on the CV response to isometric work. To assess the role of the SNS in this process beta-adrenergic blockade was used. Both isometric hand grip and isometric quadriceps exercise were used as the static stressors. The training program was held three days per week for five weeks. The exercise consisted of treadmill work, bicycling, and bench stepping. In the control group VO2max was increased 21%. Maximal oxygen uptake was unaltered by training in the propranolol treated group. The propranolol treated group exhibited decreased HR and SBP responses to static quadriceps work after training. Also, no changes were seen during isometric work in response to dynamic training. The control group's response to isometric hand grip was not changed as a consequence of a lower body aerobic conditioning program. This finding was discussed as

a specificity of training phenomenon. Morgan and co-workers concluded that beta-adrenergic activity was necessary for CV modifications during dynamic and/or isometric training.

Sinyor et al.(1983) examined aerobically trained and untrained subjects during a mental arithmetic test. They hypothesized that since trained persons respond to exercise (physical) stress more efficiently, they would respond to emotional situations more efficiently. Heart rate, plasma E and NE, and other biochemical measures were taken. Aerobic fitness was estimated by a nomogram so that a true index of fitness could not be established. The authors suggested that the groups exhibited different response profiles. The HR's of trained subjects returned to baseline more quickly and peak NE response occurred earlier. However, cardiac and bichemical measures were similar in both groups during the task. The interesting finding in this study was that the plasma E and NE levels were generally higher in the trained subjects.

CHAPTER III

METHODS

I. SELECTION OF SUBJECTS

Sixteen college-aged males participated in this investigation. Eight subjects were active but untrained individuals. These subjects did not participate regularly in any form of aerobic exercise. The other eight subjects were well-trained endurance athletes selected on the basis of a maximal oxygen uptake of at least 60ml(kg min)-1.

Maximal Oxygen Uptake Tests

Each subject took a maximal oxygen uptake test. Prior to the treadmill test each subject was shown the equipment and signed a consent form. Following this the EKG electrodes were placed on the subject, then he rested in a chair next to the treadmill for 10 minutes. A brief warm-up followed the rest period. During this period the subject walked and/or ran on the treadmill until he was comfortable. A two minute recovery period preceeded the actual test.

The trained subjects took a continuous treadmill test. The subjects ran at approximately 250 meters per minute on a starting grade of 0%. The grade was increased 2.5% every two minutes until exhaustion.

The untrained subjects took a Super Standard Balke test. These subjects walked at 100 meters per minute on a starting grade of 4%. The grade was increased 2% every two minutes until exhaustion. One minute bags of expired ventilatory gases were collected continuously from the second minute of the test until exhaustion for trained and untrained subjects.

Measurement of Oxygen Uptake

We measured oxygen uptake by the open circuit method using meteorological balloons and a Daniels valve. An Applied Electrochemistry model S-3A O2 analyzer and a Beckman model LB2 CO2 analyzer were used to measure the gas fractions. The analyzers were calibrated with standardized gases previously measured by the Scholander method. A Parkinson-Cowan CD4 dry gas meter and a Narco Biosystems DMP-4A recorder was used to measure and record inspired minute ventilation. Oxygen uptake was calculated according to the Haldane transformation.

II. PROCEDURES

Experimental Protocol

All subjects reported to the laboratory 2-3 hours following their last meal. They were asked to refrain from coffee, tea, and/or cola drinks and cigarettes the day of the test. Upon arrival to the laboratory heart rate electrodes and a blood pressure cuff were placed on the subjects.

The subjects sat in a reclining chair for placement of the catheter. After placement of the catheter in the dorsal aspect of the left hand the subjects were given a twenty minute rest period. During the rest period the subjects remained in a semi-reclined position. Attention was directed at the subjects' position to assure that all subjects were in the same degree of recline. At the conclusion of the twenty minute rest period a 3-4ml blood sample was taken. Also, during the final two-minutes of rest, heart rate as well as systolic and diastolic blood pressure measurements were recorded. Thereafter, heart rate was recorded continuously throughout each of the experiments.

Orthostatic Stressor

Following the rest period the subjects stood quietly for 10 minutes. Care was taken so that muscular movement to the standing position was minimized as much as possible. Blood was sampled at minutes 1:00-1:30 and 9:30-10:00. Blood pressures were recorded at minutes 0:15-0:45, 2:00-2:30, 4:30-5:00, 7:00-7:30, and 9:00-9:30. Each subject rested for 10 minutes immediately after the orthostatic task. During the last three minutes of this rest period blood pressures were recorded. When heart rate and blood pressure approached baseline the next test was started.

Cold Pressor Test

Following the rest period, the subjects placed their

right hand, wrist deep, in an ice bath at a temperature of approximately 5 C for two minutes. A blood sample was collected during the last half of the second minute of the test. A Blood pressure recording was taken from minute 1:45-2:00. Heart rate and blood pressure recordings were monitored during the last three minutes of a five minute rest period following the cold-pressor test. The next task was started when these recordings were at or near baseline.

Isometric Handgrip Test

A workload of 30% of maximal hand grip strength, based on the mean of three maximal isometric handgrip contractions, was calculated for each subject. They held the calculated load for five minutes. A blood sample was taken at minute 4:30-5:00. Arterial blood pressure measurements were taken at minutes 0:15, 1:00-1:30, 2:30-3:00, and 4:00-4:30. Subsequent to the isometric hand grip test there was a 10 minute rest period. During the last three minutes of this rest period heart rate and blood pressure readings were checked to determine when to start the next test. Also, a blood sample was taken during the final minute of this rest period.

Reaction Time Avoidance Task

The subjects were told that a rapid button push in response to a light signal was required to avoid a one-second, 3.5mA shock to the lower leg. They were told

that a small red light would turn on at random intervals during this task and to react as quickly as possible. If they improved upon their preceding time or approached their best they would avoid all shocks. If they were slower than their preceding time they might receive a shock, but it would come 5 to 10 seconds after the light reaction signal, not immediately. After all questions were answered, the electrode was placed on the lower right leg. If this was the first reaction time task of the session, the subjects were told that they would receive three practice trials to acquaint them with the procedure. After the practice trials the subjects were given a sample shock. The subjects were given notice of the application of the sample shock then the experimenter signalled the start of the session. Each subject received 15 trials. The inter-signal interval averaged 15 seconds, with a range of 10 to 20 second intervals. The frequency of shocks was held to two per subject excluding the sample shock. No shocks were given during the first five trials, one occured during the next three trials and one in the succeeding three trials. In all cases, the shocks were given after those trials in which the subject failed to show improvement with respect to the previous trial.

Reaction Time Appetitive Task

The instructions and protocol were essentially the same as for RT-AV. The major difference was the potential to win

money rather than receive a shock. If the subjects responded at or near their best the display screen flashed 1.00 five to ten seconds after the criterion response was made. They were told that, this signal represented one-dollar, and the accumulated total would be paid to them after completion of the experiment. If the RT-AP task was given before RT-AV, practice trials as were described for RT-AV were given before the actual session began.

After all tasks were completed and the last rest period had occurred the heart rate electrodes, the blood pressure cuff, and the catheter were removed from the subjects. Each subject was paid the money he had earned and thanked for his participation.

Experimental Design

Each subject was exposed to five experimental tasks, separated by 5 or 10 minute periods of rest. The order of the tasks was determined by a Latin square design so that there were four possible combinations: 1. ISO, C-P, RT-AV, RT-AP; 2. C-P, RT-AV, RT-AP, ISO; 3. RT-AV, RT-AP, ISO, C-P; 4. RT-AP, ISO, C-P, RT-AV. The subjects were randomly assigned to the task orders such that equal filling occurred. The orthostatic stress task was always conducted first in the order of tasks, thus it was not included in the Latin square design of tasks.

Statistical Procedures

The analysis of the data involved the use of multiple t-tests for independent means to test for statistical differences between the trained and untrained groups for each of the experimental tasks (Bruning and Kintz, 1977).

III. APPARATUS AND MATERIALS

Experimental Chamber

The experimental sessions were conducted in a small room adjacent to the room housing the recording equipment. The experimental room contained a lounge chair, a small shelf, and a table. The ice container was placed to the right of the lounge chair to allow immersion of the right hand into the ice bath. The table was placed to the left of the reclining chair for placement of the catheterized hand. Also, a curtain was placed in the area of the left arm of the subject to minimize the effect of blood withdrawal.

Physiological Monitoring Equipment

Heart rate was recorded with a Grass 7D4F preamplifier as part of the Grass 7D polygraph. Three bipolar regular electrodes tranduced the EKG. One electrode was placed on the right side below the clavicle, another over the fifth intercostal space on the left side of the rib cage and the ground electrode was placed over the fifth intercostal space on the right side of the rib cage.

The blood pressure was measured with an Arteriosounde blood pressure monitoring device. The principle of operation was based on the Doppler effect. Systolic and diastolic pressure were registered on two separate mercury columns which held the last detected value. This device was calibrated several times against a mercury manometer for each subject.

Handgrip Dynamometer

The dynamometer was manufactured by the Stoelting Co. It was calibrated by direct force application.

Shocker

The shocker used in the RT-AV task was a Lafayette model #82426. It had a maximum output of 5mA, with a voltage source of 2500 VAC. The output meter was calibrated with known resistances and an ammeter. A single electrode was connected to the subject via an output in the rear panel. The concentric circle electrode allowed a maximum current density of 4mA per cm2.

Reaction Time

The measurement of reaction times, delivery of signals, control of shock, and reward signals were done with transistor, transistor logic (TTL). The components were housed in a small plexiglass box situated in the recording room.

Catheterization

The catheterization process outlined below was used for each subject.

A 21-guage disposable needle and a 5ml plastic syringe were used to draw 4.0ml of sodium heprin from its vial. This volume was added to the vial containing 30ml of sterile saline. Another 5ml syringe and a 21-guage needle were used to withdraw 5ml of the heprinized saline into the syringe.

After determination of the vein to be punctured, the skin was cleansed with alcohol and the catheter (Deseret Minicath-PRN Catheter, 3/4 inch, 21-guage) was secured in place by tape. Approximately 1-2ml of heprinized saline was infused into the vein to clear the catheter of blood.

A 3-4ml blood sample was taken during specified time intervals of each experimental task. The syringe containing the sample was taken from the catheter and replaced by a syringe containing the heprinized saline to flush the catheter. This process was repeated for each sampling period.

Blood Samples

Blood samples were taken as previously outlined above. During each sampling period approximately 3-4ml of blood were taken for determination of plasma epinephrine, and norepinephrine.

Immediately after each sample of blood was withdrawn it

was placed in cold test tubes containing EGTA and glutathione. These were added to give a final concentration of 1.8mg and 1.2mg per ml of blood, respectively. The plasma was immediately separated by centrifugation at 4000rpm for ten minutes and placed into plastic tubes, capped, and frozen for analysis at a later date.

Blood Analysis

The catecholamine analysis followed a modification of the radioisotope assay developed by Peuler and Passon(1975). A 100pg E and NE standard was run as an internal standard with every third plasma sample. The interassay coefficient of variation for norepinephrine in this study was 12%, while that for epinephrine was 11%.

CHAPTER IV

RESULTS

I. BIOGRAPHICAL INFORMATION

Data on subject age, height, and weight are listed in Table 2. There was a significant difference between the groups for age ($p<0.005$). The trained group had a mean age of 23.8 while the untrained group had a mean age of 19.9. There was also a significant difference between the groups for the variable of weight ($p<0.05$). The mean weight of the untrained group was 78.0 kg while that of the trained group was 65.8 kg. There was no significant difference between groups for the variable of height ($p<0.67$).

II. OXYGEN UPTAKE

Data on mean maximal oxygen uptake are listed in Table 2. The data indicate a highly significant difference between the trained and untrained groups. The VO2max for the trained group was calculated to be 4.65 liters per minute as compared to 3.54 liters per minute for the untrained group ($p<0.0003$). When the VO2max was related to individual body weight the trained group exhibited a mean VO2max of 70.63 mlO2(kg min)-1 while the mean VO2max of the untrained group was 45.54 mlO2(kg min)-1 ($p<0.0001$).

TABLE 2. Biographical Information.

	AGE (yrs)	HEIGHT (cm)	WEIGHT (kg)	VO2max ml(kg min)-1	l/min
C	19.9±2.8	177.5±3.6	78.0±1.5	45.5±1.1	3.54±0.1
T	23.8±0.9	179.1±2.5	65.8±2.2	70.6±0.8	4.65±0.2

Values are mean ± SEM.

III. EPINEPHRINE

Data on plasma epinephrine concentrations during rest and the experimental tasks are listed in Table 3. No significant differences were observed at rest or for any of the experimental tasks between the trained and untrained groups. Figure 1 illustrates this point. As can be seen from Figure 1, however, epinephrine levels for both groups were increased above rest values during all of the experimental tasks. Also, from Figure 1 it can be seen that the trained group exhibited small but consistantly higher epinephrine levels during most of the experimental tasks.

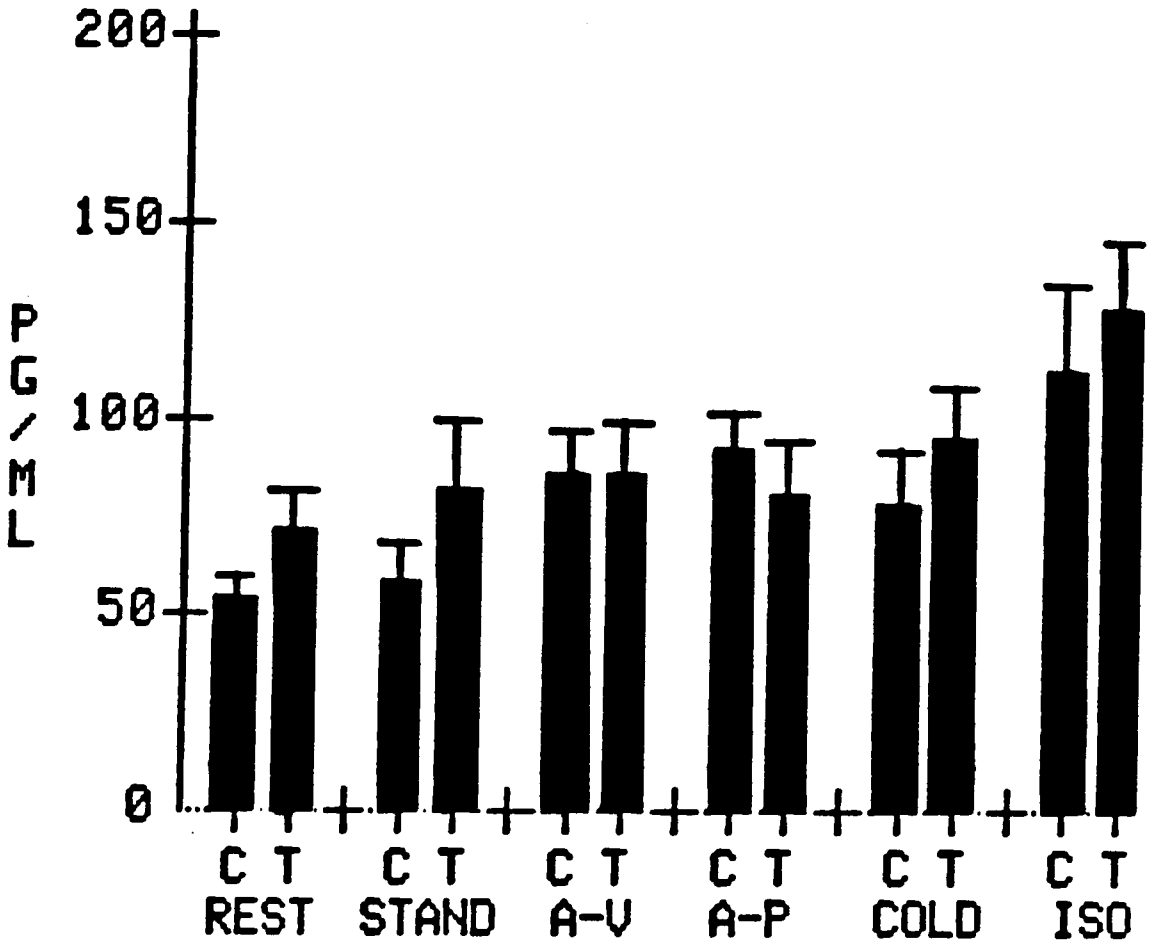
IV. NOREPINEPHRINE

Analysis of the data on the plasma norepinephrine concentrations during rest and the experimental tasks indicates that there were no significant differences between the experimental groups (Table 4). Again, as with the epinephrine data, the rest values for norepinephrine were less than the norepinephrine values for all of the experimental tasks (Figure 2). Further, the trained group exhibited non-significant but consistently higher norepinephrine levels during the experimental tasks, except during the orthostatic task (Figure 2).

TABLE 3. Plasma Epinephrine Concentrations During Rest and the Experimental Tasks.

	REST	STAND	RT-AV	RT-AP	COLD	ISO
C	53±5	58±10	91±11	92±10	77±14	112±14
T	71±11	81±14	94±16	82±13	95±13	128±21

Values are Epinephrine in picograms per milliliter of blood expressed as mean ± SEM.



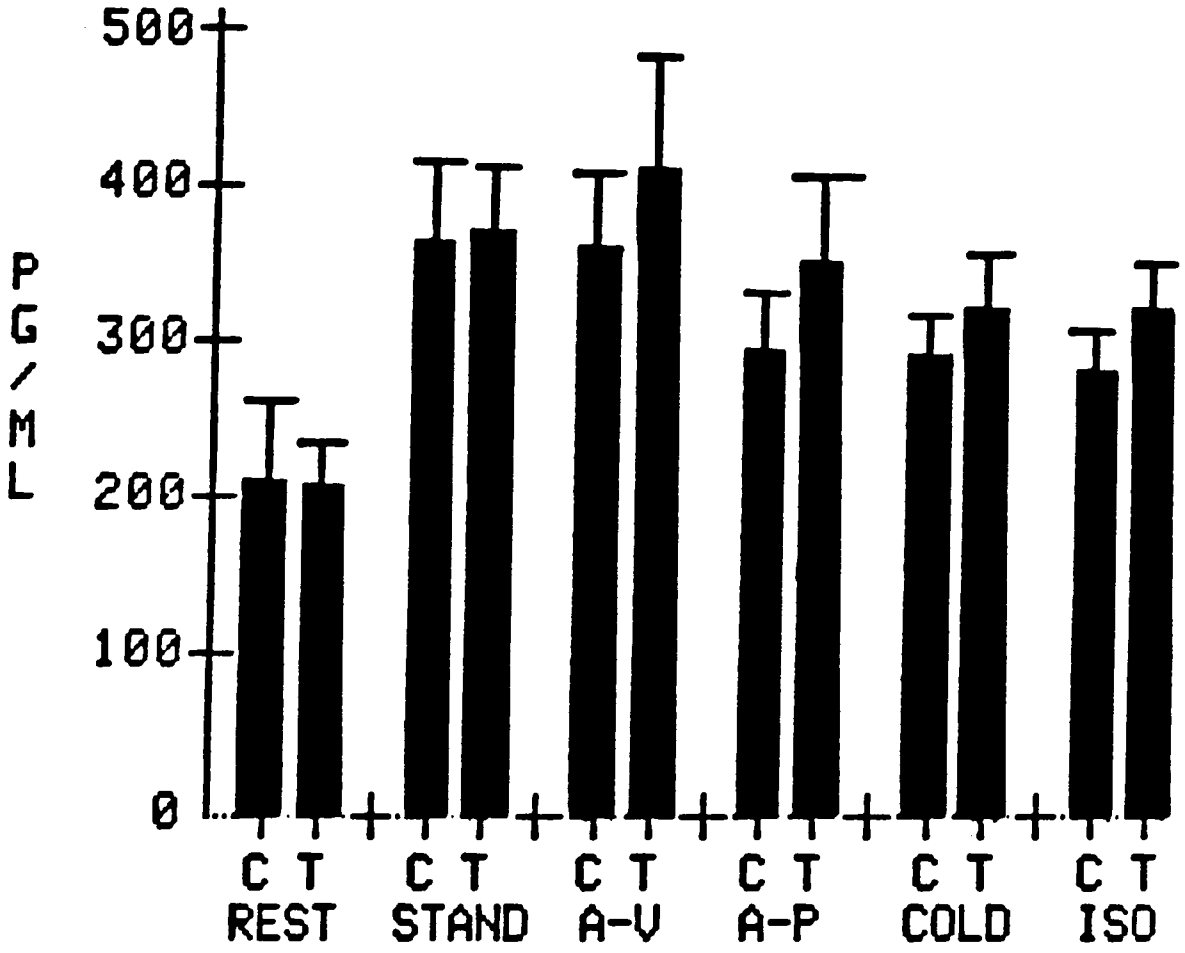
Values are epinephrine in picograms per milliliter of blood expressed as mean ± SEM.

FIGURE 1. Epinephrine Concentrations for Each Task

TABLE 4. Plasma Norepinephrine Concentrations During Rest and the Experimental Tasks.

	REST	STAND	RT-AV	RT-AP	COLD	ISO
C	210±29	362±23	359±49	293±28	290±25	279±26
T	201±22	368±41	409±85	356±62	321±40	318±36

Values are Norepinephrine in picograms per milliliter of blood expressed as mean ± SEM.



Values are norepinephrine in picograms per milliliter of blood expressed as mean ± SEM.

FIGURE 2. Norepinephrine Concentrations for Each Task

V. HEART RATE

Mean heart rate data are listed in Table 5. Heart rates were averaged during each experimental treatment to get mean values. The mean heart rate at rest was found to be significantly lower for the trained group as compared to the untrained group ($p<0.05$). There were no significant differences between the groups during any of the experimental tasks. As can be seen from Figure 3, the untrained group exhibited non-significant but consistantly higher mean heart rates for each of the experimental tasks.

Figure 4 represents a comparison of the peak heart rate responses for the experimental groups during rest and each of the experimental tasks. Although the values for peak heart rate at rest approached significance ($p<0.06$), there were no significant differences between the groups for any of the experimental tasks. The untrained group exhibited consistently higher peak heart rates for each of the dependent variables. Also, the heart rate values taken during the experimental tasks were higher than those taken at rest (Figure 4).

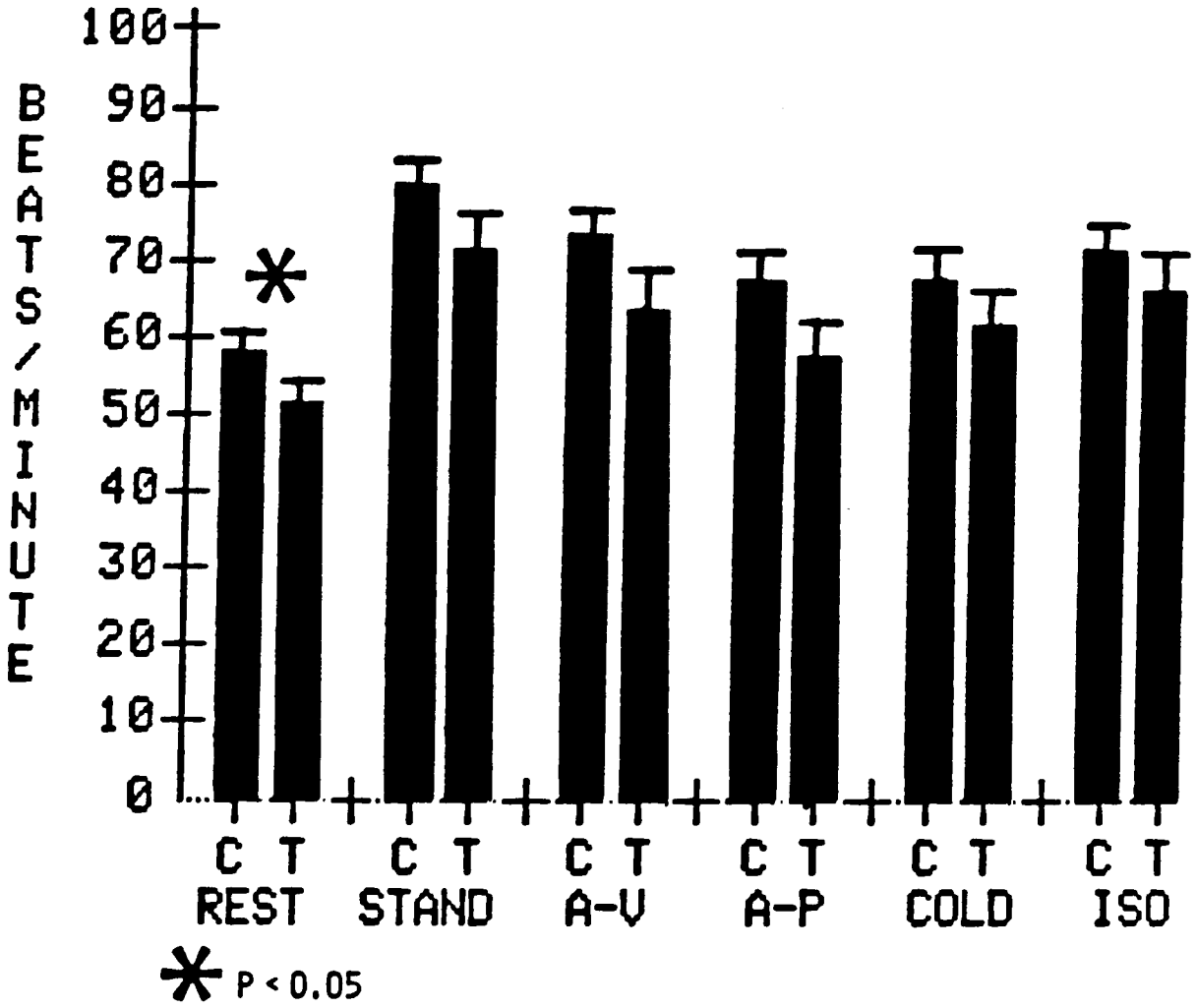
VI. SYSTOLIC BLOOD PRESSURE

Table 6 lists the peak systolic blood pressure measurements for rest and for each of the experimental tasks. The measurements taken during the experimental tasks were

TABLE 5. Mean Heart Rate Response to Rest and the Experimental Tasks.

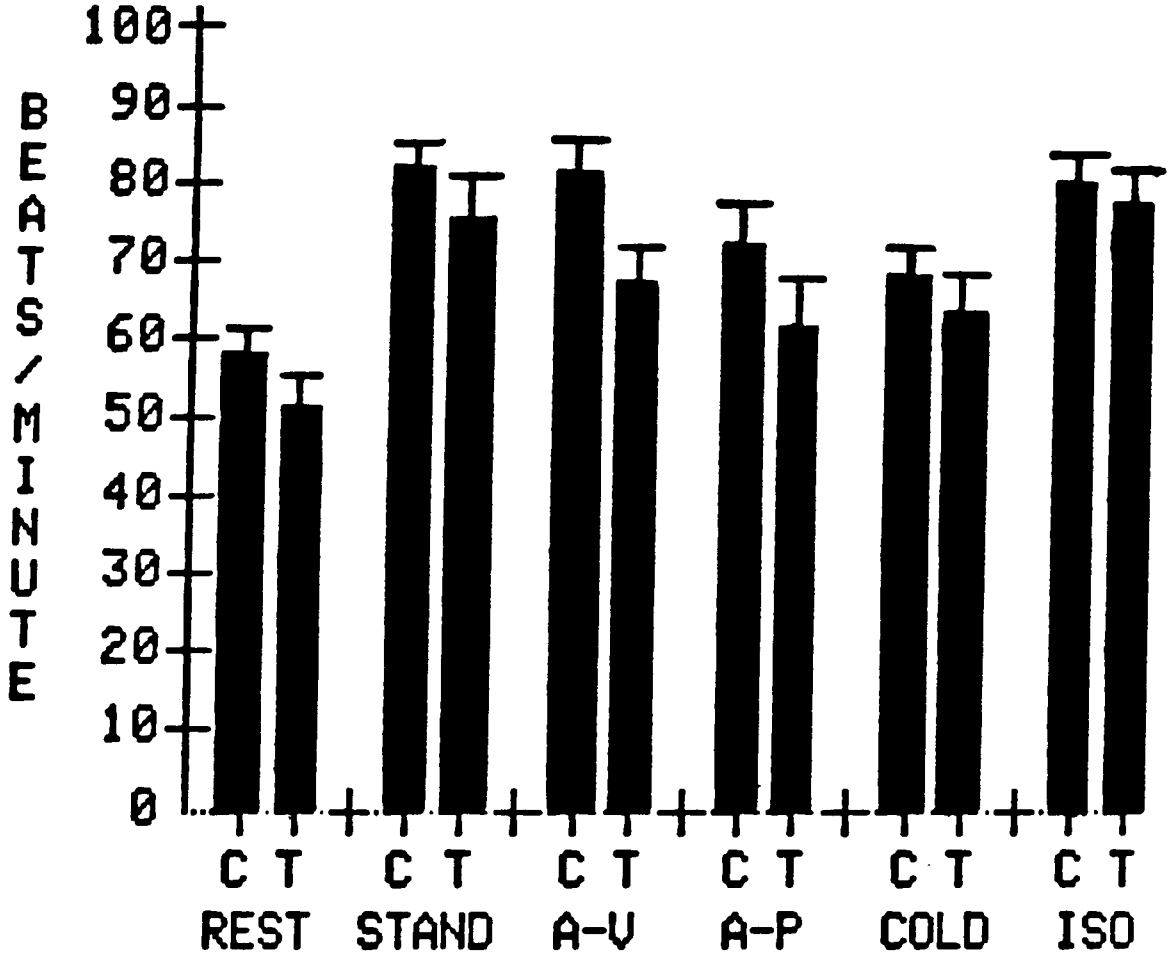
	REST	STAND	RT-AV	RT-AP	COLD	ISO
C	59±2	80±3	73±2	67±3	67±4	71±3
T	51±2	71±5	63±5	57±4	61±4	66±5

Values are Heart Rate in beats per minute expressed as mean ± SEM.



Values are heart rate in beats per minute expressed as mean ± SEM.

FIGURE 3. Mean Heart Rates for Each Task



Values are heart rate in beats per minute expressed as mean ± SEM.

FIGURE 4. Peak Heart Rates for Each Task

TABLE 6. Peak Systolic Blood Pressure Response to Rest and the Experimental Tasks.

	REST	STAND	RT-AV	RT-AP	COLD	ISO
C	103±3	134±7	140±8	132±6	138±3	143±3
T	113±3	132±3	138±9	128±6	141±5	154±8

Values are peak Systolic Blood Pressure in millimeters of mercury expressed as mean ± SEM.

higher than the measurements taken at rest. There were no significant differences between the groups either at rest or for any of the experimental tasks (Figure 5).

Data on mean systolic blood pressure were consistent with those of peak systolic blood pressure in that there were no significant differences between the groups for any of the experimental tasks. The systolic BP recordings were averaged during each experimental treatment to get a mean value.

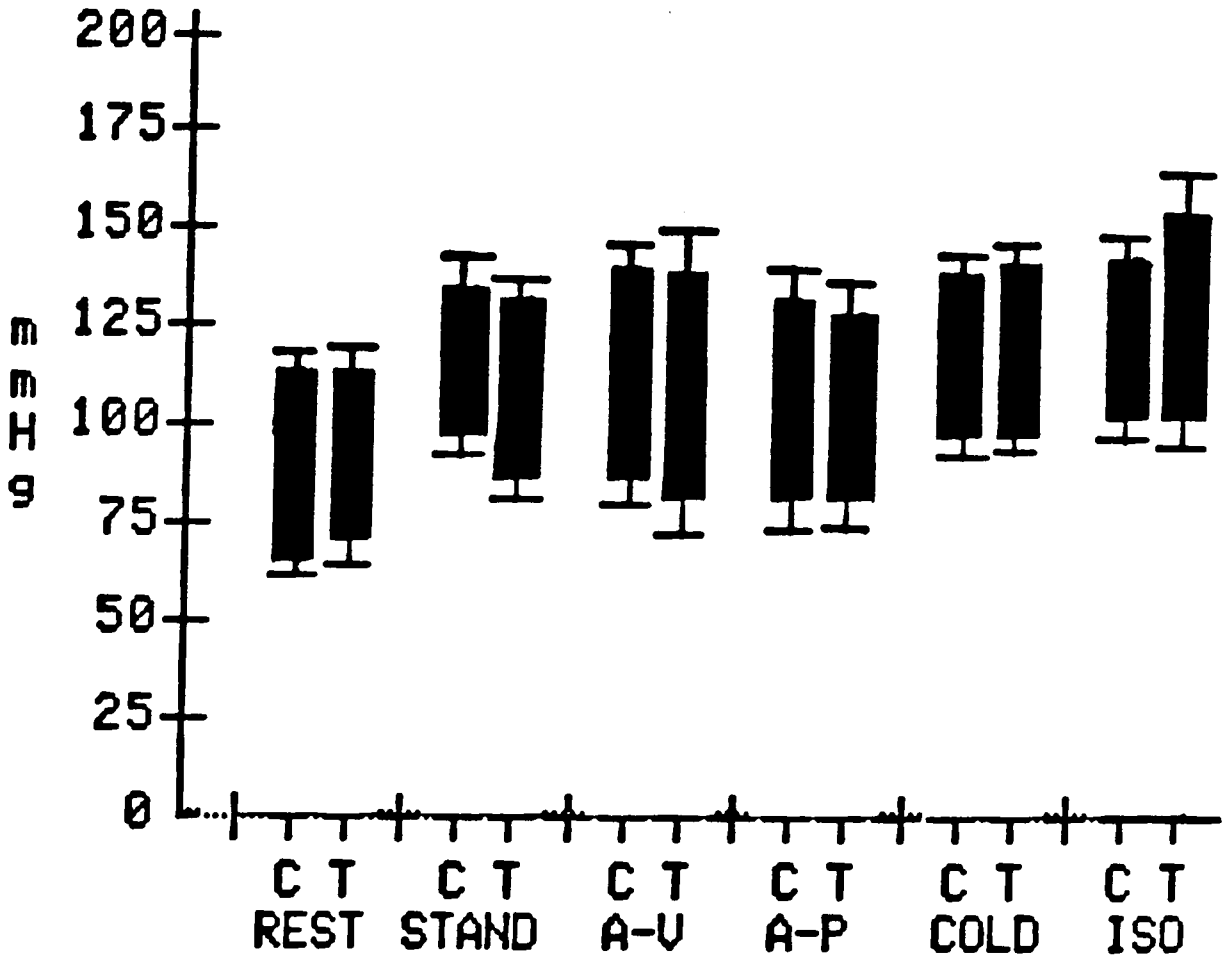
VII. DIASTOLIC BLOOD PRESSURE

Data for peak diastolic blood pressure are listed in Table 7. There were no significant differences between the groups for any of the dependent variables.

Also, the mean diastolic blood pressure recordings between the groups were not significantly different at rest or during any of the experimental tasks. However, as can be seen from Figure 5, the mean diastolic blood pressure recordings taken during the experimental tasks were higher than those taken at rest.

VIII. MEAN ARTERIAL BLOOD PRESSURE

Peak mean arterial blood pressure data are listed in Table 8. No significant differences were observed between the groups during any of the experimental tasks.



Values are peak systolic and diastolic blood pressure expressed in millimeters of mercury as mean ± SEM.

FIGURE 5. Peak Systolic and Diastolic Blood Pressure Responses for Each Task

TABLE 7. Peak Diastolic Blood Pressure Response to Rest and the Experimental Tasks.

	REST	STAND	RT-AV	RT-AP	COLD	ISO
C	67±2	99±9	87±5	84±3	100±4	103±4
T	72±3	90±3	86±4	84±4	97±3	105±5

Values are peak Diastolic Blood Pressure in millimeters of mercury expressed as mean ± SEM.

TABLE 8. Peak Mean Arterial Blood Pressure Response to Rest and the Experimental Tasks.

	REST	STAND	RT-AV	RT-AP	COLD	ISO
C	82±2	110±9	105±6	100±3	113±3	116±4
T	85±3	106±3	101±4	98±4	111±3	121±5

Values are peak Mean Arterial Blood Pressure calculated by: peak diastolic blood pressure + 1/3 (peak systolic blood pressure - peak diastolic blood pressure) in millimeters of mercury expressed as mean ± SEM.

CHAPTER V

DISCUSSION

The primary focus of this investigation was to determine whether a high state of aerobic fitness induced a cross tolerance to distinct physical and psychological stressors. In an attempt to clarify the role of cross resistance as a physiological phenomenon trained and untrained college-aged males were subjected to physical and psychological laboratory stressors that had previously been shown to elicit cardiovascular and catecholamine responses. During these tasks E, NE, HR, and systolic and diastolic BP measurements were taken to assess hemodynamic and SNS responsiveness to these stressors. This design permitted the study of a number of stressors and facilitated discussion as to whether participation in a chronic exercise program does, in fact, influence the physiological response to other stressors.

The physical characteristics of the two groups of subjects in this study were different. The mean age of the trained group was slightly but significantly greater than the untrained group. This observation is of minimal importance when the narrow age range of the subjects is taken into account and the fact that all subjects were considered to be young adults. Also the trained group of subjects weighed significantly less than the control group. Although the difference between the groups for body weight was significant

the magnitude of the difference was relatively small considering the nature of the two groups. The largest and most significant difference between these groups was maximal oxygen uptake. The trained group of subjects exhibited a VO2max approximately 75% greater than that of the untrained subjects. This factor was of critical importance to the study as VO2max was considered to be the variable upon which distinctions between the groups were made.

Although the two groups of subjects were physically different the measured physiological responses to the experimental tasks were for the most part not significantly different.

I. REST

The mean resting heart rate of the trained group was significantly lower than that of the untrained group. This observation was not surprising as one of the hallmarks of the endurance athlete is a slow heart rate at rest(Lewis et al., 1980). Many studies have shown that endurance athletes exhibit a resting bradycardia(Scheuer and Tipton, 1977).

The mean resting heart rate values of the groups differed but arterial systolic and diastolic BP and plasma catecholamine concentrations did not significantly differ. Also plasma epinephrine and norepinephrine values at rest were in general agreement with the existing literature (Cryer et al., 1974; Lake et al., 1976; Peronnet et al., 1981; Goldstein et al., 1982).

II. ORTHOSTATIC STRESSOR

I hypothesized that the trained group would exhibit a greater catecholamine response to this task to counterbalance the decreased baroreceptor reflex pattern as a result of repeated exercise stimuli (Dworkin et al., 1979). However, the results of the orthostatic task indicated that there were no significant differences between the experimental groups for any of the physiological parameters during this task. Although there was no evidence of group differences during this task the magnitude of the plasma NE increase in response to this task was approximately two fold above the rest values for both groups. These data and the plasma E data are in general agreement with Cryer et al. (1974); and Lake et al. (1976) in their discussions of orthostatic stress and plasma catecholamine concentrations.

III. PSYCHOLOGICAL CHALLENGE

The reaction time-avoidance of shock (RT-AV) task and the reaction time-appetitive (RT-AP) task were used in this study as a means to produce physiological responses from the cognitive or mental processes.

During the RT-AV task the experimental groups did not differ significantly in the measured physiological responses but both groups did exhibit large plasma NE and peak systolic

and diastolic blood pressure responses to this task.

Norepinephrine levels increased approximately two-fold and peak systolic and diastolic BP increased approximately 30mmHg and 10mmHg, respectively. These changes in blood pressure are similar but slightly greater than changes reported during less aversive cognitive tasks (Manuck et al., 1978). The plasma E and NE values reported by Sinyor et al., 1983 are in close agreement with the values obtained in the present study. It is interesting to note that the trained group exhibited consistent but insignificantly greater plasma NE values during the experimental task in the Sinyor et al. (1983) study. The same finding occurred in our study. Also the plasma NE values attained during the RT-AV task were as great or greater than any of the other experimental tasks involved in this study. This finding did not correspond with the data of LeBlanc et al. (1979). These authors found that plasma NE exhibited a greater increase in response to acute cold while plasma E was increased to a higher degree during a mental arithmatic test. While the amount of change in plasma NE levels during the cognitive tests are similar, LeBlanc et al. (1979) reported a much greater increase in the plasma E concentration during the mental task than did our study. LeBlanc and coworkers reported approximately 100 pg/ml increase in plasma E during the experimental task while we reported approximately a 25 pg/ml increase. This discrepency could be attributed to the difference in the cognitive tasks and/or to the individual differences in the subjects.

The results of the RT-AP task did not suggest any significant differences between the experimental groups for any of the measured physiological parameters. The magnitude of change for all of the physiological variables during the appetitive task were similar to those of the avoidance of shock task. Although the feelings of the subjects suggest that, the avoidance of shock task was more aversive than the appetive task, the physiological variables did not reflect this.

IV. COLD PRESSOR TEST

The cold pressor test has been used by many as an index of one's reaction to pain wherein hemodynamic and SNS responses have been measured (Wolf and Hardy, 1941 and Hardy, 1951). Also the pressor response of acute cold stimulus has been discussed as being mediated by a reflex neurogenic arc(Winer and Carter, 1977). In this study the cold pressor test was used as one method of elicting cardiovascular and SNS responses that are physical and reflexive in nature.

Although there were no significant differences between the experimental groups for any of the physiological variables measured during the cold pressor test, the plasma NE, HR, systolic and diastolic BP, and mean arterial pressure(MAP) values are in close agreement with previous studies using the cold pressor test (Lake et al., 1976; Winer and Carter, 1977). Also our change scores for the plasma

catecholamine concentrations, HR, and systolic and diastolic blood pressure are consistently higher but in general agreement with those values of LeBlanc et al. (1979). However, LeBlanc and co-workers(1979) suggested that plasma E concentrations were greater in response to a mental test than those of the cold test and that heart rate was increased to greater extent during the mental test. Our results do not support these findings. Inspection of our results suggest that the cold-pressor task was no more aversive than any of the other tasks used in this study even though it was described by a majority of the subjects as the "most disliked task". This same finding was noted by Lake et al. (1976).

V. ISOMETRIC HANDGRIP TASK

The isometric hand grip task was used as another physical stressor to provoke the cardiovascular system and the sympathetic nervous system. The mechanism of provocation of the adrenergic system has been hypothesized to be reflexive in nature in response to muscular exercise(Lind et al., 1964 and Donald et al., 1967).

I hypothesized that as result of chronic dynamic muscular exercise the trained group would exhibit a smaller response to the static exercise task in comparison to the untrained group. This hypothesis was unsubstantiated. The results of this study suggest that the experimental groups did not differ significantly in response to the isometric

task. The magnitude of the cardiovascular parameters are in general agreement with other studies of this nature (Nazar et al., 1979; Kozlowski et al., 1973; Martin et al., 1974; Longhurst et al., 1980; Morgan et al., 1982). Morgan et al. (1982) reported similar hemodynamic responses to isometric handgrip but slightly higher values during isometric quadriceps exercise. This could be attributable to the increased muscle mass used during this exercise. Longhurst et al. (1980) reported similar but slightly higher cardiovascular responses to handgrip. In effect, they used a higher percentage of MVC(40%) and maintained the contraction for a shorter time period. These procedural differences may provide an explanation for the differences in the results. Longhurst also found that an aerobically trained group responded significantly less than the control group for heart rate at time 1/2 and at time max. Our data did not support this finding.

The catecholamine concentrations reported in our study are much lower than the data reported by several studies concerning static exercise (Kozlowski et al., 1973; Few et al., 1975; Lake et al., 1976). Although Lake et al. (1976) reported plasma NE concentrations approximately twice those of our study the difference may be a result of procedural dissimilarities. On the other hand Kozlowski et al.(1973) reported plasma catecholamine values during static hangrip work that were equivalent to moderate work on a bicycle ergometer. The plasma NE and E values reported for static

exercise in our study are similar to values reported for sitting on a bicycle ergometer at rest.

VI. AEROBIC FITNESS AND PHYSIOLOGICAL ADAPTATION

Although the trained group exhibited a significantly higher VO2max and a significantly lower mean resting heart rate there were no significant differences between the groups for any of the measured variables during any of the experimental tasks. Several recent studies have shown that aerobic training may not induce significantly different circulatory and biochemical responses during mental tasks and isometric exercise (Longhurst et al., 1980; Morgan et al., 1982; Sinyor et al., 1983). Morgan et al. (1982) found no hemodynamic differences in an isometric hand grip test after a short period of lower body aerobic training. They did find a significantly decreased HR and SBP response to isometric quadriceps exercise in the aerobically trained group. These findings were discussed as an example of the specificity of training.

Longhurst et al. (1980) studied a cross-sectional population of aerobically trained and untrained individuals. They found no significant differences between the groups in the BP response to isometric handgrip but did find a significantly decreased HR response to isometric handgrip in the trained group. Upon inspection of the data the difference in the HR response may actually be a function of

the differences in resting HR between the groups. However, LeBlanc et al. (1978) showed that a physically fit group exhibited a decreased HR and SBP response to a cold pressor test. Decreased SNS activity was implicated as the maechanism for this response.

At present there is confusion in the literature as to whether training (fitness) really does induce a differential response to other stressors. The underlying assumption in nearly every study regarding the effect of fitness on the physiological adaptation to novel stressors has been that a diminished catecholamine response to these stressors is a beneficial result. This assumption may have developed from the studies that showed diminished catecholamine responses to exercise after training (Galbo et al., 1977; Winder et al., 1979; Peronnet et al., 1981). Possibly the validity of this assumption should be considered. A greater catecholamine response to a myriad of potential stressors may suggest that there is greater catecholamine synthesizing capabilities in the system (Kvetnansky et al., 1970). If there is an increased potential to release catecholamines but a decreased catecholamine response to repeated stressors such as exercise (Ostman and Sjostrand, 1972; Winder et al., 1979; Peronnet et al., 1981) and forced immobilization (Kvetnansky et al., 1970) as a result of central afferent habituation then the enhanced capacity to produce and release catecholamines may allow the system to exhibit an intensified catecholamine response to different and/or new stimuli (Kvetnansky, 1980).

This may be considered a type of dual adaptation that permits greater control of the catecholamine supply and demand in the sympathetic-adrenomedullary system. This implies that the increased potential to synthesize and thus release catecholamines may be beneficial with respect to repeated exposure to the changing stressful situations encountered in everyday life.

CHAPTER VI

CONCLUSIONS

From the results of this study it may be concluded that:

1. There is no evidence of a "cross-adaptation" to these particular laboratory stressors as a result of chronic aerobic exercise. However the intensity of these stressors may not have been great enough to reveal an adaptive effect in the trained individuals.
2. These particular stressors, relative to intensity, evoked an SNS response approximately equal to that for standing upright and/or extraction of the third molar (Goldstein et al., 1982).
3. Self reported disinclination toward the tasks did not affect the physiological response to those tasks. There was no correlation between the "most disliked task" and the magnitude of the circulatory and the biochemical responses.
4. The trained group of subjects exhibited consistently greater but non-significant concentrations of plasma NE during each of the experimental tasks. This response may be a previously unrecognized type of adaptation that occurs with chronic aerobic training.

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APPENDIXES

APPENDIX A

Informed Consent

Informed consent for participation in the study to measure the effect of various laboratory stressors on the concentration of plasma epinephrine and norepinephrine.

Description of the Project

This experiment is designed to measure the changes in plasma epinephrine and norepinephrine and cardiovasculas responses during five experimental tasks. The tasks are: 1) a reaction time task, in which a slow time is punished with an electric shock; 2) a reaction time task in which each fast time is given a $1.00 reward; 3) a task in which some simple arithmetic problems must be mentally computed; 4) a five minute isometric contraction on a hand-grip dynamometer and 5) a two minute hand immersion in ice water.

For this experiment a catheter will be placed in a superficial vein on the back of your hand. A 3 ml sample of blood will be taken during particular phases of the test. The total blood taken during this experiment will be less than 2 oz.

A second aspect of the study requires that you take a maximal work capacity test. This involves walking on a treadmill. The elevation of the treadmill will be gradually increased. The test will continue until the point of voluntary exhaustion, which you alone will determine.

Possible Risks and Discomforts

The placement of the catheter may cause temporary pain and there may be soreness on the back of your hand for several days following the test. The possibility of infection due to the insertion of the catheter also exists, although this is very improbable under the circumstances of this experiment. The electric shock and the hand immersion involve discomfort, but minimal risk. You will perceive fatigue during the maximal work capacity test. The possibility that you could experience muscle soreness for several days after the test also exists. While there are risks associated with the exercise test, they are very small for someone your age who is in good health.

Having read the above statement, I understand my role in this study and am aware of the risks involved. The procedures for the experiment have been explained and demonstrated and any questions I have regarding this experiment have been answered to my satisfaction. I am aware that I may withdraw from this research at any time. I further understand that should any adverse health effects occur because of my participation in this study, financial compensation is not available and medical treatment is not provided free of charge.

Signature _____

Date _____

Witness _____

APPENDIX B

CATECHOLAMINE ANALYSIS

Principle of Operation

The epinephrine and norepinephrine of the plasma are converted to ^3H metanephrine and ^3H normetanephrine respectively during incubation with catechol-o-methyl-transferase (COMT) and ^3H s-adrensyl methionine (^3H-SAM). The corresponding methanephrines are extracted from other organic products with a series of toluene-isoamyl alcohol washes. Metanephrine and noremetanephrine are separated with thin layer chromatography (TLC). They are eluted from the TLC silica gel and oxidized to vanillin with sodium periodate. This is done because vanillian in more soluble in toluene, the organic solvent in which the radioactivity is counted, than are the methalated catecholamines.

Reagents:

1. Buffer. To 10 ml of water (distilled) add: 6.05 of THAM; 1.9 gm EGTA · Na_2; 3.05 gm $MgCl_2 \cdot 6H_2O$. Adjust pH to 8.3 with concentrated HCl or NaOH. The initial pH will be close to this. Bring volume to 25.0 ml with water.
2. .1 molar Gluthathione. Add 30.7 mg to a small test tube and add 1 ml of water. Vortex lightly, if necessary. Make prior to using and keep in ice bath.
3. Stopping solution. A 1.0 m boric acid and .2 m EDTA Na_2 buffer is prepared by adding 1.55 gm boric acid and .93 gm EDTA · $2H_2O$ · Na_2 to 20 ml of water. Adjust pH to 11.1 and bring to 25 ml volume with water. To 5 ml of this borate EDTA stopping solution, add 4.67 mg of metaephrine and 4.39 mg of normetanephrine prior to use. A 50 ul aliquot will then provide .2 moles of each carrier.
4. Toluene-isoamyl alcohol (3:2). Combine 300 ml of toluene (Fisher #T-324) and 200 ml of isoamyl alcohol (Fisher #A-393).
5. .1 Acetic acid. 2.95 ml of glacial acetic acid to 500 ml.
6. 4% w/v $NaIO_4$. 1 gm up to 25 ml of water--prepare fresh.
7. 10% Glycerol V/V. 1 ml up to 10 ml of water.
8. .05 NH_4OH. .33 ml up to 100 ml of water.
9. 1.0N NCl 8.3 ml of concentrated HCl up to 100 ml.
   .01 HCl 1.0 ml of 1.0NHCl to 100 ml.
   .001 HCl 1.0 ml of 1.NHCl to 1000 ml.
10. 100 pg Standards. Unstable, prepare only before use.

(10. Continued)

a. 100 ul of 50 ug/ml E stock and 100 ul of 50 ug/ml are brought to a volume of 50 ml with .01 HCl
b. Bring 10 ml of this solution to 100 ml with .001 HCl
c. 10 ul of this solution equals 100 pg of E and 100 pg of NE.

11. Enzyme. From Axelrod and Tomcheck (1958) and Painter (1976).

Procedure

1. Turn on water bath and set to 37°C.
2. Prepare two sets of test tubes (13 x 100 mm) in triplicate. The first set is for reaction and incubation and should be kept in ice bath, the second is for extraction.
3. Remove enzyme, samples, buffer, ^{3}H SAM, and stopping colution from freezer. Thaw and store in ice bath prepared from ice, water, and NaCl.
4. Use a conical centrifuge tube that has been in ice bath and add in the following order in amounts for assay plus 2 (see below): Buffer solution, Gluthatione and ^{3}H SAM; vortex lightly; COMT enzyne solution; vortex lightly; keep in ice.

Assay	x1	x20	x50	x100
Buffer	5 ul	100 ul	250 ul	500 ul
Gluthatione	1 ul	20 ul	50 ul	100 ul
^{3}H SAM	10 ul	200 ul	500 ul	1000 ul
Enzyme	24 ul	480 ul	1.2 ml	2.4 ml
Total value	40	800	1.95 ml	4.0 ml

5. Incubation mixture. Use a glass micropipette for accuracy in pipetting. The first set of test tubes will receive the following:
   a. Blanks
      1. 50 ul of sample vehicle (i.e., H_2O that is mixed with sample tubes)
      2. 40 ul of enzyme cocktail (#4)
      3. 10 ul of .001 HCl
   b. Standards (Internal)
      1. 50 ul of plasma
      2. 40 ul of enzyme cocktail
      3. 10 ul of 100 pg standard
   c. Plasma Samples
      1. 50 ul of plasma
      2. 40 ul of enzyme cocktail
      3. 10 ul of .001 HCl
   d. Vortex tubes lightly and centrifuge briefly (30 seconds).

6. Incubation. One hour at 37°C in an oscillating water bath.
7. In second set of test tubes, add 100 ul of .1 N acetic acid. An automatic pipette is adequate.
8. Stop incubation by placing reaction tubes in an ice bath and adding 50 ul of Borate-EDTA-Metanephrine buffer solution (vortex well).
9. Extraction.
   a. Add 2 ml of (3:2) toluene-isoamyl alcohol to incubation tubes. Vortex vigorously. Centrifuge 2 minutes at 800 x g.
   b. Quick freeze: by submerging tube to level of aqueous phase for 15 seconds. Use a timer.
   c. Blot outside of tube. Decant the organic phase into its corresponding tube with .1 N acetic acid. (Discard aqueous phase.)
   d. Vortex and centrifuge. (Solution should be clear.)
   e. Quick freeze. Aspirate off organic phase without touching suction tube to the frozen pellet. (Tilt tube.)
   f. Thaw the aqueous phase. Add 1 ml of 3:2 toluene-isoamyl alcohol. Vortex vigorously and centrifuge. Quick freeze, aspirate, and discard as in step 5.
10. TLC
   a. Add 100-150 ul of absolute ethanol to the thawed acetic acid from step f (above). Vortex briefly and centrifuge at #4 for 1 minute (add ethanol only for the number you are about to spot--avoid evaporation).
   b. Pull some ethanol into spotting syringes and gently expel so that needle still contains ethanol. This will eliminate air bubbles.
   c. Slowly pull acetic acid-ethanol solution into syringe. Do not pull air into syringe.
   d. Turn on dryer and spotter.
   e. Place dryer approximately 3 cm from plates and set temperature control between 200-300.
   f. Position syringes so that tips touch TLC plates. Set plunger speed to slowest possible speed.
   g. Prepare 44 ml of developing solution (6:2:3) in a 50 ml graduate.
      1. 24 ml tertiary amyl alcohol
      2. 8 ml benzene
      3. 12 ml methylamine
      4. Mix gently
   h. Put developing solution in developing tank immediately before use. Carefully place plates in tank. Develop for 50 minutes (solution should be clear).

i. Dry plates and visualize spots under UV. Utilizing a scalpel, carefully outline the spots.
j. Scrape spots into acid washed scintillation vials (use a scalpel). The metanephrines are the top zone and normetanephrines are the bottom zone.

11. Oxidation
a. Add 1 ml of .05 M NH_4OH to vials. Vortex vigorously.
b. Line up vials and add 50 ul of 4% periodate solution at time intervals. Vortex vigorously.
c. Stop reaction by adding 50 ul of 10% Glycerol solution, 5 minutes after step b. Maintain order and timing of step b.
d. All 1 ml of .1 M acetic acid to each vial and vortex.
e. Add 10 ml of toluene-Liquifluous (1000:50 v/v) to each scintillation vial. Shake by hand vigorously (for about 10 seconds).
f. Count each vial for a minimum of 10 minutes.

Reference:

Upjohn Diagnostics with modifications by Painter, P. Changes in plasma epinephrine, norepinephrine, cyclic AMP, and cyclic GMP in men subjected to the same degree of progressive and continuous work. Dissertation. The University of Tennessee, Knoxville. 1976.

VITA

Randal Paul Claytor was born in Chillicothe, Ohio on July 22, 1958. He resided in Piketon, Ohio; attended public schools there and was graduated from Piketon High School in May 1976. He entered Capital University located in Columbus, Ohio in August of that year. He participated in varsity football for four years and received a Bachelor of Arts degree in Health and Physical Education from that instituation in May 1980.

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