THE ROLE OF THE BAROREFLEX IN DIVING BRADYCARDIA

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ABSTRACT

Large inter-individual differences exist in the degree of bradycardia induced by breath-hold facial immersion. The purpose of this study was to examine baroreceptor sensitivity in subjects who exhibit a strong response and in those who exhibit a minimal response. Thirty-nine healthy volunteers were screened with three trials of breath-hold facial immersion during mild steady-state cycling. The six subjects displaying the greatest bradycardia were selected as responders and the six showing the least as non-responders. Baroreceptor sensitivity was estimated in each subject by examination of the heart rate and blood pressure responses to a controlled Valsalva manoeuvre and to isometric handgrip exercise. Regression lines for changes in systolic blood pressure over time showed a flatter response in the responders both during isometric handgrip exercise ($p<.05$) and over the 25 s immediately following release ($p<.01$). One interpretation of these findings is that the non-responders are less able to maintain a resting level of arterial blood pressure. As well, regression lines for the change in diastolic blood pressure over the period 25 to 55 s post-release of isometric handgrip exercise had different slopes in the two groups ($p<.05$). A positive mean slope calculated for the responders and a negative mean slope calculated for the

non-responders, when plotted with the average intercepts, suggested an undershoot in diastolic blood pressure upon release in the responders. This may represent an attempt to regain resting levels of arterial blood pressure through peripheral vasodilitation. Direct measures by arterial catheter, in a sub-sample of four subjects, suggested that the blood pressure overshoot during the recovery phase of the Valsalva manoeuvre may not have been large enough to demonstrate group differences in baroreceptor sensitivity.

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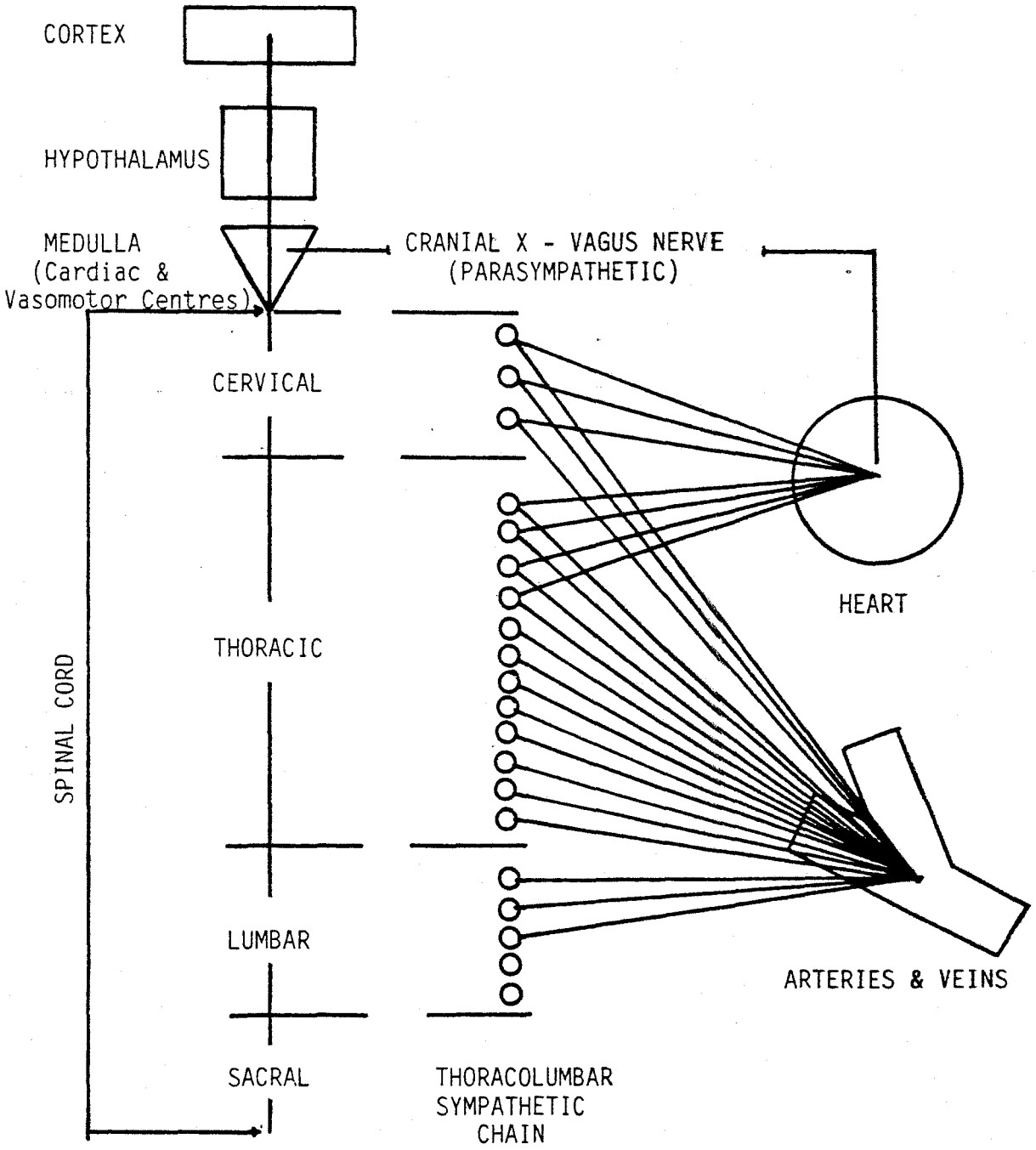
CHAPTER 1

INTRODUCTION

Submersion in water results in an immediate slowing of heart rate and constriction of peripheral blood vessels in most mammals (Andersen, 1966) (Figure 1a p. 2). Attempts to understand the physiological mechanisms which cause these responses in man have focused on the role of temperature receptors in the face and of arterial chemoreceptors (Figure 1b p. 4). Brick (1966) demonstrated the importance of facial immersion to the quick initiation of diving bradycardia. Moreover, the magnitude of the heart rate response to facial immersion has been found to increase with colder water temperatures (Paulev, 1968; Whayne and Killip, 1967). Blood gas changes reach levels capable of intensifying the heart rate response between 28 s (Kawakami et al, 1967) and 95 s (Moore et al, 1973; Hong et al, 1971) after the initiation of breath-hold facial immersion.

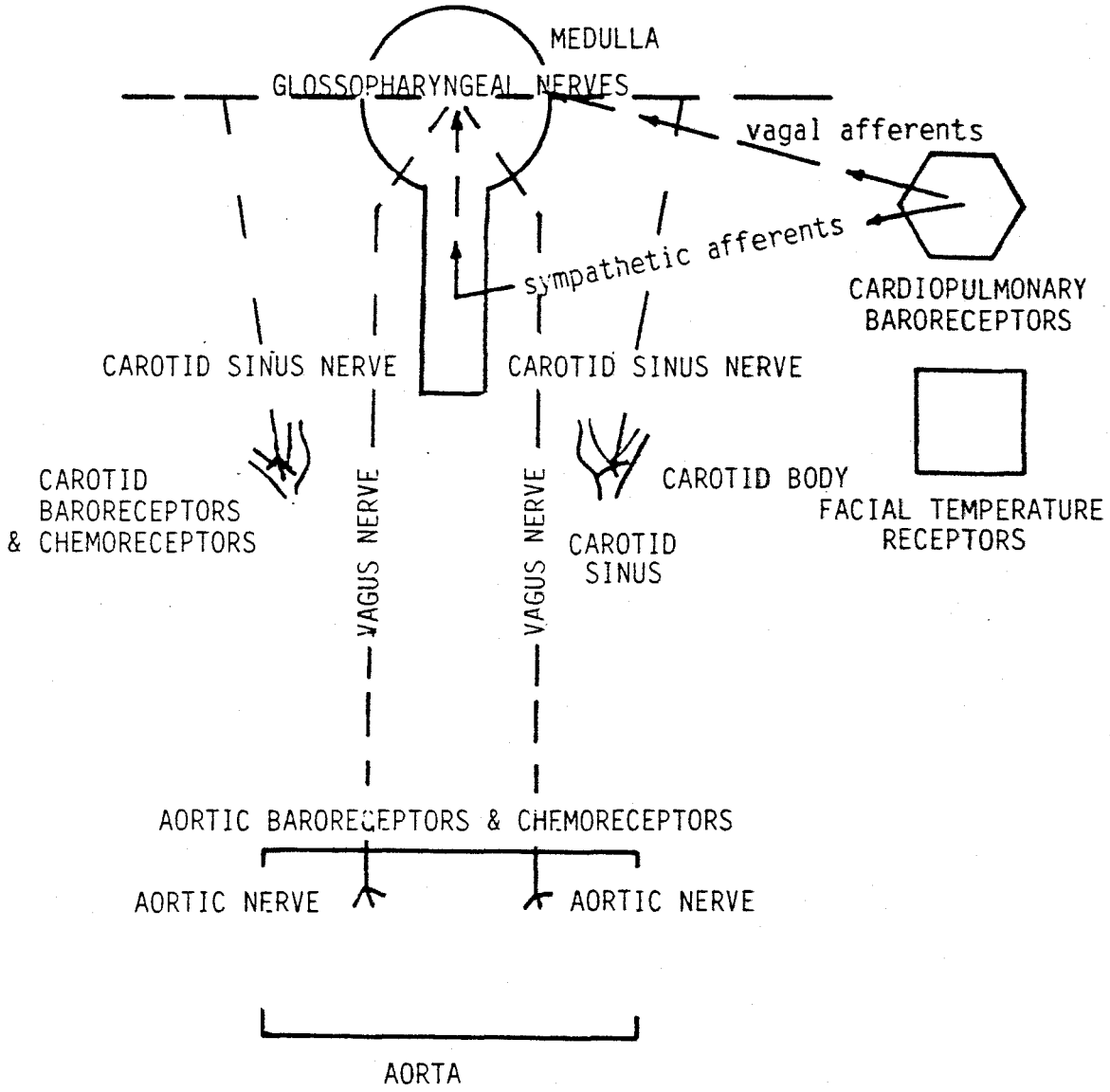
The heart rate response to breath-hold facial immersion may also be directly related to the baroreceptor reflexes (Figure 1b p. 4). Breath-hold after a maximal inspiration results in an increase in intrathoracic pressure which is transmitted to the arterial system (Paulev, 1968). Kawakami et al (1967) reported an initial transient decrease in blood pressure both with simple breath-hold and with breath-hold facial

Figure 1a. The efferent sympathetic and parasympathetic pathways involved in the diving response.



It is not known whether sympathetic control of heart rate plays a role in the diving response in man (Finley et al, 1979; Heistad et al, 1968).

Figure 1b. The afferent pathways for the three mechanisms involved in the discussion of diving bradycardia; arterial chemoreceptors, arterial and cardiopulmonary baroreceptors and facial temperature receptors.


MEDULLA
GLOSSOPHARYNGEAL NERVES
vagal afferents
sympathetic afferents
CARDIOPULMONARY
BARORECEPTORS
CAROTID SINUS NERVE
CAROTID SINUS NERVE
CAROTID
BARORECEPTORS
& CHEMORECEPTORS
VAGUS NERVE
VAGUS NERVE
CAROTID BODY
CAROTID
SINUS
FACIAL TEMPERATURE
RECEPTORS
AORTIC BARORECEPTORS & CHEMORECEPTORS
AORTIC NERVE
AORTIC NERVE
AORTA

immersion. Whether this reflects a decrease in cardiac output as a result of the increased pressure within the chest is unknown. Alternatively, these changes may be a baroreceptor-mediated response to increases in arterial blood pressure. Following any initial decrease in blood pressure during breath-hold manoeuvres, circulatory adjustments result in a gradual increase in mean arterial pressure (Heistad et al, 1968; Kawakami et al, 1967).

Heistad et al (1968) recorded a continuous trace showing increases in both systolic and diastolic blood pressure during facial immersion and simple breath-hold in man. The magnitude of the mean arterial pressure response was greater with facial immersion than with breath-hold alone. Since the decreases in heart rate during breath-hold facial immersion did not coincide with the increase in mean arterial pressure in each subject, the authors concluded that bradycardia is probably not entirely dependent upon the baroreceptor response.

Finley and associates (1979) reported a reduction in the bradycardia response to cold water facial immersion when subjects were administered atropine, a vagal blocker. Neither beta adrenergic blockers, which reduce increases in heart rate and contractility, nor alpha blockers, which weaken the peripheral vasoconstrictor response, had an effect on diving bradycardia. Cuff measures of systolic blood pressure taken in three subjects supported a decrease in, or elimination of, these sympathetic baroreceptor stimuli during facial immersion. The researchers

concluded that hypertension due to sympathetic stimulation is not essential to the decrease in heart rate seen with facial immersion.

The interpretation of the data collected by Finley and associates is complicated. For example, circulatory adjustments may have occurred in response to the autonomic blockade. Without measures of diastolic blood pressure during the breath-hold facial immersions, it is not known whether increases in mean or pulse pressure were providing a stimulus for the baroreflex. In addition, interactions between the sympathetic and parasympathetic control of the heart have been reported (Levy et al, 1971). Finley and associates did not discuss the possible effects of interference with the sympathetic changes within the heart on the parasympathetic control of heart rate and, therefore, on the diving response.

1.1 Statement of the Problem

Baroreflex-mediated responses to increases in arterial blood pressure represent a possible mechanism for diving bradycardia.

Reference is made in the literature to subjects who show strong and weak responses to breath-hold facial immersion (Gooden et al, 1970; Asmussen and Kristianson, 1968; Irving, 1963). In addition, pilot data showed a wide range in the

magnitude of the bradycardia response to facial immersion (Appendix A). It is therefore possible to identify a population who show exaggerated responses and a population who show weak responses to facial immersion. Similarly, differences in baroreceptor sensitivity have been found within a group of young healthy subjects (Bevegard et al, 1966). Baroreceptor sensitivity was measured as the absolute levels of decrease in heart rate and blood pressure in response to the application of negative pressures to the neck (ie. stretch of the carotid baroreceptors). A demonstration of a higher level of baroreceptor sensitivity in responders than in non-responders to breath-hold facial immersion would provide support for a role of the baroreceptor in diving bradycardia.

1.2 Purpose of the Study

The purpose of this study was to compare measures of baroreceptor sensitivity in subjects who have demonstrated a marked slowing of heart rate upon facial immersion in cold water with those who have demonstrated little or no change in heart rate.

1.3 Definition of Terminology

Diving bradycardia- Decreases in heart rate during breath-hold facial immersion.

Baroreceptor sensitivity- The ability of the arterial baroreceptors to detect

	fluctuations in arterial blood pressure and to initiate cardiovascular changes aimed at restoring normal pressure levels.
Valsalva manoeuvre-	Forced expiration against a closed glottis.
Isometric exercise-	Sustained muscle contraction in which there is no change in muscle length.
RR interval-	The length of time between two consecutive QRS complexes (ventricular depolarization) recorded on an electrocardiagraph.

CHAPTER II

REVIEW OF THE LITERATURE

This chapter will provide the reader with an understanding of circulatory control mechanisms as they relate to the purpose of the study. Measures of baroreceptor sensitivity were compared between subjects who demonstrate a strong and subjects who demonstrate little or no heart rate response to breath-hold facial immersion. Important to this chapter, therefore, is a review of the role of the baroreceptor in cardiovascular control and a discussion of the concept of barosensitivity. The heart rate and blood pressure responses to the Valsalva manoeuvre and to isometric exercise, the measures of barosensitivity used in this study, will also be reviewed. As well, subjects were classified as responders and non-responders according to their heart rate responses to breath-hold facial immersion performed during dynamic exercise. The final sections discuss the effect of dynamic exercise on barosensitivity and review previous literature examining the role of the baroreceptor in diving bradycardia.

2.1 Cardiovascular Control

2.1.1 Overview

An interaction of the two branches of the autonomic nervous system provides efferent cardiovascular control (Levy, 1971; Copen et al, 1968; Kabat, 1939). The parasympathetic branch of the nervous system plays a dominant role in the regulation of heart rate (Levy and Zieske, 1969). Stimulation of the parasympathetic nerves results in a decrease in heart rate, while the withdrawal of vagal (parasympathetic) tone results in an increase in heart rate (Levy and Martin, 1979). The primary effects of stimulation of the sympathetic branch of the nervous system are peripheral vasoconstriction (Åstrand and Rodahl, 1977), an increase in heart rate and improved cardiac contractility (Levy et al, 1979). Sympathetic stimulation also activates the release of hormonal transmitters from the adrenal medulla. These act to reinforce the changes mediated through the nervous system (Smith and Kampine, 1980). In addition, the vascular beds vary in the density of sympathetic efferent nerve fibers and in the types of specialized receptors present (Åstrand et al, 1977). This permits a finer control of blood flow distribution. The total amount of blood flow, or cardiac output, is determined by four factors; heart rate, cardiac contractility, the amount of blood returning to the heart and the pressure against which the left ventricle must work (Parmley and Talbot, 1979).

The success of these various control mechanisms is monitored through chemosensitive and pressure sensitive receptors.

A. Chemosensitive receptors

Chemoreceptors in the aortic and carotid bodies are stimulated through decreases in the arterial pH, decreases in the arterial pressure of oxygen and increases in the arterial pressure of carbon dioxide. Stimulation of the carotid chemoreceptors results in peripheral vasoconstriction, bradycardia and a decrease in cardiac contractility (Coleridge and Coleridge, 1979). Although the aortic chemoreceptors are equally effective in mediating vascular changes (Daly and Ungar, 1966), they play little (Angell-James and Daly, 1969) or no (Katzin and Rubenstein, 1974) role in the control of heart rate.

B. Pressure sensitive receptors (baroreceptors)

Baroreceptors, the mechanisms for and consequences of their stimulation are discussed in the following sections. Most important to the present study are the types of pressure stimuli capable of stimulating baroreflex mediated changes in heart rate and blood pressure.

2.1.2 Baroreceptors

The cardiovascular system is equipped with a series of stretch or mechanoreceptors that regulate heart rate and vasomotor tone in the maintenance of mean arterial pressure. The arterial receptors are located in the vessel walls of the carotid sinus and the aortic arch. Cardiopulmonary receptors may be found in the atria, the venae cavae, the ventricles and the lungs (Smith et al, 1980).

Receptor deformation is the result of pressure changes at these sites. More common names for these structures, therefore, are pressoreceptors or baroreceptors. With the exception of those located in the ventricular walls, cardiopulmonary receptors respond to low pressure stimuli and systemic arterial receptors respond to high pressure stimuli (Smith et al, 1980).

Stimulation of these stretch receptors produces a receptor current which, after travelling over a spike initiating zone, results in baroreceptor discharge (Eyzaguirre and Kuffler, 1955). Both increases in impulse frequency in individual nerve fibers and the recruitment of new receptors accompany increases in blood pressure (Bronk and Stella, 1932; Landgren, 1952). As well, the amplitude of the electrical potentials becomes larger with this greater total afferent activity (Pelletier et al, 1972).

Baroreceptors have been classified according to the size of the discharge spike recorded in their afferent fibers (Bronk

and Stella, 1935; Bronk et al, 1932). The larger amplitude of the electrical potentials with increased baroreceptor activity may be the result of selective recruitment of baroreceptors with the larger amplitude spike (Pelletier et al, 1972). Alternatively, these larger amplitude spikes may represent the summation of two or more impulses that were fired simultaneously (Spickler and Kezdi, 1969).

2.1.2.1 Arterial baroreceptors

In man, increases in mean arterial pressure within the range of 62 to 215 mmHg are accompanied by increases in mean impulse frequency of the carotid sinus afferent nerves. At these pressure levels, the aortic baroreceptors are substantially less sensitive to a given pressure stimulus (Pelletier et al, 1972).

Bevegard and Shepherd (1966) reported decreases in cardiac output and vasodilatation in the resistance vessels of the forearm with increased carotid sinus baroreceptor activity. The changes in cardiac output were the result of a decrease in heart rate. That stroke volume did not increase in order to maintain cardiac output (Ross et al, 1965) suggested a negative inotropic (cardiac contractility) effect of the baroreceptor stimulation. Venodilatation did not play a role in the baroreceptor response. In contrast, increases in arterial pressure mediated through the baroreceptors are thought to be the result of an increase in cardiac output, with little or no change

in peripheral resistance (Mancia et al, 1979).

The heart rate response to a decrease in arterial blood pressure is an initial decrease in cholinergic activity. This signal is then reinforced through an increase in beta adrenergic activity (Eckberg, 1980). The beta adrenergic system, however, is not involved in the decrease in heart rate which follows an increase in carotid sinus discharge (Robinson et al, 1966; Glick and Braunwald, 1965).

The cardiovascular system is thought to provide a better antihypotensive than antihypertensive defense (Smith et al, 1980). This is attributed to the response characteristics of the carotid baroreceptors (Mancia et al, 1979). The aortic baroreceptors are primarily antihypertensive and ineffective in buffering decreases in pressure to below normal levels (Pelletier and Shepherd, 1973).

The carotid sinus has been shown to be sensitive to the rate of change of pressure (Schmidt et al, 1972; Stegeman and Tibes, 1969; Ead et al, 1952). Pulse pressure is a major component of this stimulus (Schmidt et al, 1972) and has been found to be most effective in stimulating the carotid baroreceptors at mean pressures of less than 150 mmHg (Koushanpour and McGee, 1969; Schmidt et al, 1972). Schmidt and associates (1972) reported that the relative contribution of changes in cardiac output and total peripheral resistance to the response to increases in pulse pressure was dependent on the

level of intrasinus pressure and varied between subjects at each intrasinus pressure level. The rate of change of pressure (Pelletier et al, 1972) and the magnitude of the pulse pressure (Angell-James and Daly, 1970), however, have comparatively little effect on the aortic baroreceptors.

Both myelinated and unmyelinated afferent baroreceptor fibers have been identified (Krauhs, 1979). Brown and co-workers (1978) found changes in the amplitude of the nervous discharge in myelinated afferents and slight changes in the discharge frequency of unmyelinated afferents in rats with changes in heart rate. These changes appeared over the physiological range of rat heart rate. Other researchers have found the effects of pulse frequency on systemic arterial pressures of the dog to be restricted to frequency ranges of 0 to 1.6 cycles per s (Stegeman et al, 1969) or 28 to 72 cycles per min (Angell-James et al, 1970).

The change from steady to pulsatile arterial blood flow is not always associated with an increase in the average frequency of nerve impulses in baroreceptor afferent fibers (Ead et al, 1952). However impulse grouping, without changes in the total number of impulses per unit time, results in decreases in arterial blood pressure (Koepchen and Sellers in Stegeman et al, 1969; Ead et al, 1952).

In addition, three sizes of baroreceptor afferent fibers have been identified. Large fibers, which produce large

amplitude spikes on an electroneurogram, are recruited in response to increases in the pulsatility of flow through the carotid sinus (Ead et al, 1952). This may provide a means through which the central nervous system detects these changes in arterial blood pressure.

2.1.2.2 Cardiopulmonary baroreceptors

The location of cardiopulmonary baroreceptors has left them technically difficult to study (Brown, 1979). Distension of small balloons at the points of venous entry in the atria is thought to imitate changes in venous return. A reflex steady-state tachycardia is achieved in one to two min.. Mean arterial pressure, however, is left unchanged (Linden, 1973). Bradycardia and hypotension follow stimulation of the ventricular mechanoreceptors (Brown, 1979).

2.1.2.3 Summary

The baroreceptors are located in the aortic arch, the carotid sinus, the great veins, the heart and the lungs. Pressure changes in these areas result in receptor deformation and changes in the afferent nervous activity. Increases in the arterial pressure are counteracted through decreases in heart rate and vasodilatation in peripheral resistance vessels. On the other hand, increases in heart rate provide the major portion of the system's response to hypotension. Carotid baroreceptors are

more sensitive to fluctuations in mean arterial pressure than those in the aorta. As well, carotid receptors may be stimulated through alterations in the rate of change of pressure or in the pulse pressure. Changes in heart rate, over certain ranges, also result in changes in afferent arterial baroreceptor discharge.

2.2 Baroreceptor Sensitivity

Baroreceptor sensitivity may be defined as the ability of the baroreceptor to detect fluctuations in arterial blood pressure and to initiate cardiovascular changes aimed at restoring normal pressure levels. Both the levels of arterial pressure which trigger the reflex (set point) and the degree of response to a set pressure change (gain) must be considered (Pelletier et al, 1972).

2.2.1 Measures of baroreceptor sensitivity

The latency of the baroreflex in animals is one to two heart beats, with the shortest stimulus response interval being approximately 80 msec (Jewett, 1964). Smyth et al (1969) examined the heart rate and blood pressure responses to angiotension-induced hypertension in humans. The changes in systolic blood pressure were best correlated with the changes in those RR intervals beginning with the next heart beat. The slope of the regression of these two measures was chosen to represent baroreceptor sensitivity.

The influence of a high level of sensitivity of the cardiodepressor component of the baroreflex, as measured by Smyth et al (1969), on the ability of subjects to maintain resting levels of arterial blood pressures has been examined. Normotensive subjects with the most sensitive baroreflex demonstrated the smallest increases in systolic blood pressure and the flattest dose response curves to three doses of each of two hypertensive agents (Conway et al, 1981). As well, large daily fluctuations in heart rate in combination with a fairly constant blood pressure was found to be an indication of a high level of baroreceptor sensitivity in mild to moderate hypertension (Ogawa et al, 1981).

2.2.2 Baroreceptor resetting

Rapid resetting of the threshold pressure for increases in the baroreceptor afferent activity has been demonstrated in rabbits (Dorward et al, 1982). This occurred with changes in mean arterial pressure which were sustained for a minimum of 15 min.. The effect was reversible and is thought to be the result of viscoelastic relaxation within the arterial wall (Dorward et al, 1982; Coleridge et al, 1981).

The baroreceptors of hypertensive individuals operate around a higher set point. As well, the sensitivity to changes from this baseline may be reduced (Ogawa et al, 1981; Brown, 1980; Downing, 1979). Increases in arterial wall stiffness,

which act to limit baroreceptor deformation, (Kezdi, 1967) and receptor destruction (Brown, 1980) have been demonstrated in established hypertension. Receptor modification or dissociation of the receptor from the vessel wall may also be involved (Brown, 1980). The major cause of early hypertension is thought to be changes within the receptor (Brown et al, 1976).

Finally, a sympathetic efferent pathway has been identified which is able to regulate the distensibility of the carotid sinus wall (Kezdi, 1954). Stimulation of these fibers results in an increase in baroreceptor afferent discharge (Koizumi and Sato, 1969). Although there is little known about the physiological role of this mechanism (Kircheim, 1976), it may provide a means for direct control of barosensitivity.

2.2.3 The central nervous system -- control of the baroreflex

Changes within the cardiovascular system are the net result of the interaction of central nervous system command mechanisms (voluntary activity and emotional responses) and afferent nerve signals (Hilton and Spyer, 1980). Integration of autonomic activity takes place in the spinal, bulbar, cerebellar and suprapontine areas (Korner, 1979).

Barosensitivity has been found to be influenced by the respiratory cycle (Eckberg and Orshan, 1977), is thought to increase with sleep (Smyth et al, 1969) and has demonstrated a daily rhythm of increases and decreases (Hossman et al, 1980).

Sustained increases in the level of discharge of the cardiopulmonary stretch receptors (increases in the positive end-expiratory pressure -- Sepe et al, 1982 and increase in central blood volume -- Billman et al, 1981; Ludbrook et al, 1981) have also modified the cardiovascular response to baroreceptor stimulation. In contrast, the atrial baroreflex appears to be independent of the level of afferent activity from the carotid sinus baroreceptors (Carswell et al, 1970).

2.3 Isometric Exercise and Baroreceptor Sensitivity

2.3.1 The cardiovascular responses to isometric exercise

Increases in blood pressure with isometric exercise have been attributed to the effects of exercise tachycardia on cardiac output (Bezucha et al, 1982; Lind et al, 1964). Decreases in blood flow as a result of mechanical occlusion (increased intramuscular pressure) are not counteracted by increased levels of vasodilatation within the contracting muscle (Perez-Gonzalez Unpublished in Perez-Gonzalez, 1981). However, evidence suggests that ischemic conditions within exercising muscle are capable of stimulating increased levels of vasoconstriction in non-active areas (Perez-Gonzalez, 1981; Higgins et al, 1972; Vatner et al, 1972; Vatner et al, 1971). This works to increase perfusion pressure, thereby assisting with the supply of adequate blood flow to the exercising muscle. Total peripheral resistance remains at pre-exercise levels both

when small (Lind et al, 1964) and when large (Bezucha et al, 1982) muscle groups are used.

Proposed mechanisms for the exercise tachycardia include increases in central command, chemoreceptor stimulation of small sensory afferent fibers and mechanoreceptor stimulation (Asmussen, 1981). The role of central mechanisms in the pressor response has been demonstrated through changes in the amount of effort required for a given task (Goodwin et al, 1972; Freychuss et al, 1970). Increases in blood pressure were found to be minimal with levels of isometric exercise that do not effect blood flow (Perez-Gonzalez, 1981). This has led to the investigation of pressor responses to blood flow occlusion. When initiated during dynamic exercise (Rowell et al, 1981), blood pressure increased. The level of increase was related to the duration of muscle ischemia. When maintained throughout an immediate post exercise (isometric [Mitchell et al, 1980] or dynamic [Rowell et al, 1981]) period, blood pressure was prevented from returning to resting levels. These results have presented a strong case for the role of ischemic changes within the contracting muscle in the pressor response to isometric exercise.

Occlusion studies using dynamic (Freund et al, 1978) and isometric (Mitchell et al, 1980) exercise have found that the strength of the pressor response is increased when a larger muscle mass is involved. It has been suggested that the number

of sensory afferent fibers is not related to muscle size (Asmussen, 1981). If this were the case, factors other than muscle ischemia must have played a role in the increases in blood pressure found with increases in muscle mass. In agreement, elimination of sensory afferent nervous signals and the blood pressure response to muscle ischemia did not eliminate the pressor response to maximal isometric contractions performed by the legs (Freund et al, 1979).

The role of the muscle mass in determining the pressor response has been demonstrated through comparisons using muscle groups of different sizes (Mitchell et al, 1980). Studies using strong and atrophied limbs (Mitchell et al in Mitchell et al, 1981) have found that it is, more specifically, the absolute level of force produced that is important. Smoothed rectified electromyography suggested that the same number of motor units were firing during conditions of the same absolute force. The increase in blood pressure with increased duration of exercise (Perez-Gonzalez, 1981; Sharratt and Bruce, 1979) may be the result of increases in voluntary effort with fatigue or may reflect the chemical changes within the muscle.

2.3.2 Baroreceptor sensitivity during isometric exercise

Cunningham and associates (1972) examined the effects of dynamic exercise (cycling - 30 to 85 watts), sustained handgrip (30% of maximal voluntary contraction) and rhythmic handgrip (30,

45 and 60% of maximal voluntary contraction) on baroreceptor sensitivity. Baroreceptor sensitivity was measured according to the method described by Smyth et al (1969) which stimulates the baroreceptor through drug-induced peripheral vasoconstriction. The decrease in the cardiodepressor effect of baroreceptor stimulation with exercise was found to be unrelated to the degree of increase in oxygen uptake. However, correlations in order of increasing strength were found with the existing values of arterial pressure, RR interval and an index made up of the two measures. Although cycling produced the greatest increase in heart rate, sensitivity was significantly lower during sustained handgrip when the exercise conditions were compared at the same heart rate. Separation of the data from the dynamic and isometric exercise trials also improved the prediction of reflex sensitivity from the heart rate - systolic blood pressure index. As well, conditions of hypocapnic hypoxia changed the response of heart rate but not that of barosensitivity to exercise.

A similar study (Ludbrook et al, 1978) produced increases and decreases in carotid sinus transmural pressure with a variable pressure neck chamber. Unlike the pharmacological stimulus used by Cunningham and associates, this technique produced sustained levels of baroreceptor stimulation. Subjects performed isometric handgrip at intensities of 35, 45, and 65% of maximal contraction. The response of mean pressure to increases or decreases in carotid sinus transmural pressure was generally

not affected by isometric exercise. The only consistent difference in the baroreflex mediated change in heart rate with isometric exercise was noted in the first 10 s of neck suction. Here, the absolute level of decrease in heart rate with carotid sinus stimulation was lower in the two highest work levels than at rest and also lower during 65% than during 35% of maximal effort. In contrast, the more gradual tachycardia caused by application of positive pressure to the neck was similar during rest and during the three intensities of isometric exercise.

Nutter and Wickliffe (1981) used direct stimulation of somatic afferent fibers in anesthetised dogs to study the cardiovascular response to isometric exercise. Afferent input from cardiopulmonary and aortic baroreceptors was eliminated through bilateral vagotomy and muscle contraction was prevented with neuromuscular blockade. The somatopressor reflex involved significant average increases in both heart rate (30%) and blood pressure (40%). The initial response included peripheral vasoconstriction, with the greatest increase in vasomotor tone in the "inactive" muscle and a delayed vasodilatation in the arterial circulation of the hind paw. When the pressure in the carotid sinus was held constant throughout the trial, the level of constriction in the muscle was increased and the secondary vasodilatation seen in the skin was replaced by a larger overall constriction which was maintained throughout nerve stimulation.

These findings were substantiated in the same animal

model by Abboud et al (1981). This group also reported that increased levels of cardiopulmonary baroreceptor stimulation weaken the vasoconstrictor response found in the kidney during isometric exercise. The strongest inhibitory effects of the cardiopulmonary afferents were found while the carotid sinus pressure was maintained at low levels.

The same authors investigated humans performing isometric handgrip exercise at 10 and 20% of maximal voluntary contraction. The combination of lower body negative pressure (decreased central blood volume) and isometric exercise resulted in significant increases in forearm vascular resistance that were greater than the summation of the effect of each treatment administered separately. In addition, the arterial blood pressure response was increased when the high intensity exercise was performed during lower body negative pressure. The heart rate response, however, was not affected.

2.3.2.1 Summary

In human subjects, isometric exercise has been associated with decreases in the degree of change in RR interval in response to drug-induced changes in systolic blood pressure. Prevailing RR interval was found to be a better indicator of the degree of change in this measure of barosenstivity than was systolic blood pressure. The best correlation, however, was given by an index incorporating both measures.

A second study also demonstrated a decrease in the cardiodepressor effect of baroreceptor stimulation (ie. the change in RR interval per unit change in systolic blood pressure) with isometric exercise in humans. However, with sustained increases in carotid sinus transmural pressure it was found that this effect is transitory lasting for only the initial 10 s of baroreceptor stimulation. Neither the sensitivity of the heart rate response to arterial hypotension, nor the absolute level of the mean arterial pressure response to increases or decreases in carotid sinus transmural pressure was affected by isometric exercise.

The carotid sinus baroreceptors have been found to dampen the peripheral vasoconstrictor response to isometric exercise in anesthetized dogs. In addition, studies using both anesthetized dogs and conscious humans have shown an inhibitory effect of cardiopulmonary afferent activity on the increases in vasomotor tone found during isometric exercise.

2.4 The Cardiovascular Responses to the Valsalva Manoeuvre

Performance of the Valsalva manoeuvre involves forced expiration against a closed glottis. The cardiovascular responses to this respiratory act have been well documented. They form a consistent pattern that has been divided into four phases (see Figure 2 p. 28).

Circulatory Response to Non-Exercise Stress

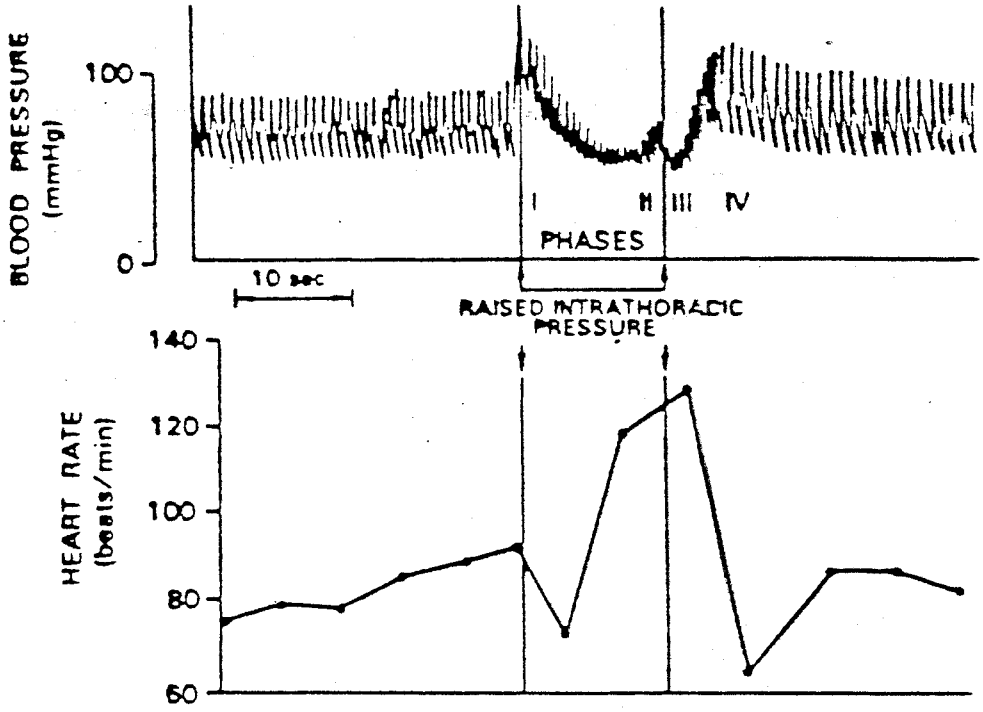


Figure 2. Change in heart rate and blood pressure in response to forced expiration. Subjects maintained an expiratory pressure of 40 mmHg for 15 s. (From J. J. Smith and J.P. Kampine, 1980.)

2.4.1 Phase one

The onset of expiratory strain results in increases in both systolic and diastolic pressure, with pulse pressure left unaffected (Stone et al, 1965; Goldberg et al, 1952). Simultaneous increases in venous pressure (Price and Connor, 1953) and in pulmonary arterial pressure (Stone et al, 1965) have also been reported. Heart rate has either shown no change (Goldberg et al, 1952) or has decreased (Korner et al, 1976). This first phase lasted only 1 to 2 s when the expiratory pressure exerted was between 20 and 45 mmHg (Price et al, 1953).

Sarnoff and colleagues (1948) proposed that the increase in intrathoracic pressure with the Valsalva manoeuvre squeezes the blood out of the pulmonary vascular tree. This would result in elevated levels of cardiac output and be able to account for a pressor response.

It has been argued, however, that increases in cardiac output would cause increases in pulse pressure (Sharpey-Schaefer, 1965). As well, the level of increase in systolic and diastolic blood pressure was found to be comparable to that of intrathoracic pressure (Stone et al, 1965). The pressor response is best explained, therefore, by a direct transmission of the increased pressure within the thorax from the left heart and the aorta to the peripheral arteries (Sharpey-Schaefer, 1965).

Korner et al (1976) had subjects perform the Valsalva manoeuvre (expiratory pressure of 20 mmHg for 30 s) both before

and after total autonomic blockade. The initial increase in mean arterial pressure was not different in the two experimental conditions. It was concluded, therefore, that neural mechanisms are not involved.

Any decrease in heart rate during this part of the Valsalva manoeuvre has been attributed to carotid sinus baroreceptor stimulation. Increases in intrathoracic pressure have an equal effect on the intravascular and extravascular pressures within the thorax. With no change in transmural pressure, the aortic baroreceptors are left unaffected (Sharpey-Schaefer, 1965).

2.4.2 Phase two

The initial pressor response is followed by decreases in systolic, diastolic and pulse pressures (Korner et al, 1976; Stone et al, 1965; Goldberg et al, 1952). Both mean and pulse pressures drop significantly below resting levels when subjects maintain an expiratory pressure of 20 mmHg (Korner et al, 1976). Decreases in mean and pulse pressures have also been found in the pulmonary arterial circulation (Stone et al, 1965; Gorlin et al, 1957; Lee et al, 1954).

Researchers have agreed that these changes in pressure reflect a diminishing cardiac output (Korner et al, 1976; Sharpey-Schaefer, 1965; Stone et al, 1965; Sarnoff et al, 1948). It has been proposed that during the Valsalva manoeuvre,

pressures within the abdomen and the thorax exceed those in the great veins thereby shutting down blood flow (Sharpey-Schaefer, 1965; Sarnoff et al, 1948). In support of this, venous pressures demonstrated a gradual increase despite a loss of pressure in the arterial circulation (Gorlin et al, 1957; Price et al, 1953). Radiographic studies showed that at least part of this increase in pressure is the result of a collection of blood in the veins below the diaphragm (Judson et al, 1955).

Zema et al (1980) pointed out that the narrowing of pulse pressure is consistent with a decrease in stroke volume. Opposing this is a gradual increase in heart rate which has been attributed to stimulation of the aortic (a decrease in both pulse and transmural pressures) and carotid (a decrease in pulse pressure) baroreceptors (Sharpey-Schaefer, 1965). This proposed activation of the baroreflex was used to suggest that increases in vasomotor tone are also involved at this point in the manoeuvre (Stone et al, 1965).

In addition, a secondary increase in mean arterial pressure (Korner et al, 1976; Stone et al, 1965; Gorlin et al, 1957; Price et al, 1953) has been reported. This was accompanied by either an increase (Korner et al, 1976) or no change (Stone et al, 1965; Gorlin et al, 1957) in pulse pressure. The minimum levels of blood pressure are reached 7 to 8 s (Price et al, 1953 - expiratory pressures of 20 to 45 mmHg) or 15 to 20 s (Korner et al, 1976 - expiratory pressure of 20 mmHg) after onset

of the manoeuvre. Other investigators (Goldberg et al, 1952; Sarnoff et al, 1948 - dogs) did not observe this reversal of the blood pressure response.

The secondary pressure increases reported by Korner et al (1976) were associated with a levelling off of heart rate. Venous pressure also reaches a plateau during this portion of the Valsalva manoeuvre, with the final level equal to intrathoracic pressure (Gorlin et al, 1957; Price et al, 1953).

Korner et al (1976) examined the importance of increases in heart rate and systemic vascular resistance to this delayed pressor response. Cardiac output was measured in the last 10 s of each 30 s forced expiration by the thermodilution technique. Total peripheral resistance was calculated as the difference between mean arterial and right atrial pressures divided by cardiac output.

Expiratory pressures of 2.5 to 30 mmHg produced a decrease in cardiac output. These manoeuvres were then repeated both after cardiac effector and after total autonomic blockade. When the expiratory pressure held was 10 mmHg or less, elimination of reflex changes in heart rate and total peripheral resistance did not affect the degree of change in cardiac output.

However, cardiac effector nerves played a significant role in maintaining cardiac output when subjects created an expiratory pressure of 20 mmHg. With the nervous system intact,

cardiac output demonstrated a 35% decrease during the Valsalva manoeuvre. Cardiac effector blockade magnified this response, leaving cardiac output at one half of the pretest level. The addition of sympathetic vasoconstrictor blockade did not significantly influence the amount of change in cardiac output.

The role of cardiac and vasomotor reflex activity in the maintenance of cardiac output was evenly weighted at the highest expiratory pressure. Forced expiration resulted in a 40% decrease in cardiac output. However, the total mechanical effect of the increased intrathoracic pressure was a loss of 60% of the resting level.

Corresponding measures of total peripheral resistance showed increases above resting values with each expiratory pressure. While manoeuvres requiring little effort (expiratory pressures of 2.5 and 5 mmHg) triggered only slight vasomotor responses, expiratory pressures of 10 to 30 mmHg resulted in increases in systemic resistance of 50 to 60% of resting values.

Although Gorlin and co-workers (1957) reported a late increase in mean pulmonary arterial pressure in some cases, the general consensus was that there is no secondary increase in this pressure (Stone et al, 1965; Lee et al, 1954; Price et al, 1953). However, the disagreement may be one of interpretation rather than of findings. Stone et al (1965), while reporting no change, discussed the difficulty in interpreting the significance of small changes. It has been argued that if the

secondary rise in arterial pressure represents an increase in venous return, the pulmonary arterial circulation should demonstrate a similar increase (Stone et al, 1965).

2.4.3 Phase three

With the release of respiratory strain, investigators have found an abrupt decrease in mean arterial blood pressure (Korner et al, 1976; Sharpey-Schaefer, 1965; Stone et al, 1965; Goldberg et al, 1952; Sarnoff et al, 1948) and in pulmonary arterial pressure (Stone et al, 1965). The absolute degree of change in these pressures was equal to that of intrathoracic pressure (Sharpey-Schaefer, 1965). Korner and associates (1976) reported that total autonomic nervous system blockade did not affect the changes in mean arterial pressure during this phase.

That the arterial pressure drops below control levels (Stone et al, 1965; Goldberg et al, 1952) may be explained by a loss of the direct effects of increased intrathoracic pressure through a period where cardiac output remains low. However venous pressure has also demonstrated an immediate decrease at the end of the manoeuvre (Price et al, 1953), suggesting an increase in venous return. It appears, therefore, that the delay in the increase in cardiac output is the result of transit time from the right atrium to the systemic circulation. This may be increased by a filling of the lungs with blood during the initial inspiration (Sarnoff et al, 1948).

The changes found in pulse pressure during this phase of the Valsalva manoeuvre are not consistent across experiments. Stone et al (1965) reported that diastolic pressure did not change, resulting in a further narrowing of pulse pressure. In contrast, an earlier study reported decreases in both systolic and diastolic blood pressure with pulse pressure normally not showing any change from the end of phase two (Goldberg et al, 1952).

In both studies pulse pressure was well below rest at the end of phase three. The group that did not find decreases in pulse pressure (Goldberg et al, 1952) also did not report a secondary parallel increase in systolic and diastolic pressure during strain. Differences in blood pressure levels at the end of phase two may account for the differences in the relative contribution of systolic and diastolic changes to the decrease in pressure during phase three.

2.4.4 Phase four

A marked overshoot in arterial pressure has been demonstrated during the final phase of the Valsalva manoeuvre (Korner et al, 1976; Stone et al, 1965; Lee et al, 1954; Price et al, 1953; Goldberg et al, 1952), with the highest pressures recorded within 7 s of release (Stone et al, 1965; Price et al, 1953). This was accompanied by increases in pulse pressure (Sharpey-Schaefer, 1965; Stone et al, 1965; Lee et al, 1954;

Goldberg et al, 1952) to levels significantly above those measured at rest (Stone et al, 1965). Additionally, one group reported that although systolic pressure showed the greatest changes, diastolic pressure also constributed to the mean arterial pressure response (Goldberg et al, 1952).

In an attempt to counteract these large increases in arterial pressure, heart rate fell below resting levels (Goldberg et al, 1952). Post-release, the increase in mean arterial pressure within the thorax was no longer balanced by an increased intrathoracic pressure. This resulted in elevated levels of transmural pressure and stimulation of the aortic baroreceptors. That this slowing of heart rate was more pronounced than that noted during the initial pressor response (phase one) has been explained by the synergistic action of the aortic and carotid baroreflexes (Sharpey-Schaefer, 1965).

Pulmonary pressures demonstrate a similar pattern of change in the mean arterial, diastolic and systolic pressures (Stone et al 1965; Lee et al, 1954). These responses, however, were of a smaller magnitude when compared to those in the brachial artery (Lee et al, 1954). The highest values were usually recorded within 5 s of release and 1 to 4 s before the systemic response (Stone et al, 1965).

Changes in pressure within the pulmonary circulation have been used to present a case for the role of increased venous return and cardiac output in the systemic pressure overshoot

(Stone et al, 1965; Lee et al, 1954). No increase in systemic arterial pressure occurred in the absence of a pressor response within the pulmonary capillaries. Moreover, the time period which separated the two pressure responses approximates transit time from the right to the left ventricle (Stone et al, 1965).

Accounts of the physiological changes with the Valsalva manoeuvre have all suggested that baroreceptor mediated vasoconstriction is involved in the arterial pressure overshoot. The decrease in pulse pressure during phase two has been selected as the stimulus for the reflex response (Korner et al, 1976; Sharpey-Schaefer, 1965; Stone et al, 1965; Gorlin et al, 1957; Judson et al, 1955; Lee et al, 1954; Price et al, 1953).

Cardiac patients in whom systolic, diastolic and pulse pressure were maintained throughout respiratory strain did not demonstrate the overshoot in pressure post-release. Radiographic studies showed a continuance of blood flow from the peripheral veins in these subjects (Judson et al, 1955).

However, cases have been reported with normal decreases in pulse pressure during the Valsalva manoeuvre in association with no pressure increase post-test (Stone et al, 1965; Judson et al, 1955). It was argued, therefore, that the vasoconstriction was not an important factor in the production of pressure changes during the fourth phase (Stone et al, 1965).

The role of baroreceptor mediated vasoconstriction in the pressor response during recovery has also been investigated

through pharmacological interference with the autonomic nervous system. The overshoot was eliminated by drugs which prevented peripheral vasoconstriction (Korner et al, 1976; Price et al, 1953; Sarnoff et al, 1948). However, the results of these studies may have been caused by blood pooling in veins with the loss of smooth muscle tone (Stone et al, 1965). Additionally, the response can be dampened by sympathetic pre-excitation with circulating epinephrine (Sarnoff et al, 1948) and l-norepinephrine (Price et al, 1953).

2.4.5 The Valsalva manoeuvre as a test of baroreceptor sensitivity

The increases in both mean and pulse pressure during the fourth phase of the Valsalva manoeuvre provide a strong stimulus to the aortic and carotid baroreceptors. Palmero and co-workers (1981) measured the cardiodepressor response of the baroreflex to this pressure overshoot. Subjects maintained an expiratory pressure of 40 mmHg for 20 s. According to the method of Smyth et al (1969), each systolic blood pressure was paired with the second RR interval following it. The regression coefficient of the line relating these two variables was used as an index of baroreceptor sensitivity.

The first few beats after the pressure increase were not associated with a slowing of the heart rate. Calculation of barosensitivity, therefore, was based on the responses of blood

pressure and heart period during the period which started with the first lengthened RR interval and ended with the highest systolic blood pressure.

Baroreceptor sensitivity measures obtained were highly correlated with those obtained in response to the injection of phenylephrine. One important advantage of the use of respiratory strain is that it does not require interference with the vasomotor response.

2.4.6 Summary

Increases in intrathoracic pressure with forced expiration result in an immediate parallel increase in systolic and diastolic pressure. After 1 to 2 s arterial pressures begin to gradually decline, with systolic pressure decreasing more rapidly than diastolic. It has been proposed that baroreceptors respond to the decreases in pulse pressure by increasing both heart rate and vasomotor tone. That these responses are involved in a secondary increase in blood pressure during strain with higher expiratory pressures, has been demonstrated.

Upon release of the Valsalva manoeuvre, mean arterial pressure is decreased by the same amount as intrathoracic pressure to levels below those measured at rest. Within 7 s post-release, this is reversed with large increases in both mean and pulse pressure. The associated bradycardia has been used as an indication of the sensitivity of the aortic and carotid

baroreceptors.

2.5 Barosensitivity During Dynamic Exercise

Bevegard et al (1966) examined the effects of baroreceptor stimulation during supine leg exercise. Negative pressures in a cuff placed around the neck were used to simulate an increase in arterial pressure through a stretch of the carotid baroreceptors. Significant and sustained decreases were found in heart rate and blood pressure during three levels of exercise. The absolute magnitude of change in heart rate and arterial pressure was not related to the initial levels of these parameters. However, only one subject reached an exercise heart rate of greater than 120 bpm.

Similar results were found with increases in the carotid sinus pressure in dogs (Melcher and Donald, 1981). During rest, mild and moderately severe exercise, the stimulus response curves for arterial blood pressure demonstrated 1) the same maximum slope at the same sinus pressure and 2) an upward displacement associated with increases in power output. As well, both initial (first 10 s) and steady-state heart rate response curves showed no difference with changes from rest to mild and moderately severe exercise except for upward shifts along the heart rate axis.

Results of these studies suggest that the baroreceptor set point but not the sensitivity or gain of the baroreflex is

changed with exercise. Melcher et al concluded that the changes in heart rate and blood pressure in response to baroreceptor stimulation are similar during rest and exercise. This conclusion was based on an argument put forth by Korner (1979). Changes in the slope of the response curves (gain) are thought to be baroreceptor dependent. Changes in the level of heart rate or blood pressure throughout the stimulus range that do not affect the pattern of the response, however, have been classified as baroreceptor independent.

In contrast, Bristow et al (1971) reported that the sensitivity or gain of the cardiodepressor component of the baroreflex (Smyth et al, 1969) was reduced in subjects performing erect bicycle exercise at heart rates comparable to those used by Bevegard and associates. Over a range of exercise intensities, the resting level of 20 to 25 msec change in RR interval per mmHg increase in systolic blood pressure approached 0 msec per mmHg when the preinjection RR interval decreased below 40 msec (150 bpm). The loss of reflex sensitivity at this exercise intensity was also apparent when expressed as the change in heart rate per unit change in blood pressure.

The investigators explained that the relationship between RR interval and systolic blood pressure is effectively linear while the relationship between heart rate and systolic blood pressure is hyperbolic. The former was chosen in order to examine changes in sensitivity of the baroreflex, therefore,

based on greater validity for the comparison of regression slopes.

The use of RR interval rather than heart rate may explain the different conclusions that have been made regarding the effects of dynamic exercise on the gain of the baroreflex. Heart rates recorded during the initial response to mild exercise in Melcher and Donald's study, when converted to RR intervals, did show a decrease in sensitivity or gain of the baroreflex control of heart rate with exercise.

Despite any decreases in baroreceptor sensitivity, the baroreceptor reflexes do play a role in determining the blood pressure responses to dynamic exercise (Melcher et al, 1981). Only small transient decreases were noted in dogs during the first 10 s of both light and moderately severe exercise when the baroreceptors were functioning normally. However with no baroreceptor input available, arterial pressure demonstrated a sustained decrease during light exercise and an initial decrease with a return to resting levels during moderately severe exercise.

2.5.1 Summary

It has been demonstrated that the response of the RR interval to increases in systolic blood pressure decreases with dynamic exercise. The ability of the baroreflex to decrease heart rate, whether expressed as the change in RR interval (msec)

or in heart rate (bpm) per unit change in blood pressure, approaches 0 with an exercise heart rate of 150 bpm. The smaller RR intervals or higher heart rates which accompany each level of systolic blood pressure during exercise, have been interpreted as a change in the set point of the baroreceptor.

Finally, that the baroreceptors play a role in the cardiovascular adjustment to exercise has been demonstrated through the comparison of blood pressure response with and without baroreceptor afferent input. Normally, arterial pressure increases with exercise despite vasodilatation within the exercising muscle. Elimination of baroreceptor afferent input in dogs resulted in either a sustained decrease in arterial blood pressure (light exercise) or an initial decrease in blood pressure with a return to resting levels (moderately severe exercise).

2.6 The Role of the Baroreceptor in Diving Bradycardia

Breath-hold facial immersion triggers three responses: apnea, bradycardia, and peripheral vasoconstriction. Moreover, each response is the result of an interaction of a number of reflexes. For these reasons, Daly et al (1979) have argued that the term "diving reflex" is misleading. This section of the paper will discuss the role of the baroreceptor reflex in diving bradycardia.

Paulev (1968) stated that there are adequate stimuli for an explanation of diving bradycardia based on a baroreceptor response to changes in arterial blood pressure. Relaxation of the respiratory muscles after a maximal inspiration results in an increase in intrathoracic pressure. These changes are transmitted to the arterial system and may, through the baroreflex, trigger decreases in heart rate.

The increase in thoracic pressure also acts as an impedance to venous return (Sharpey-Schaefer, 1965). In support of this, an initial hypotension during simple breath-hold and breath-hold combined with a variety of cold stimuli applied to the face has been reported (Kawakami et al, 1967). Diving bradycardia was found to be independent of changes in esophageal pressures within the range of -5 to +16 cm H_2O. The high esophageal pressures were created by closing the glottis. Whether the manoeuvre was initiated at the end of a normal expiration or at the end of a maximal inspiration did not make a large difference in these measures.

Two studies (Heistad et al, 1968; Kawakami et al, 1967) have documented gradual increases in systolic and diastolic blood pressure during breath-hold facial immersion. With a water temperature of 20° to 25° C, mean arterial pressure reached levels that were an average of 20% above resting levels (Heistad et al, 1968).

These increases in blood pressure are the result of

peripheral vasocontriction. Increases in vasomotor tone may be a direct effect of temperature receptor (Heistad et al, 1968) or arterial chemoreceptor (Coleridge et al, 1979) stimulation. Alternatively, the peripheral vasoconstriction may represent a baroreceptor mediated response to any initial decrease in venous return and cardiac output.

Two studies have examined the role of the baroreceptor in diving bradycardia. The first (Heistad et al, 1968) reported that decreases in heart rate did not parallel increases in blood pressure during breath-hold facial immersion in each of their subjects. The authors were unable to accept or reject the role of the baroreceptor in diving bradycardia based on this evidence. Decreases in heart rate separate of increases in blood pressure may have been the result of stimulation of temperature receptors in the face (Heistad et al, 1968; Paulev, 1968; Whayne et al, 1967; Kawakami et al, 1967; Brick, 1966) or of arterial chemoreceptors (Stromme and Blix, 1976; Moore et al, 1973; Kawakami et al, 1967).

The second study (Finley et al, 1979) examined the importance of increases in blood pressure to the diving bradycardia response. Breath-hold facial immersion (6° C water) was performed both at rest and while exercising at 60% of maximal oxygen uptake. Both the increases in systolic blood pressure and the decreases in heart rate during the resting trials were potentiated by the addition of exercise. Neither alpha nor beta

adrenergic blockade had an effect on the decrese in heart rate during breath-hold facial immersion. Alpha blockers weaken the bodies peripheral vasoconstrictor response, while beta blockers reduce increases in heart rate and cardiac contractility.

Cuff measures of systolic blood pressure supported a decrease in or elimination of sympathetic baroreceptor stimuli during the breath-hold facial immersions as a result of each pharmacological intervention. However, circulatory adjustments may have occurred in response to the autonomic blockade. Increases in either mean arterial or pulse pressure could have provided baroreceptor stimuli during the breath-hold facial immersion trials. As well, interactions exist between the sympathetic and parasympathetic control of the heart (Levy et al, 1971). Interference with one of these branches of the nervous system makes it difficult to interpret the final response, in this case the heart rate changes during breath-hold facial immersion.

2.6.1 Summary

Diving bradycardia may represent a baroreceptor mediated response to increases in arterial blood pressure. One study found that the decrease in heart rate appeared to follow the increases in blood pressure in some subjects. If these subjects were also those who demonstrated a strong heart rate response to breath-hold facial immersion, the role of the baroreceptor in

diving bradycardia would have been supported

2.7 General Summary

The baroreceptor reflex responds to increases in arterial blood pressure through decreases in heart rate and peripheral vasodilatation, and to decreases in arterial blood pressure through increases in heart rate. The majority of studies examining the reflex have used changes in RR interval in response to drug-induced increases in systolic blood pressure, as an indication of baroreceptor sensitivity. Subjects classified as baroreceptor sensitive with this measure also demonstrated large daily fluctuations in heart rate and an ability to maintain a relatively constant arterial blood pressure.

The present study used two manoeuvres to stimulate the arterial baroreceptors. The measurement of the relationship between changes in systolic blood pressure and changes in RR interval during the blood pressure overshoot in the recovery of the Valsalva manoeuvre has been validated against measures using drug-induced increases in blood pressure. Isometric exercise has not been used to examine baroreceptor sensitivity in previous studies. However, it has been shown that the system's ability to regulate arterial pressure is not changed during isometric exercise.

The purpose of this study was to compare measures of baroreceptor sensitivity in responders and non-responders to

breath-hold facial immersion. Subjects were placed into these groups based on their heart rate responses to breath-hold facial immersion performed during dynamic exercise. The addition of dynamic exercise to breath-hold facial immersion results in a heightened blood pressure response and a larger percent decrease in heart rate. The level of exercise used in the present study has been shown to reduce, but not eliminate, the cardiodepressor component of the baroreflex.

CHAPTER III

METHODS

3.1 Design

The purpose of this study was to compare measures of baroreceptor sensitivity in those individuals who demonstrate a pronounced slowing of pulse rate during breath-hold facial immersion (responders) and those who show little or no bradycardia (non-responders).

Volunteer university students performed three trials of breath-hold facial immersion during rest and three trials during mild steady-state cycling. Subjects were placed in groups of responders, non-responders and weak responders based on their heart rate response during the exercise trials. Thirty-nine students were screened in order to find a minimum of six who decreased their heart rate by greater than 35% and six who decreased their heart rate by less than 10% during the initial 10 s of each trial. The six with the strongest responses were classified as responders and the six with the weakest as non-responders. The remaining 27 subjects were labelled weak responders. Maximal oxygen uptake was measured during cycle ergometry using the open-circuit method in the six responders and the six non-responders on a separate occasion.

Each of the 39 students tested for their response to breath-hold facial immersion returned to the lab to perform three trials of forced expiration (Valsalva manoeuvre) and three trials of isometric handgrip exercise. Systolic and diastolic blood pressures were measured as often as possible (every 20 s) with a standard sphygmomanometer, both during the manoeuvres and during a 2 min recovery period. Heart rate was monitored continuously over the same period on a physiograph. The systolic blood pressure, diastolic blood pressure and heart rate response patterns of the responders and non-responders to breath-hold facial immersion were analyzed for possible differences in baroreflex sensitivity.

3.2 Pretest (Screening)

Twenty-one male and 18 female university students, aged 19 to 30 years, were pretested in order to identify six responders and six non-responders to breath-hold facial immersion. Subjects were classified according to their heart rate response to facial immersions performed during dynamic exercise.

The subjects were seated on a Quinton constant workload bicycle (model #844) with a pan of cold water (4°-6° C) supported at handlebar level. Both heart rate and rhythm were recorded on a single channel Cambridge electrocardiograph (model VS4) from a modified V lead. The paper speed was set at 50 $mm.s^{-1}$.

Breath-hold was initiated following a maximal inspiration. Subjects were instructed to breathe normally before the full inspiration and were taught to avoid forced breath-hold or a Valsalva manoeuvre. A maximal breath-hold effort was encouraged with each trial. The subjects assumed a position with their face over the water pan while 15 s pre-immersion and 30 s post-emersion electrocardiographic traces were recorded.

Subjects performed three facial immersions during rest. They then began cycling at a constant rate of 50 rpm. Power output on the ergometer was increased each minute until a heart rate of approximately 130 bpm was reached. This level of exercise was maintained until a second set of three facial immersions had been completed. A minimum of 4 min separated the facial immersion trials, both during rest and during exercise. Consecutive 1 min counts of heart rate were compared in order to ensure that the subject was in steady-state before initiating each facial immersion.

Pre-immersion heart rates were calculated from the average RR interval in the 12 s period preceding the full inspiration. The longest two-beat interval within the initial 10 s of the exercise facial immersions and the longest over the total duration of the resting facial immersions were chosen to represent the post-immersion heart rates.

Criteria for the classification of subjects were based on results from 21 students tested in a pilot study (Appendix A).

The screening was continued until a minimum of six subjects decreased their heart rate by greater than 35% of the pre-immersion level and a minimum of six decreased their heart rate by less than 10% of the pre-immersion level during the first 10 s of all three exercise breath-hold facial immersions. At that point, the six subjects with the strongest responses were selected as responders and the six with the weakest as non-responders. All subjects not placed into one of these two categories (27) were classified as weak responders.

3.3 Procedures

3.3.1 Direct measurement of maximal oxygen uptake

Direct measures of oxygen uptake were obtained using open-circuit spirometry as described by MacDougall et al (1982). Subjects exercised to the point of exhaustion on a Monark cycle ergometer (model #868). The initial workload was 300 kpm.min^{-1}. This was increased by 200 kpm.min^{-1} every 2 min for the females and by 300 kpm.min^{-1} every 2 min for the males.

During the final workloads, subjects wore a noseclip and breathed through a one-way valve. The volume of inspired air was measured with a Hewlett-Packard digital pneumotachometer (model # 4000VR). The linearity of the electrical output from the pneumotachometer was checked against actual flow measures using a 500 ml calibration syringe. A Godart oxygen analyzer (model #176) and a Hewlett-Packard capnograph (model #47210A) provided a

#47210A) provided a continuous assessment of the oxygen and carbon dioxide concentrations in the expired air. These measures were calibrated with two gas samples containing a known concentration of oxygen and carbon dioxide. Heart rate was monitored using a V lead system. All measures were recorded on a Narco Biosystems physiograph (model #PMP-4A).

3.3.2 Valsalva manoeuvre

The Valsalva manoeuvres were performed with a modified sphygmomanometer. Trials consisted of forced expiration through a mouthpiece against the mercury column.

A noseclip was worn during the manoeuvre. However, a small leak in the system (.5 - 1 $mmHg.s^{-1}$) was established with a two-way connector placed between two sections of tubing. A constant flow of air through this leak assured the experimenter that the subject had maintained an open glottis throughout the trial.

The Valsalva manoeuvre was initiated following a maximal inspiration. The subject then brought the mercury column to the 30 mmHg mark and maintained that level of respiratory effort for 40 s. The time from the initiation of the maximal inspiration to the start of the trial was not more than 5 s. A 7 min rest period followed each Valsalva manoeuvre.

3.3.3 Isometric exercise

Isometric exercise was performed with a Lafayette handgrip dynamometer (model #78010). The handle position was adjusted to fit each subject's grip size (ie. second phalangeal joint placed under the handle). Two maximal handgrip efforts, separated by 1 to 2 min of rest, were used to measure maximal voluntary contraction. These were completed approximately one half hour before the isometric trials.

During the experimental trials the participant maintained 70% of their maximal force of contraction for as long as possible. A loss of greater than 20% of this force level signalled the end of the trial due to fatigue. Instructions were given throughout the trials to involve only the dominant forearm muscles in the exercise. As well, subjects continuously reported the level of force being produced in order to avoid breath-hold. The time between the isometric manoeuvres was approximately 12 min.

3.3.4 Data collection

Subjects were seated while they performed three trials of forced expiration (Valsalva manoeuvre) and three trials of isometric handgrip exercise. Heart rate, systolic blood pressure and diastolic blood pressure were recorded during the manoeuvres and during a 2 min recovery period. Using a stethoscope and a standard sphygmomanometer, systolic and diastolic blood pressure

could be measured approximately every 20 s. Trials were repeated if fewer than two systolic and two diastolic measures were recorded during a manoeuvre. The cuff was placed on the nondominant arm and diastolic pressures were read at the point of muffling of the arterial sounds. Heart rate was monitored using a V lead system. A Narco Biosystems physiograph (model #PMP-4A) recorded the signal throughout the trials at a paper speed of 5 $mm.s^{-1}$. Baseline measures were recorded before each trial. Heart rate was counted over a 1 min period and paired with a simultaneous blood pressure reading. Trials began 1 min after these levels were recorded.

3.4 Data Analysis

Heart rates were estimated from the number of QRS complexes in each 10 s period during the Valsalva manoeuvre. Due to the varying length of the isometric trials, heart rates were counted over the 10 s preceding the end of the first, second, third and fourth quarter of the manoeuvre. Where these tests lasted less than 40 s, 5 s heart rate counts were used. Recovery heart rates for both manoeuvres were taken from consecutive 10 s strips on the physiograph during the initial 1.5 min post-release. All heart rate counts were estimated to the nearest half beat.

Heart rate, systolic blood pressure and diastolic blood pressure measures were converted to values which represented the

change from baseline levels. These data were then plotted over time using a Minitab computer program (Appendix D). Each plot contained data from one of three groups; responders, non-responders or weak responders. Visual examination of these plots was used to select the portions of the heart rate, the diastolic blood pressure and the systolic blood pressure responses that would best fit a linear regression model (Table 1 p. 57). However, points on the scatterplots did not distinguish between subjects or between trials. It is possible, therefore, that the pattern of change represented by the scatterplots did not accurately reflect the pattern of changes in heart rate and blood pressure during isometric exercise.

Direct measures in a small sub-sample (Appendix E) showed large increases and decreases in systolic and diastolic blood pressure which followed no set pattern during the first 7 s of recovery from the Valsalva manoeuvre. If this is a typical blood pressure response, cuff measurements taken during this period would represent random samples rather than a pattern of change over time. For this reason, cuff measurements taken during this period were excluded from the analyses.

The heart rates recorded in responders and non-responders during each time interval of the Valsalva manoeuvre and isometric exercise trials (Table 1) were entered into a separate repeated measures analysis of variance (BMDP-2V). The mixed design (ie. within and between subjects variables) examined the effects of 2

TABLE 1

The time intervals chosen for the analyses

		VALSALVA MANOEUVRE			ISOMETRIC HANDGRIP EXERCISE		
		Heart Rate	Systolic Blood Pressure	Diastolic Blood pressure	Heart Rate	Systolic Blood Pressure	Diastolic Blood pressure
TIME INTERVALS	1	test duration	test duration	test duration	test duration	test duration	test duration
	2	release to 40 s post-release	8 to 25 s post-release	8 to 55 s post-release	release to 20 s post-release	release to 25 s post-release	release to 25 s post-release
	3		25 to 55 s post-release		20 to 60 s post-release	25 to 55 s post-release	25 to 55 s post-release

groups by 3 repetitions by 3 or 4 time points. These analyses identified any group effects on the change in heart rate over time. The orthogonal option provided by this statistical program was used to examine group differences in any significant linear or quadratic components of change in heart rate over time.

However, blood pressure measures were recorded at different points in each trial and the number of measures varied across trials. In order to examine the pattern of change of these measures, simple regressions (SPSS) were performed for each subject using the data points from all three trials. Each regression line described the change in either systolic or diastolic blood pressure over one time interval (Table 1). Group comparisons (ie. responders vs non-responders) tested the differences in the slopes and then, where the rate of change of pressure was the same in the experimental groups, the differences in the intercepts of these lines. Data from each time interval of each pressure measure were entered separately into a one-way analysis of variance.

The results of all group comparisons were checked through an analysis of covariance (BMDP-2V). This statistical program was used to separate out any effects of group differences in factors other than the responsiveness to breath-hold facial immersion. The role of the baseline levels of the dependent variable being examined (ie. heart rate, systolic or diastolic blood pressure), as well as that of the subjects' fitness levels

were analyzed. Additional covariates were examined in the analysis of the isometric handgrip data. These were maximal grip strength and the average length of time to fatigue.

RESULTS

CHAPTER IV

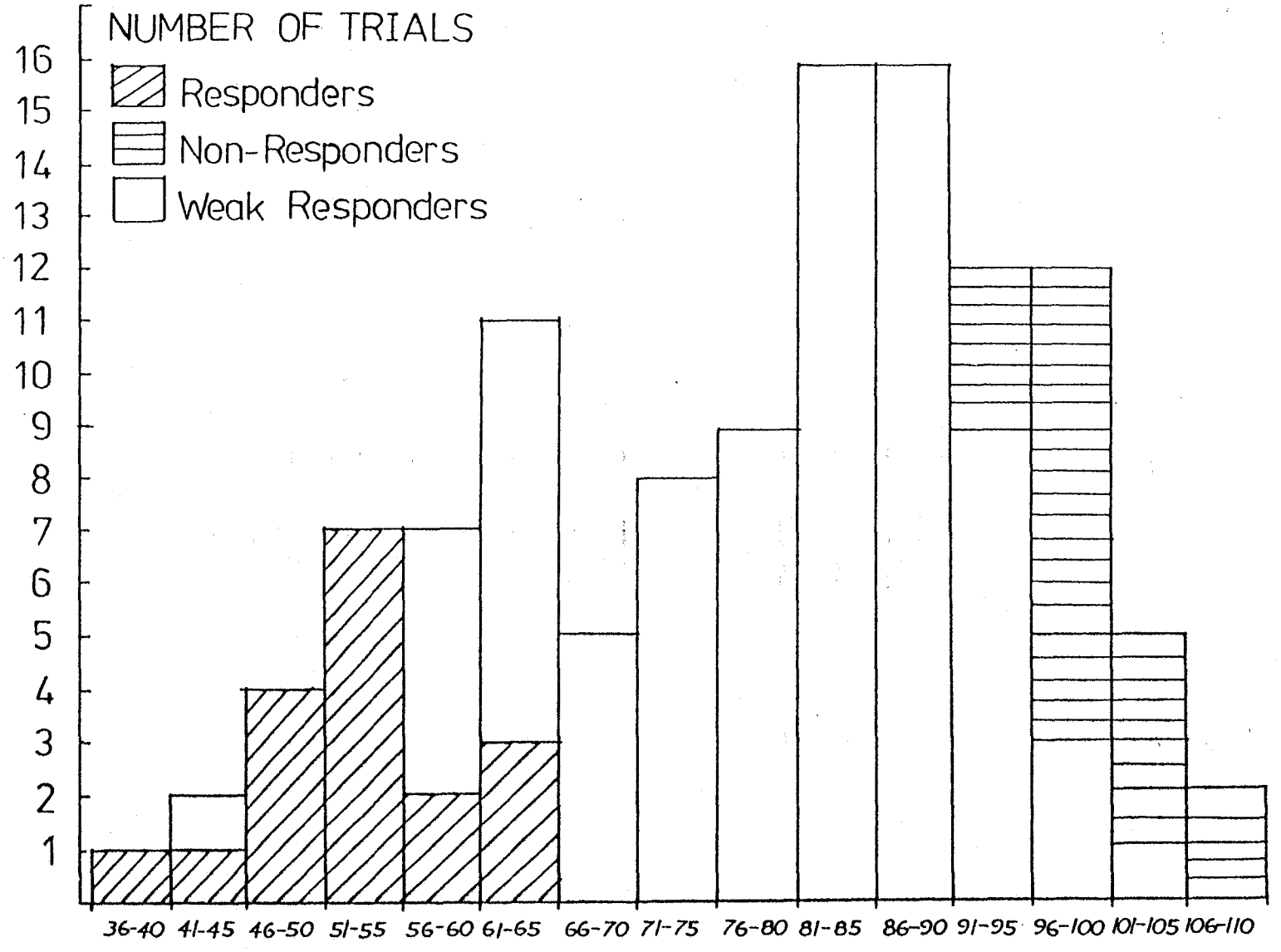
4.1 Pretest (Screening)

Subjects (N=39) cycled at a mean power output of 667 ± 34 $kpm.min^{-1}$ (range 300 - 1300 $kpm.min^{-1}$) during the exercise facial immersions. Pre-immersion heart rates in these trials ranged from 115 to 147 bpm. The mean pre-immersion heart rate, calculated from each subject's average measure across trials, was 132 ± 1 bpm. The corresponding values for responders and non-responders were 132 ± 3 and 130 ± 2 bpm, respectively.

Eight of 39 subjects exceeded the minimum response levels set for classification as a responder to breath-hold facial immersion, while 6 of 39 met the criteria for classification as a non-responder. The six subjects selected as responders (4♀, 2♂) were 22 ± 2 and the six selected as non-responders (2♀, 4♂) were 21 ± 1 years of age. Mean values for maximal oxygen uptake in these two groups were 41 ± 3 (range 32-51) and 47 ± 3 (range 35-56) $ml.kg.min^{-1}$, respectively. The 27 weak responders (12♀, 15♂) were 22 ± 0 years of age.

Figure 3 (p. 61) demonstrates the distribution of heart rate responses to the 117 trials of breath-hold facial immersion performed during exercise (ie. 3 trials for each of 39

Figure 3. The distribution of heart rate responses to 117 breath-hold immersion trials (ie. three trials for each of 39 subjects) performed during mild steady-state exercise. Post-immersion heart rates were calculated from the longest two beat interval in the initial 10 s of the manoeuvre.



POST-IMMERSION HEART RATE EXPRESSED AS A % OF PRE-IMMERSION HEART RATE

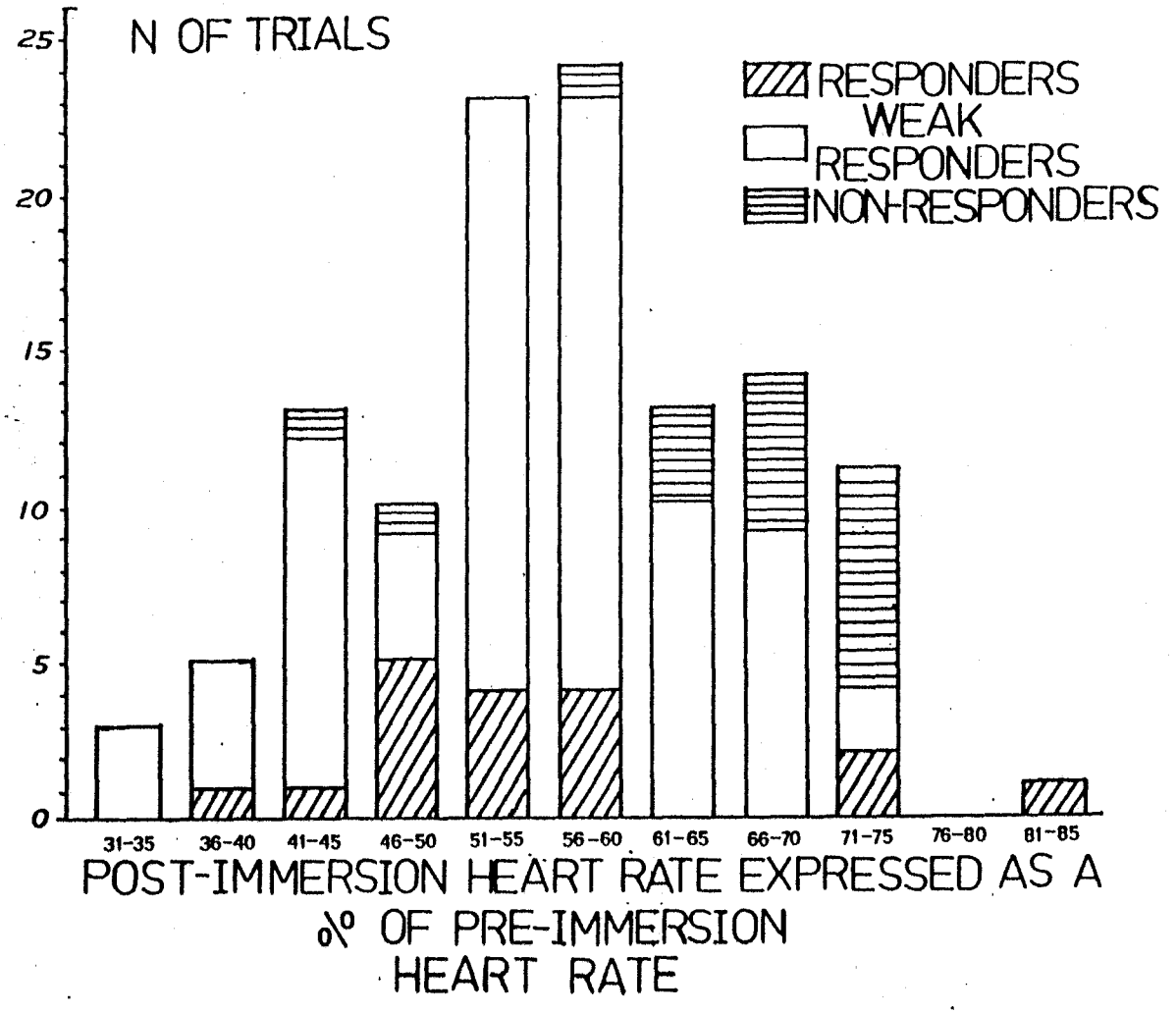
subjects). The longest two beat interval during the initial 10 s of facial immersion represented an increase in heart rate from the pre-immersion level in 6% of these trials (5 subjects). In the same number of trials (4 subjects) this measure represented a decrease in heart rate of 50% or greater. Forty-eight % of the trials produced two beat intervals within the first 10 s which equalled heart rates of 81 to 100% of the baseline level. The average within subject variance of the post-immersion heart rates expressed as a percentage of the pre-immersion heart rate (Figure 3) was 36.8 in the responders and 26.7 in the non-responders.

The degree of bradycardia found during the resting breath-hold facial immersions is illustrated in Figure 4 (p. 64). Each trial has been coded according to the strength of the response of the subject to the same manoeuvre performed during exercise (ie. responder, non-responder or weak responder). The average percent decrease in heart rate during resting trials for each subject showed little or no relationship (r=.22, 37df, N.S.) to the average exercise response.

Heart rate decreased by 18 to 67% in the resting breath-hold facial immersion trials. In 40% of the trials subjects reached heart rates that were just over one half (51-60%) of their pretest rate. The subject's average breath-hold time (range 23-125 s; mean 51 $\pm$ 4 s) was not related to their average percent decrease in heart rate (r=.003, 37 df, N.S.).

The mean value calculated from each subject's average

Figure 4. The distribution of heart rate responses to breath-hold facial immersion performed during rest. Post-immersion heart rates were calculated from the longest two beat interval. Each trial has been coded according to the strength of the response of that subject during the exercise trials (ie. responder, non-responder or weak responder).


N OF TRIALS
25
20
15
10
5
0
RESPONDERS
WEAK RESPONDERS
NON-RESPONDERS
31-35
36-40
41-45
46-50
51-55
56-60
61-65
66-70
71-75
76-80
81-85
POST-IMMERSION HEART RATE EXPRESSED AS A % OF PRE-IMMERSION HEART RATE

pre-immersion heart rate in the resting condition was 83± 2 bpm. Baseline measures ranged from 57 to 121 bpm. Subjects who decreased their heart rate by 50% or more in all three trials had an average pre-immersion heart rate of 88± 4 bpm (4 subjects). In comparison, those who maintained a heart rate that was 61% of the pretest heart rate or greater in all three trials had a mean baseline heart rate of 75± 3 bpm (8 subjects).

4.2 Time Intervals Chosen for the Examination of the Change Over Time in the Dependent Measures

Table 1 (p. 57) gives the time intervals chosen from scatterplots for the analyses. The repeated measures statistical programs were applied to the heart rate data collected in responders and non-responders during the isometric handgrip and the Valsalva manoeuvre trials. Over each time interval, heart rate demonstrated a significant ($p<.05$) linear component of change over time. In addition, significant ($p<.05$) quadratic components were identified in the change in heart rate during isometric exercise and over the second time interval for both the isometric and Valsalva manoeuvre trials. However, groups did not differ significantly in the linear or quadratic components of the change over time.

4.3 Valsalva Manoeuvre

No significant differences between responders and

non-responders to breath-hold facial immersion were found in heart rate, systolic or diastolic blood pressure responses to the Valsalva manoeuvre. The average baseline heart rate for the Valsalva manoeuvres was 72 ± 2 bpm. This measure was associated with a systolic pressure of 119 ± 2 mmHg and a diastolic pressure of 79 ± 1 mmHg. Heart rates of more than 20 bpm below baseline levels were recorded during the first 40 s of recovery (ie. the second time interval p. 57) in 13 subjects. Values were as low as 39 bpm below the baseline levels. Systolic blood pressure measures greater than 20 mmHg above baseline were recorded during the same portion of the recovery traces in 34 subjects, with values as high as 54 mmHg above baseline. In addition, diastolic blood pressures of 20 mmHg above baseline were recorded during the first 40 s of recovery in 2 subjects.

4.4 Isometric Handgrip Exercise

The mean pretest heart rate for the isometric trials was 75 ± 2 bpm. Mean baseline blood pressure was 119 ± 2/76 ± 1 mmHg.

Figures 5 (p.68) and 6 (p. 70) illustrate the relationship between handgrip strength and the maximal increase over three isometric trials in systolic and diastolic blood pressure, respectively. Handgrip strength varied from 29 to 67 kg across subjects. Similarly, the highest recorded systolic pressure response (Figure 7 p. 72) and the highest recorded diastolic pressure response (Figure 8 p. 74) in individual subjects have

Figure 5. The relationship between each subject's (N=38) grip strength and the maximal recorded increase in systolic blood pressure over three isometric trials.

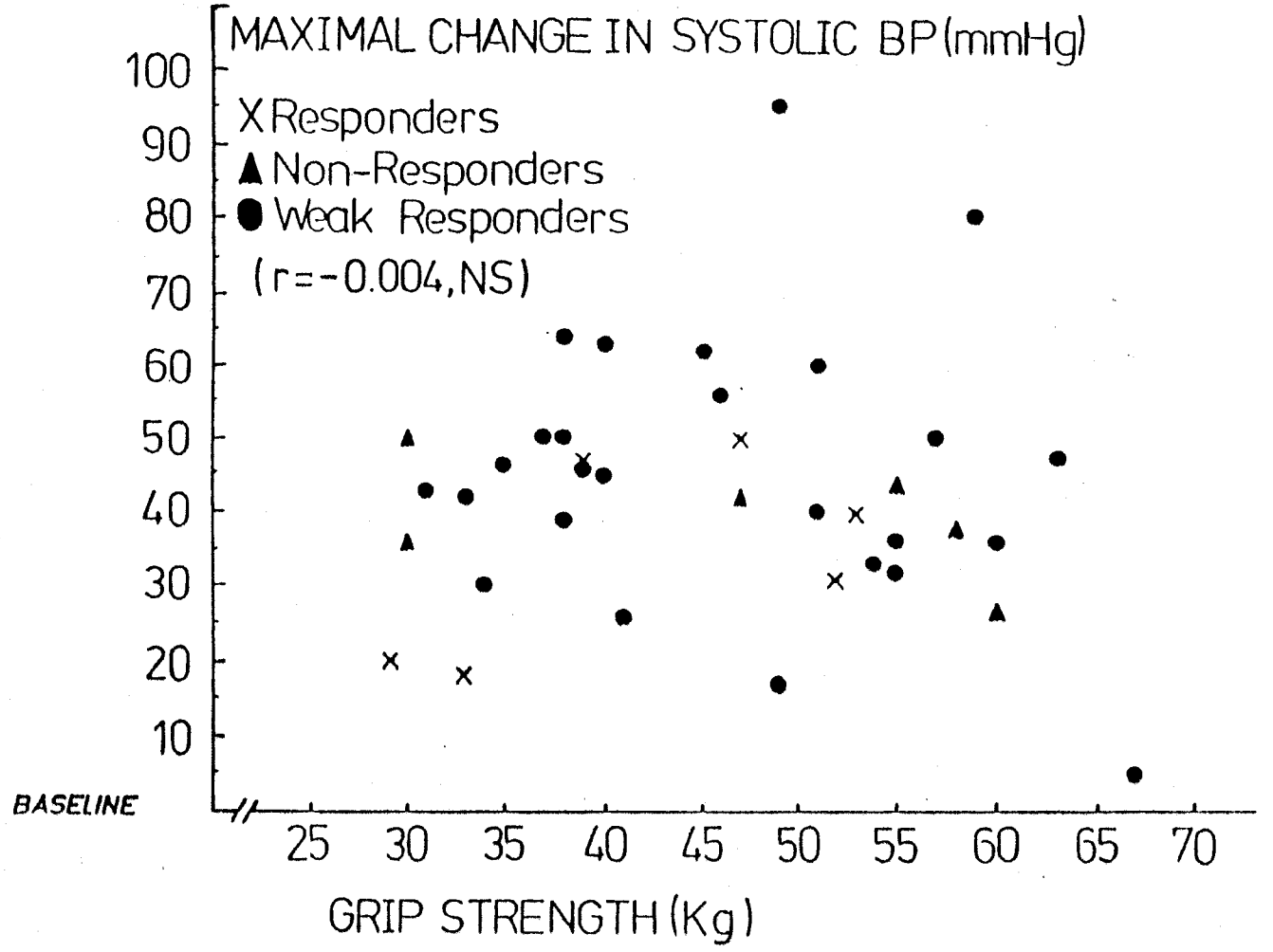

MAXIMAL CHANGE IN SYSTOLIC BP (mmHg)
X Responders
▲ Non-Responders
● Weak Responders
(r=-0.004, NS)
100
90
80
70
60
50
40
30
20
10
BASELINE
25
30
35
40
45
50
55
60
65
70
GRIP STRENGTH (Kg)

Figure 6. The relationship between each subject's (N=36) grip strength and the maximal recorded increase in diastolic blood pressure over three isometric trials.

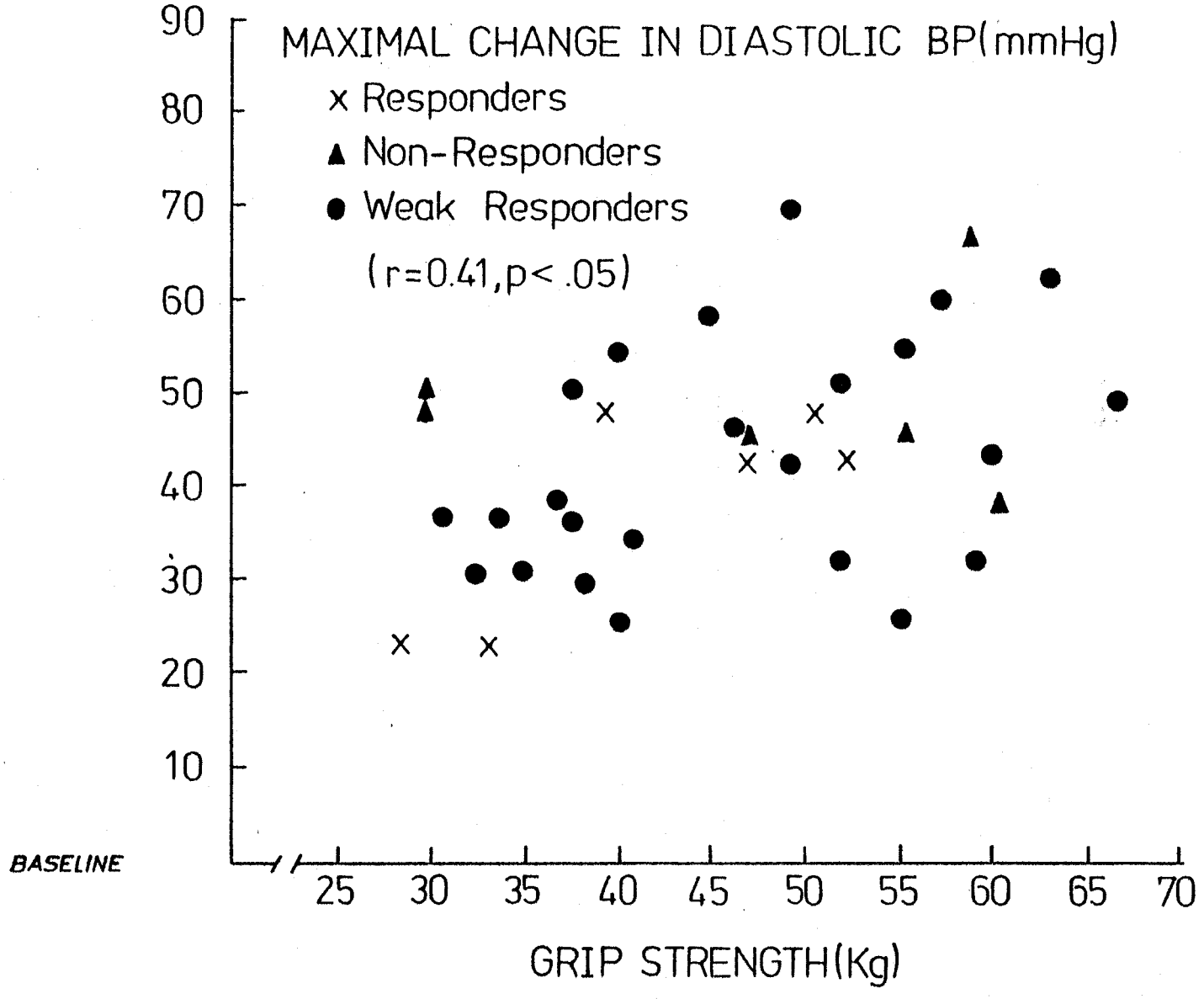

MAXIMAL CHANGE IN DIASTOLIC BP(mmHg)
x Responders
▲ Non-Responders
● Weak Responders
(r=0.41, p< .05)
90
80
70
60
50
40
30
20
10
BASELINE
25
30
35
40
45
50
55
60
65
70
GRIP STRENGTH(Kg)

Figure 7. The relationship between each subject's (N=38) average length of time to fatigue and the maximal recorded increase in systolic blood pressure over three isometric trials.

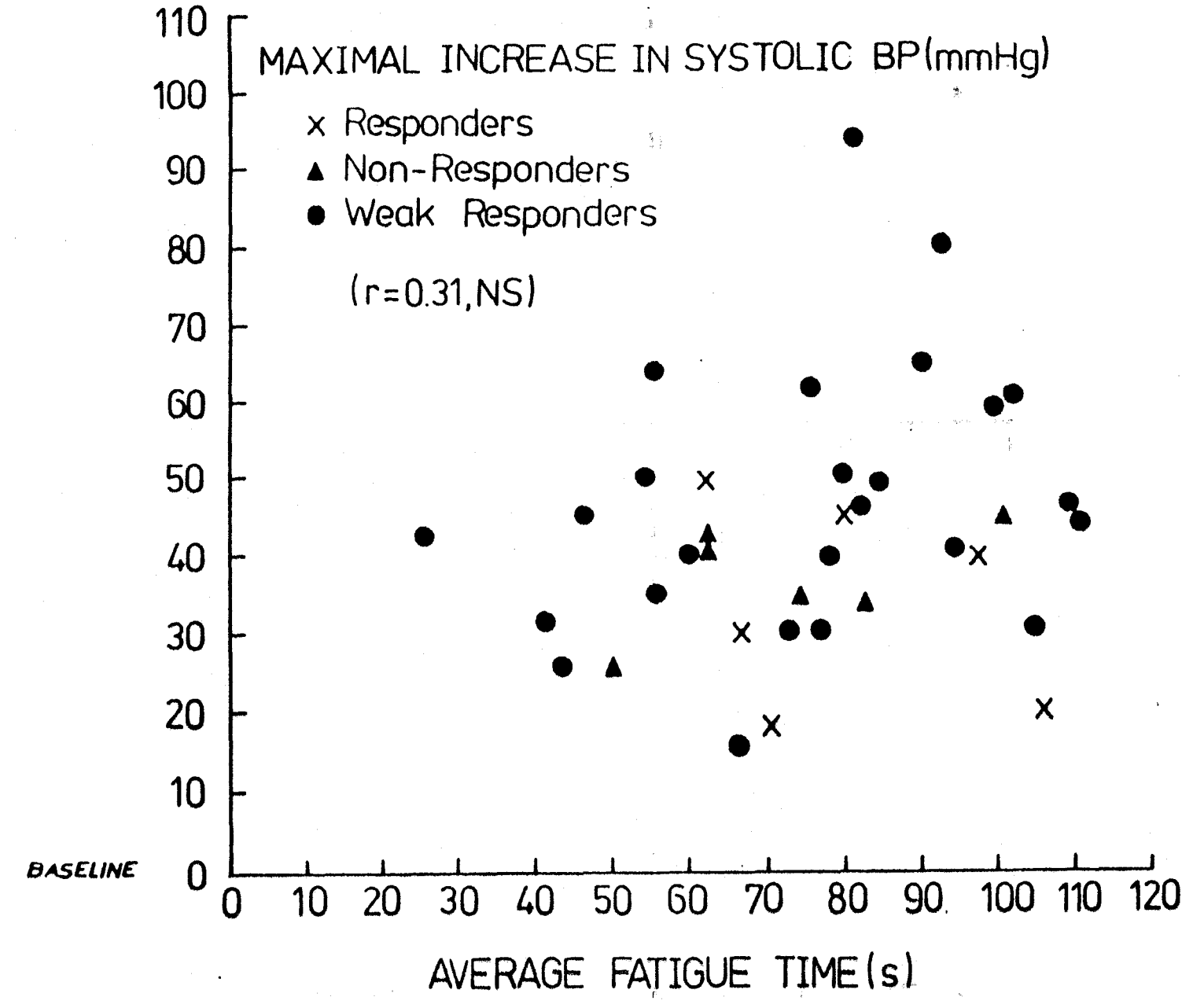
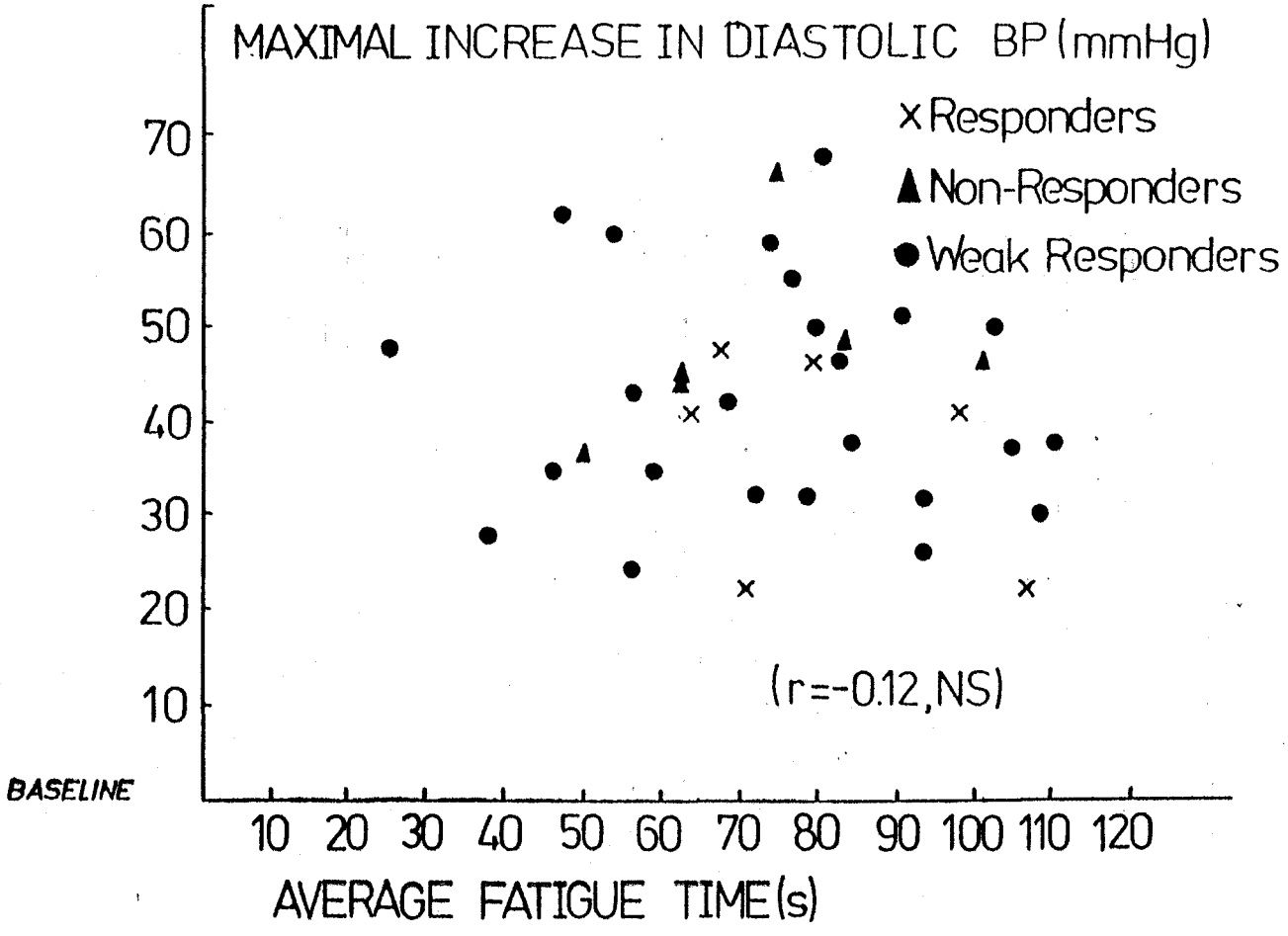

MAXIMAL INCREASE IN SYSTOLIC BP(mmHg)
x Responders
▲ Non-Responders
● Weak Responders
(r=0.31,NS)
110
100
90
80
70
60
50
40
30
20
10
0
BASELINE
0 10 20 30 40 50 60 70 80 90 100 110 120
AVERAGE FATIGUE TIME(s)

Figure 8. The relationship between each subject's (N=36) average length of time to fatigue and the maximal recorded increase in diastolic blood pressure over three isometric trials.

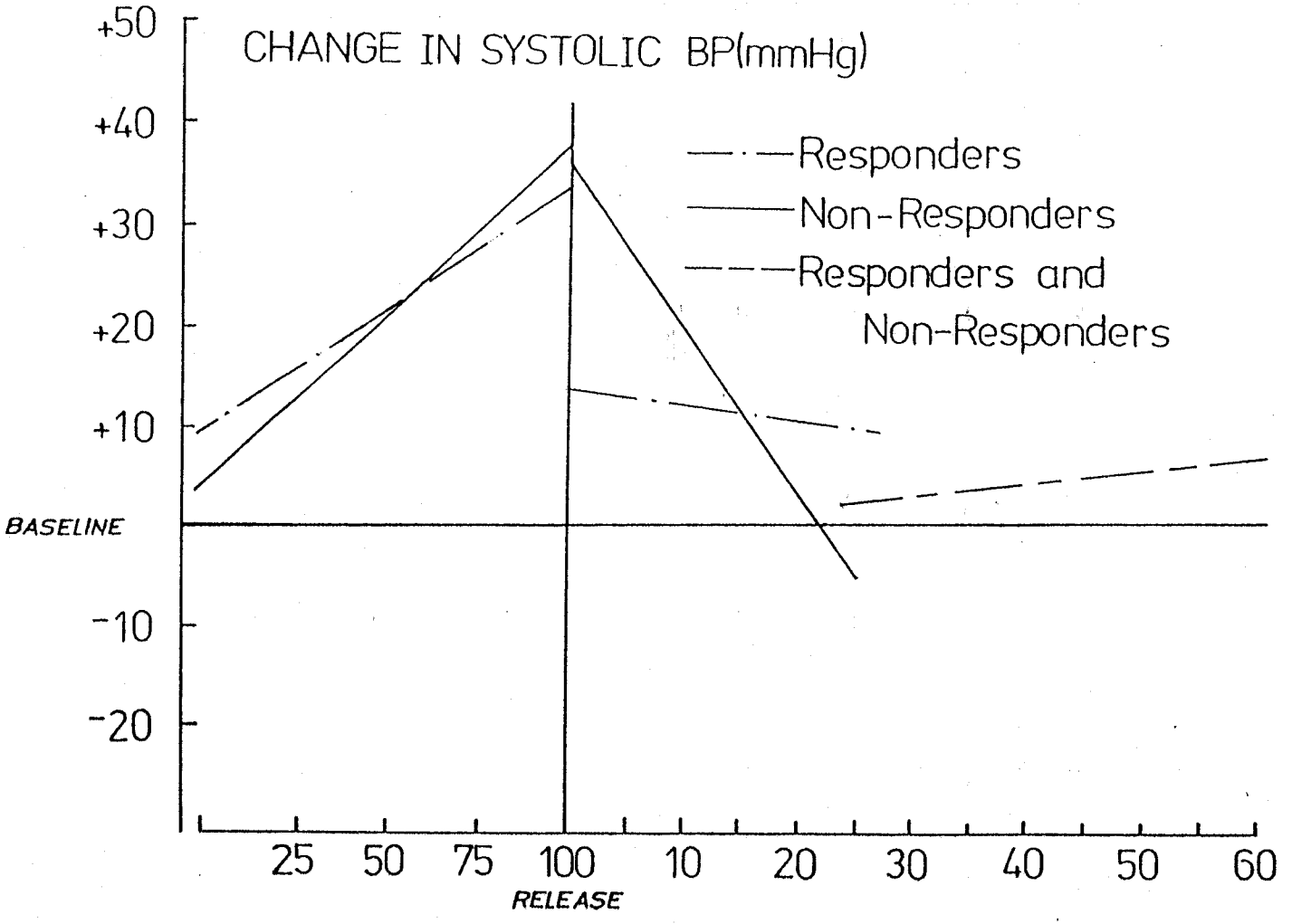

MAXIMAL INCREASE IN DIASTOLIC BP (mmHg)
× Responders
▲ Non-Responders
● Weak Responders
70
60
50
40
30
20
10
BASELINE
(r=-0.12, NS)
10 20 30 40 50 60 70 80 90 100 110 120
AVERAGE FATIGUE TIME (s)

been plotted against the average length of time to fatigue over the three isometric trials. Individual trials of isometric handgrip exercise lasted from 23 to 151 s. Those subjects without a blood pressure recording in the last quarter of at least one trial were not included in the scatterplots. The only significant relationship was between handgrip strength and each subject's (N=36) maximal increase in diastolic blood pressure over the three isometric handgrip trials ($r=.41$, 34 df, $p<.05$).

The mean maximal recorded increase in systolic blood pressure over the three isometric trials was 43 ± 2 mmHg (N=38). The corresponding measure of the maximal increase in diastolic blood pressure response was 43 ± 2 mmHg (N=36). In one trial of one subject, systolic blood pressure increased by 95 mmHg and diastolic blood pressure increased by 68 mmHg. This represented an elevation in mean arterial pressure of 77 mmHg. In contrast, all systolic and diastolic blood pressure measures taken in two subjects were within 25 mmHg of the pretest level.

An analysis of variance revealed a significant difference ($F[1,10]=5.33, p<.05$) in the slope of the increase in systolic blood pressure (see Methods p. 58) during the isometric trials between the responders and the non-responders to breath-hold facial immersion (Figure 9 p. 77). Mean values for these two groups were $.64 \pm .12$ and $.95 \pm .05$ mmHg of increase in systolic blood pressure per unit of time (length of trial in seconds/40), respectively. In addition, responders showed a significantly

Figure 9. Changes in systolic blood pressure in response to isometric handgrip exercise. One regression line was calculated for each time interval from the measures recorded over three trials of each subject. The lines on the graph represent an average slope and an average intercept. The slope of the response was higher in the non-responders, both during the isometric trials ($p<.05$) and over the first 25 s of recovery ($p<.01$). Responders and non-responders did not differ in the average slope or the average intercept of the lines representing the systolic blood pressure response from 25 to 55 s post-release. The regression line for the response over this period represents data collapsed over groups.


CHANGE IN SYSTOLIC BP(mmHg)
+50
+40
+30
+20
+10
BASELINE
-10
-20
Responders
Non-Responders
Responders and
Non-Responders
25
50
75
100
RELEASE
10
20
30
40
50
60
Isometric Exercise
(∂° trial duration)
Recovery(s)
TIME

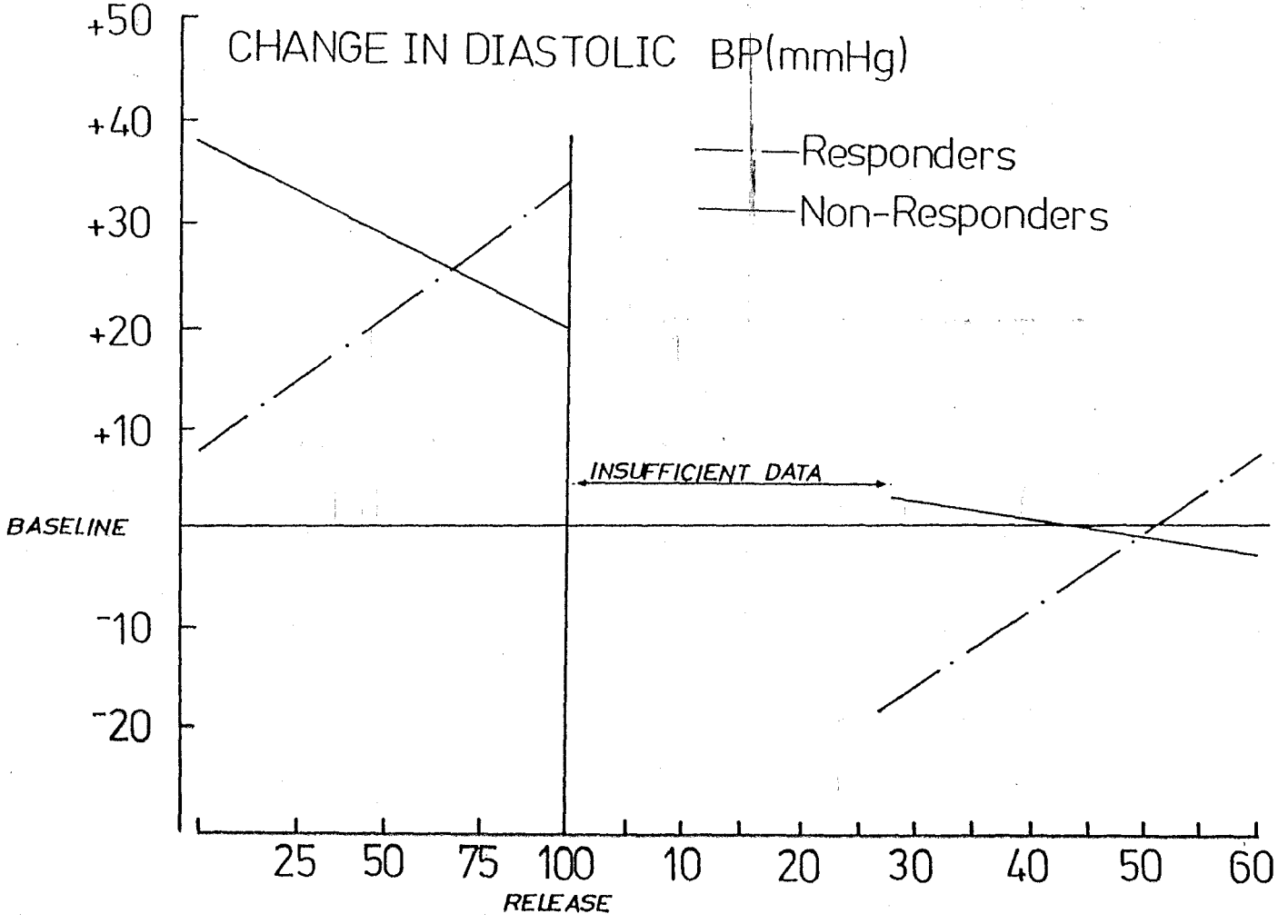
lower rate of decrease in systolic blood pressure (-.02 ± .36 mmHg.s^{-1}) than the non-responders (-1.6 ± .25 mmHg.s^{-1}) over the initial 25 s of recovery (analysis of variance - $F[1,10]=12.07, p<.01$).

Differences between responders and non-responders were also found in the diastolic blood pressure response to isometric exercise (Figure 10 p. 80). The mean slope of the response during isometric exercise represented an increase in diastolic blood pressure in the responders (.63 ± .15 mmHg per unit increase in time), while that of the non-responders (-.38 ± .12 mmHg per unit increase in time) represented a decrease in diastolic blood pressure (analysis of variance - $F[1,10]=28.89$, $p<.001$).

Too few diastolic pressure measures could be taken over the first 25 s of recovery to compare the extreme groups. However, significant group differences (analysis of variance - $F[1,10]=5.26$, $p<.05$) in the slope of the response were found over a period which began 25 s post-release and ended 55 s post-release. The mean slope of the response over this time interval was .92 ± .48 mmHg.s^{-1} in the responders and -.21 ± .11 mmHg.s^{-1} the non-responders. The regression lines calculated for 4 of the 6 responders had a positive slope and for 5 of the 6 non-responders had a negative slope.

Finally, the mean change in heart rate over the time period from 15 to 55 s post-release was significantly different (analysis of variance - $F[1,10]=6.64$, $p<.05$) in the responders

Figure 10. Changes in diastolic blood pressure in response to isometric handgrip exercise. One regression line was calculated from the data collected over the three trials of each subject. The lines on the graph represent an average slope and an average intercept. Group differences were found in the slope of the response both during the isometric trials ($p<.001$) and over a time interval from 25 to 55 s post-release ($p<.05$).

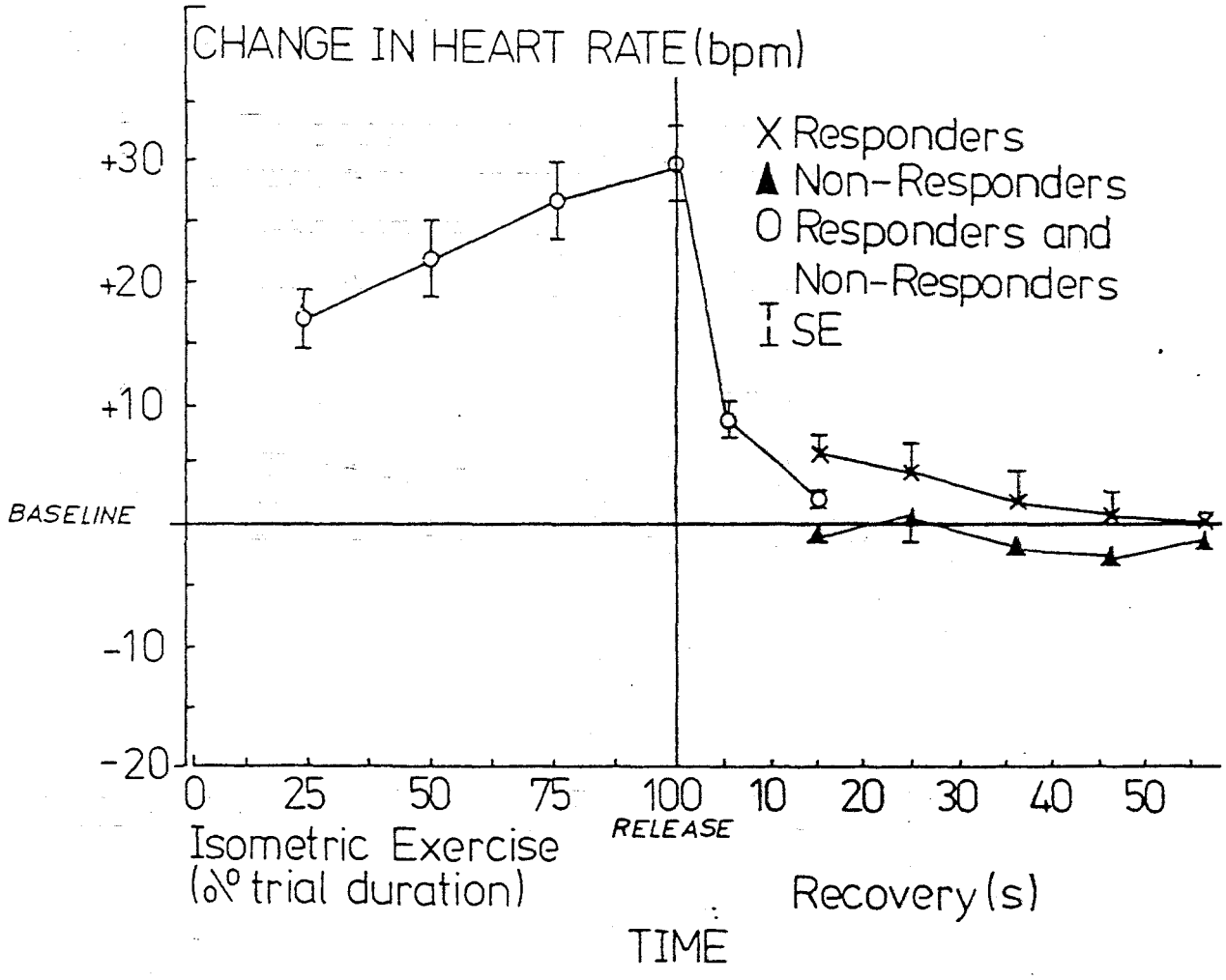

+50
+40
+30
+20
+10
BASELINE
-10
-20
CHANGE IN DIASTOLIC BP(mmHg)
Responders
Non-Responders
INSUFFICIENT DATA
25
50
75
100
RELEASE
10
20
30
40
50
60
Isometric Exercise
(% trial duration)
Recovery (s)
TIME

(+3.6 bpm) and non-responders (-1.2 bpm) to breath-hold facial immersion (Figure 11 p. 83). The slope of the heart rate response over the same time interval was similar in the two groups (time/group interaction N.S.).

4.5 Analyses of Covariance

The level of the pretest heart rate was related to the change in heart rate both over the duration of the isometric trials ($F[1,6]=10.9$, $p<.05$) and during the initial 40 s post-release of the Valsalva manoeuvre ($F[1,9]=15.9$, $p<.01$). As well, a relationship was demonstrated between the pretest level of systolic blood pressure and the intercept of the regression line for the change in systolic blood pressure during isometric exercise ($F[1,8]=8.52$, $p<.05$). A portion of the variance in both the slope ($F[1,6]=6.69$, $p<.05$) and the intercept ($F[1,6]=7.74$, $p<.05$) of the regression lines for the change in systolic blood pressure between 8 and 25 s post-release of the Valsalva manoeuvre may be accounted for by subject differences in maximal oxygen uptake. In each of these instances, neither the analysis of covariance nor the analysis of variance demonstrated a significant group effect.

Figure 11. Changes in heart rate ($X \pm SE$) in response to isometric exercise. These values were not different in the reponders and non-responders to breath-hold facial immersion, either during the isometric trials or over the initial 15 s of recovery. Mean values plotted over these time intervals represent data collapsed over the two groups. The analysis of variance for the data collected between 15 and 55 s post-release revealed a significant ($p<.05$) group effect and a nonsignificant time by group interaction.


CHANGE IN HEART RATE (bpm)
+30
+20
+10
BASELINE
-10
-20
X Responders
▲ Non-Responders
O Responders and Non-Responders
I SE
0
25
50
75
100
10
20
30
40
50
RELEASE
Isometric Exercise (0° trial duration)
Recovery (s)
TIME

DISCUSSION

CHAPTER V

The results of this study indicate that differences in the blood pressure response to isometric handgrip exercise exist between responders and non-responders to breath-hold facial immersion performed during dynamic exercise.

5.1 Breath-hold Facial Immersion

Preliminary invasive data collected in 2 responders and 2 non-responders (Appendix E) showed increases in mean arterial pressure of 27±5 mmHg and in pulse pressure of 12 ± 4 mmHg during resting breath-hold facial immersion. Heistad et al (1968) reported a mean increase of 15 mmHg in mean arterial pressure during 30 s breath-hold facial immersions. Colder water temperatures in the present investigation (4°-6° C vs 20°-25° C) may partially explain the stronger pressor response (Heistad et al, 1968).

Breath-hold facial immersions performed during exercise produced larger increases in mean arterial (35 ± 5 mmHg) and pulse pressure (26 ±4 mmHg) than were found in the resting trials (direct measures). This is in agreement with the findings of

Finley and associates (1979). They reported a heightened systolic blood pressure response during breath-hold facial immersions performed during cycling at 60% of maximal work capacity.

The heart rate responses to breath-hold facial immersion performed during exercise were investigated in a pilot study (Appendix A). The results showed that the differentiation between responders, non-responders and weak responders occurred within the initial 10 s. In this portion of the invasive exercise trials, responders demonstrated increases (ie. >10 mmHg) in both mean arterial (12 to 24 mmHg) and pulse pressure to levels above those measured before the manoeuvre. All increases in pulse pressure were associated with bradycardia. Non-responders, on the other hand, did not show pulse pressures above baseline levels. Each non-responder increased their mean arterial pressure in the initial 10 s of one breath-hold facial immersion trial (16 and 24 mmHg).

Heistad and associates (1968) reported decreases in heart rate during breath-hold facial immersion that were not preceded by increases in mean arterial pressure. Examples of this were also found during the invasive trials. Each of the responders demonstrated an initial bradycardia in the resting breath-hold facial immersions which was not associated with increases in either mean or pulse pressure. Similarly, one responder (CA) showed a decrease in heart rate at the initiation of both

exercise trials before mean or pulse pressure began to increase. In addition, heart rate in one responder (BL) decreased from 82 to 60 bpm with only transient increases in mean arterial pressure of approximately 5 mmHg during one resting breath-hold facial immersion.

In Tables A (resting breath-hold facial immersion) and B (breath-hold facial immersion performed during exercise) of Appendix E, all breath-hold trials with 0 data points did not show an increase in the respective blood pressure measure. Both mean arterial and pulse pressures remained at or below baseline levels in one resting (responder) and in one exercise (non-responder) trial.

Ignoring those breath-hold facial immersion trials with less than 7 data pairs (Tables A and B), correlation coefficients suggest a wide variability in any cardiodepressor effect of increases in mean arterial and pulse pressure. The low and negative correlation values cannot be explained through opposite changes in mean arterial and pulse pressures. Except for a few beats at the initiation of breath-hold facial immersions performed during exercise in one responder (CA), these two pressure measures always changed in the same direction. The strength of the relationship between changes in blood pressure and RR interval may depend on the level of activity of other mechanisms known to cause heart rate changes during breath-hold facial immersion (ie. chemical and temperature receptor

stimulation).

The role of cardiopulmonary baroreceptor stimulation in the diving response must also be considered. Atrial receptor stimulation results in tachycardia, while bradycardia with a resultant hypotension is triggered through stimulation of the ventricular receptors (Brown, 1979). As well, animal work has shown that changes in central blood volume (Billman et al, 1981; Ludbrook et al, 1981) and increases in the positive end-expiratory pressure in the lung (Mancia et al in Sepe et al, 1982) may influence the heart rate response to arterial baroreceptor stimulation.

Cardiopulmonary baroreceptor stimulation may occur during breath-hold facial immersion as a result of increases in intrathoracic pressure or in response to any resultant decreases in venous return. In addition, the increases in pulse pressure over pretest levels which were found during the invasive trials of breath-hold facial immersion may reflect increases in venous return and, therefore, blood volume changes throughout the cardiopulmonary system. Whether any of these changes are strong enough to play a role in the heart rate response during breath-hold facial immersion is not known.

In a pilot study, echocardiographic measures of left ventricular dimensions were obtained in one subject performing erect bicycling at a workload of 600 kpm.min^{-1}. The addition of breath-hold did not obscure the view of the left ventricle pro-

vided that the amount of air in the lungs was no greater than 50% of vital capacity.

5.2 Valsalva Manoeuvre

Palmero et al (1981) reported that the increase in systolic blood pressure during the recovery phase of the Valsalva manoeuvre could be used as a barostimulus for the measurement of barosensitivity. These researchers focused on the portion of the invasive blood pressure traces which began with the first elongated RR interval and ended with the highest systolic blood pressure. The regression coefficients representing the msec change in the RR interval per unit increase in systolic blood pressure were only considered measures of baroreceptor sensitivity if the correlation coefficient was greater than .65. However, the authors did not report the number of data points included in each correlation or the significance level of the correlation coefficients.

Direct measures (Table C Appendix E) did not show a significant relationship between increases in blood pressure and increases in the RR interval during the recovery phase of the Valsalva manoeuvre. Those trials with the highest number of data pairs (8 or 9) showed correlation coefficients of -.2 and .15 between measures of change in pulse pressure and RR interval, and of -.14 and .29 between measures of change in mean arterial pressure and RR interval. These low values suggest that the

baroreceptor response to increases in arterial pressure did not play an important role in the control of heart rate during the recovery from forced expiration (Valsalva manoeuvre).

In experiments performed by Palmero and associates (1981), the Valsalva manoeuvres were held for 20 s at an expiratory pressure of 40 mmHg. However in the present study, subjects maintained a mouth pressure of 30 mmHg for 40 s. The 25% lower mouth pressure was associated with a 46% lower (33 ± 8 -- direct measures vs 60.8 ± 4.2 mmHg) maximal change in systolic blood pressure during the recovery phase. The different intensities of forced expiration may also have resulted in a shorter time period over which mean arterial and pulse pressure were increasing during recovery in the present study. If this were the case, fewer data points would be available for the calculation of the regression coefficients.

In three of the four subjects (DA and DM--non-responders, CA--responder) involved in the invasive trials, secondary increases in pulse pressure (ie.>10 mmHg) were observed during both Valsalva manoeuvres (Figure D Appendix E). Final levels were either below, equal to or above those measured before the test. Increases in pulse pressure during this phase of the Valsalva manoeuvre were also reported by Korner et al (1976). That other investigators (Stone et al, 1965; Gorlin et al, 1957) did not find secondary increases in pulse pressure may be explained by their use of higher expiratory pressures maintained

over a shorter time period. The increases found in the invasive trials may represent some ability to regain stroke volume. It is the decrease in venous return and the increases in peripheral resistance in response to a diminished pulse pressure that are thought to be responsible for the blood pressure overshoot during the recovery from the Valsalva manoeuvre (Stone et al, 1965).

The regression lines describing the heart rate and blood pressure responses to the Valsalva manoeuvre were not different in the responders and non-responders in the present investigation. This suggests that these two groups are equally barosensitive. However with heart rates counted over 10 s periods and 20 s between blood pressure measures, rapid changes which might have reflected differences between the two groups may have been missed.

It is also possible that wide variability in the measures used in this study was able to mask group differences. For each subject the absolute workload performed during the VM trials (30 mmHg for 40 s) represented a different percentage of their maximal capacity for forced expiration. Differences in the heart rate and blood pressure responses to work performed by the respiratory muscles, therefore, would account for a portion of this variability.

A check of mean levels of heart rate for the responders and non-responders at the different time points did not suggest that variance was a problem or that group differences could be

demonstrated with a larger number of subjects. However, group differences in the blood pressure responses (ie. the slopes and intercepts of the regression lines) may have been missed due to high variability of the measures. For example, the slope of the diastolic blood pressure response over a period from 8 to 25 s post-release represented a net change of 18 mmHg in the non-responders compared to a net change of 77 mmHg in the responders.

5.3 Isometric Handgrip Exercise

The regression line for systolic pressures during isometric exercise in the non-responders demonstrates a greater average increase per unit of time than that of the responders (Figure 9 p. 77). One interpretation of this finding is that the the non-responders are less able to maintain a resting level of arterial blood pressure. Ogawa and co-workers (1981) demonstrated a negative correlation between baroreflex sensitivity and the variability of systolic blood pressure. However, the changes in systolic blood pressure must be considered along with the diastolic blood pressure responses which would have a greater effect on mean systemic pressure (Figure 10 p. 80). In the present study, non-responders showed a trend toward a decrease in diastolic blood pressure during isometric exercise. In comparison, the regression line for the responders represents increases in diastolic blood pressure over

the test duration.

The use of regression lines limits the interpretation of these results. Without actual measures of systolic and diastolic blood pressure at set time points, a comparison of the levels of baroreceptor stimuli (e.g. mean arterial pressure and pulse pressure) in the two groups cannot be made. As well, the collapsing of data over trials in order to calculate the regression line for each subject may have introduced artifact. For example, only two non-responders actually showed a decrease in diastolic blood pressure during a single isometric exercise trial. However, the regression lines for five of these subjects had a negative slope (Appendix C). Therefore, we do not know whether the responders were better able to regulate arterial pressure during isometric exercise than the non-responders.

Differences in the regression lines for blood pressure responses over the next two time intervals (Table 1 p. 57) suggest higher levels of baroreceptor sensitivity in the responders. Over the initial 25 s of recovery, responders showed the flattest systolic blood pressure response (Figure 9 p. 77). Measures taken during the last 2 s of the isometric trials were included in the data which produced these regression lines. However, only three responders and three non-responders had systolic blood pressures recorded during this period before release. The mean of these subjects' average values for the change in systolic blood pressure at the end of the isometric

trials were 30± 5 mmHg in the responders and 34± 6 mmHg in the non-responders. No readings were taken over the 8 s period following release (Appendix D). The response patterns for changes in systolic pressure over the next 30 s were similar in the two groups.

During the second phase of recovery (26-55 s post-release), diastolic pressure measures in the responders produced regression lines with a positive mean slope while those of the non- responders produced regression lines with a negative mean slope. The illustration in Figure 10 (p. 80) suggests that the non-responders are decreasing their diastolic blood pressure towards the baseline level. The pattern for the responders, on the other hand, suggests that they are recovering from a drop in diastolic blood pressure to levels below those recorded before the test. Actual measures (Appendix D) show diastolic pressures in both groups that are lower than pretest levels during this time interval. It is possible, however, that the immediate recovery response was more marked in the responders but not detected because of the time lag for measuring diastolic pressure. A large drop in diastolic blood pressure in the responders upon release of the handgrip may represent an attempt to regain normal levels of arterial pressure through peripheral vasodilatation.

The heart rate responses to isometric exercise (Figure 11 p. 83) do not support a stronger cardiodepressor effect of baroreceptor stimulation in the responders. Levels of change from baseline were not different in the responders and non-responders either during the isometric trials or over the first 15 s post-release. Mean values of these measures did not suggest that group differences were not demonstrated as a result of a high level of variance. Furthermore, the mean change in heart rate from pretest levels over the period from 15 to 55 s post-release represented an increase in the responders (+3.6 bpm). This measure differed significantly from the negative values calculated for the non-responders (-1.2 bpm). Group differences in these levels of change in heart rate remained consistent over this part of the recovery. A faster decrease in heart rate upon termination of the isometric contraction and/or lower levels of heart rate with respect to the baseline levels, would be expected in the most barosensitive group if the baroreceptor relied upon a bradycardia to return blood pressure to baseline levels post-release. Higher heart rates with respect to baseline measures in the responders may reflect a baroreceptor mediated response to the suggested undershoot of diastolic blood pressure during recovery (Figure 10 p. 80).

Direct measures of blood pressure recorded during isometric exercise and over the 25 s period following release (Appendix E) do not support the noninvasive findings. Responders

and non-responders showed the same rate of increase in systolic (Figure B) and diastolic (Figure C) blood pressure during isometric exercise, with higher levels of change in both measures at each time point in the responders. Levels of change in systolic and diastolic blood pressure over the initial 25 s of recovery were similar in the two groups. However, only two responders and two non-responders were involved in the invasive trials. Slopes and intercepts which represent group comparisons similar to those found with the direct measures could be selected from the noninvasive data (Appendix C). The discrepancy between the invasive and noninvasive group comparisons may also be a result of error introduced by the form of calibration used for the invasive data (Methods Appendix E).

5.4 General Discussion

The role of temperature receptor stimulation in diving bradycardia has been well established (Heistad et al, 1968; Paulev, 1968; Whayne et al, 1967; Brick, 1966). The addition of facial immersion (10° - 17° C) to breath-hold resulted in both a quicker initiation and a decrease in the tendency for heart rate recovery in the latter part of the manoeuvre (Kawakami et al, 1967). As well, decreases in water temperature have resulted in a potentiation of the bradycardia response (Paulev, 1968; Whayne et al, 1967).

Decreases in heart rate have been reported during

breath-hold in air (Oldridge et al, 1978; Moore et al, 1973; Brick, 1966). Moore and associates (1973) demonstrated a potentiation of the heart rate response to a 40 s breath-hold facial immersion with a decrease in the alveolar pressure of oxygen. The level shown to provide hypoxic stimulation in Moore's experiment (69 mmHg) is reached after 45 s (functional residual capacity) to 95 s (total lung capacity) of breath-hold performed during rest (Hong et al, 1971). Hypercapnia is also thought to play a role in the intensification of diving bradycardia (Kawakami et al, 1967) provided that the arterial pressure of oxygen is decreased (Stromme and Blix, 1976). Breath-hold did not potentiate the heart rate response to 30 s of facial immersion with snorkel breathing (Kawakami et al, 1967).

The study of the role of the baroreceptor in diving bradycardia is more complex. A variety of pressure stimuli present during the manoeuvre must be considered. Secondly, the reflex may respond through changes in vasomotor tone, changes in heart rate or through some combination of these two effector mechanisms.

An initial increase in intrathoracic pressure occurs with muscle relaxation after a full inspiration (Paulev, 1968). This change is transmitted directly to the arterial system (Scharpey-Schaefer, 1965). However, an initial increase in arterial blood pressure during breath-hold or breath-hold facial immersion was not reported by those who recorded continuous measures of blood

pressure (Heistad et al, 1968; Kawakami et al, 1967). One of four subjects involved in the invasive trials (DA) showed increases in systolic and diastolic blood pressure with the onset of breath-hold facial immersion performed both during rest (Figure E Appendix E) and exercise. A second subject (DM) experienced a slight increase in these pressures at the point of initiation of one resting facial immersion. Both of these subjects were non-responders to breath-hold facial immersion. This data would suggest that a baroreceptor response to increases in pressure with the onset of breath-hold cannot explain the different diving responses found in our subjects.

Kawakami et al (1967) reported initial transient decreases in blood pressure with both simple breath-hold and breath-hold facial immersion. These drops in blood pressure were also found in the invasive breath-hold trials (Figures E, F & G Appendix E). The gradual decline began immediately or 1 to 2 s into breath-hold and extended for 2 to 5 s.

A comparison may be made between the responses to breath-hold facial immersion and to forced expiration. The decrease in pressure at the beginning of the Valsalva manoeuvre (Figure D Appendix E) has been attributed to a decrease in cardiac output (Gorlin et al, 1957; Judson et al, 1955; Price et al, 1953) as a result of pressure increases within the thorax and the abdomen (Sharpey-Schaefer, 1965). A striking part of the pressure response to the Valsalva manoeuvre is a large decrease

in pulse pressure (Korner et al, 1976). This is thought to reflect a decrease in stroke volume (Zema et al, 1980).

Kawakami and associates (1967) did not report a decrease in pulse pressure during simple breath-hold or breath-hold facial immersion. In the same study cardiac index was measured over a 5 s period within the first 15 s of the manoeuvres. Values were only lower than normal resting levels during breath-hold facial immersion. As well, these decreases could be accounted for by simultaneous changes in heart rate.

In the invasive trials, decreases in blood pressure during the breath-hold manoeuvres generally involved both systolic and diastolic blood pressure. In 7 of 8 resting facial immersions and 5 of 8 exercise facial immersions, the pulse pressure was decreased. In all but one facial immersion (resting) these diminished pulse pressures were associated with a decrease or no change in heart rate. The muscle pump and higher levels of sympathetic and venomotor tone present during the exercise trials, may have assisted in the maintenance of venous return and therefore of stroke volume. Alternatively, that pulse pressure did not decrease during three of the exercise trials may have been the result of simultaneous decreases in heart rate.

The gradual climb in arterial blood pressure which follows (Heistad et al, 1968; Kawakami et al, 1967) may be partially explained as a vasomotor reflex initiated through

chemoreceptor stimulation. Heistad and co-workers (1968) demonstrated the role of temperature receptor stimulation in the secondary increases in pressure. Both the degree of peripheral vasoconstriction and the strength of the mean arterial pressure response were increased with the addition of facial immersion in 20° to 25° C water to breath-hold.

The baroreceptor may be involved in this peripheral vasoconstriction initially in response to any decrease in mean arterial or pulse pressure. However, sustained vasoconstriction occurs despite elevated pressure levels. Direct measures showed increases in mean arterial pressure of 27 ± 4 mmHg during the resting facial immersions and of 35 ± 5 mmHg during the exercise trials. As well, pulse pressure increased after the initial decrease. Levels reached (1 of 8 exercise facial immersions and 4 of 8 resting facial immersions) or exceeded pretest levels. These changes in pulse pressure are not necessarily the result of increases in venous return with the increased levels of vasomotor tone. Again, they may reflect increases in stroke volume with the diving bradycardia. In addition, increases in sympathetic tone (Finley et al, 1979) may be involved through increases in cardiac contractility.

Finally, it is of interest that mean arterial pressure reached levels during the recovery period of the majority of the invasive breath-hold facial immersion trials (both rest and exercise conditions) that were higher than those recorded before

or during the manoeuvres (Figures E, F & G Appendix E). The study of a similar blood pressure response post-release of the Valsalva manoeuvre led researchers to believe that this results from an increase in venous return at a point where vasomotor tone is still above resting levels (Stone et al, 1965).

That diving bradycardia is a baroreceptor mediated response to increases in blood pressure has been considered in two previous studies. Heistad et al (1968) used decreases in heart rate during breath-hold facial immersion that occurred separate of an increase in blood pressure to argue against the role of the baroreceptor. Finley and co-workers (1979) reported that diving bradycardia was not significantly affected by the use of an alpha or a beta blocking agent. The elimination of blood pressure responses by the sympathetic blocking agents in these trials was supported through cuff measures of systolic blood pressure.

The direct measures were used to examine the relationship between increases in blood pressure and any simultaneous decreases in heart rate during breath-hold facial immersion (Methods Appendix E). The results suggest that, in support of the conclusions made by Finley et al (1979) and by Heistad et al (1968), the arterial baroreceptors did not play a major role in the production of diving bradycardia. In agreement, responders and non-responders to breath-hold facial immersion did not demonstrate differences in the heart rate and blood pressure responses

to forced expiration in the present study.

Differences were found between the responders and non-responders in the systolic and diastolic blood pressure responses to isometric exercise. One possible explanation for the systolic response patterns found in the present study (Figure 8) is that the responders are more barosensitive and, therefore, better able to maintain arterial blood pressure at resting levels. Diastolic blood pressure responses (Figure 9) suggest that this was achieved through peripheral vasodilatation upon release. However, stretches of time without blood pressure measures (Appendix D) and the collapsing of data over trials makes it difficult to make strong statements about barosensitivity from the noninvasive findings. The group differences found with the direct measures (Figures B & C Appendix E) contradict the noninvasive findings. This may simply reflect the wide within group variability in the blood pressure responses (Appendix C) and the small number of subjects represented by the invasive data.

In the case that the responders and non-responders did differ in baroreceptor sensitivity, similar heart rate and blood pressure responses to the Valsalva manoeuvre in the two groups may be explained two ways. First, the blood pressure responses and therefore the degree of baroreceptor stimulation may not have been strong enough during the recovery phase of the Valsalva manoeuvre. Previous research (Palmero et al, 1981)

showing the Valsalva manoeuvre to be a reliable index of barosensitivity used a shorter, more intense manoeuvre and achieved higher levels of systolic blood pressure overshoot post-release (ie. 60.8±4.2 vs 33±8 mmHg -- direct measures). However, the mean arterial blood pressure responses during isometric exercise (systolic 43 ±2, diastolic 43 ± 2 mmHg -- indirect measures) and during the recovery phase of the Valsalva manoeuvre (mean arterial pressure 35 ± 7 mmHg -- direct measures) were similar in this study. As well, pulse pressure levels from 11 to 45 mmHg above pretest levels were recorded post-release of the Valsalva manoeuvre. Second, the group differences in the response to blood pressure increases may be specific to the vasomotor effector mechanism. Different manoeuvres used to increase the blood pressure may call upon different mechanisms to return the blood pressure to pretest levels.

Direct measures did not support the theory that differences in vasomotor responsiveness to arterial pressure changes account for the different diving responses found in our subjects. The decrease in mean arterial and pulse pressure at the initiation of the breath-hold manoeuvres was followed by increases in mean arterial blood pressure during the initial 10 s of most exercise trials, with no consistent difference in the level of response between the two groups.

The differences between the blood pressure responses to isometric exercise found in the responders and non-responders may

be unrelated to the baroreceptor. Subjects were classified based on their diving bradycardia response to breath-hold facial immersion performed during dynamic exercise. Research has suggested that the cardiodepressor effect of baroreceptor stimulation is reduced (heart rate >120 bpm) or eliminated (heart rate $\geq$ 150 bpm) during dynamic exercise (Bristow et al, 1971). Decreases in the sensitivity of this reflex have also been demonstrated during isometric exercise (Cunningham et al, 1972). However, this change in cardiodepressor activity is limited to the first 10 s of baroreceptor stimulation and is compensated for by more pronounced vasomotor responses (Ludbrook et al, 1978). As well, Table B (Appendix E) suggests that the baroreceptor does not play a major role in the heart rate responses to breath-hold facial immersions performed during exercise. If this were the case, any connection between the blood pressure responses to isometric handgrip exercise and the heart rate responses to breath-hold facial immersion during dynamic exercise would point to the existence of another mechanism which is common to both tests.

Increases in the level of central command (Freychuss; Goodwin et al in Perez-Gonzalez, 1981) and chemoreceptor stimulation of small sensory afferent fibers within the muscle (Rowell et al, 1981) are thought to be primarily responsible for the pressor response to isometric exercise. Any influence of the absolute tension level produced or of the duration of the

exercise trials on the blood pressure responses recorded during this experiment were covaried out of the group comparison.

Those subjects who demonstrated a strong heart rate response to breath-hold facial immersion performed during exercise were not necessarily strong responders to the same manoeuvre performed during rest. This suggests that different mechanisms are involved in the diving bradycardia found in these two conditions. Direct measures showed that the levels of increase in mean arterial and pulse pressure were higher in the exercise trials. In addition, there was a tendency for fewer exercise trials (5 versus 7) to demonstrate an initial decrease in pulse pressure and for more exercise trials (7 versus 4) to involve increases in pulse pressure above resting levels. The levels of pulse pressure may reflect changes in end-diastolic volume. On the other hand, levels of baroreceptor sensitivity may be reduced during the levels of dynamic exercise used in this experiment (Bristow et al, 1971). Therefore, the level of involvement of the arterial and cardiopulmonary baroreceptors in the heart rate response to breath-hold facial immersion may be different during rest and exercise conditions.

5.5 Summary and Conclusions

Two previous investigations examined the role of the baroreceptor in diving bradycardia. The first (Heistad et al, 1968) reported that decreases in heart rate during

breath-hold facial immersion were not always preceded by increases in blood pressure. This is not surprising as the role of both chemical and temperature receptor stimulation in diving bradycardia have been well established. A more recent study (Finley et al, 1979) found that the level of heart rate response to breath-hold facial immersion during rest and exercise was not affected by either alpha or beta blockers. Cuff measures of systolic blood pressure provided the only evidence that pressure stimuli were eliminated by these treatments.

The purpose of the present investigation was to compare measures of baroreceptor sensitivity in those subjects who demonstrate a strong response (responders) and in those subjects who show little or no response (non-responders) to breath-hold facial immersion performed during exercise. The heart rate and blood pressure responses to isometric handgrip exercise and the Valsalva manoeuvre in these two groups were compared. The only differences between responders and non-responders were found in response to isometric exercise. Responders demonstrated a flatter systolic blood pressure response both during the isometric exercise and over a period beginning immediately before release through 25 s of recovery. Diastolic blood pressure responses were also different in the two groups. Too few diastolic measures were recorded over the ~~initial~~ 25 s of recovery to compare the response in the two groups. However, diastolic measures taken after this time period suggested that this

pressure measure dropped below baseline levels in the responders upon release of the handgrip. These findings were not supported by direct measures taken in two of the six responders and in two of the six non-responders.

Attempts to measure the cardiodepressor effect of increases in mean arterial and pulse pressure during breath-hold facial immersion (both rest and exercise conditions) and during the recovery from forced expiration in the invasive trials were unsuccessful. There were two reasons for this. First, in a large number of the trials there were too few blood pressure measures that were both higher than those recorded before the test and associated with an elongated RR interval. Second, considering only those trials with the largest number of data pairs (blood pressure and corresponding RR interval) the correlation coefficients were either low or showed a wide between trial and between subject variability.

The reasons for certain subjects to consistently experience large decreases in heart rate and for other subjects to show little or no change in heart rate with breath-hold facial immersion performed during exercise are not known. While direct measures suggested that the baroreceptor does not play an important role in diving bradycardia, noninvasive results suggested that these subjects differ in the blood pressure response to isometric exercise. Direct measures in approximately six responders and six non-responders would be necessary in order to confirm

these results. It is also suggested that, with continuous traces of blood pressure, Valsalva manoeuvres performed over a shorter time period and at a higher expiratory pressure would provide a better measure of barosensitivity. The use of responders and non-responders remains an interesting way to examine mechanisms involved in diving bradycardia.

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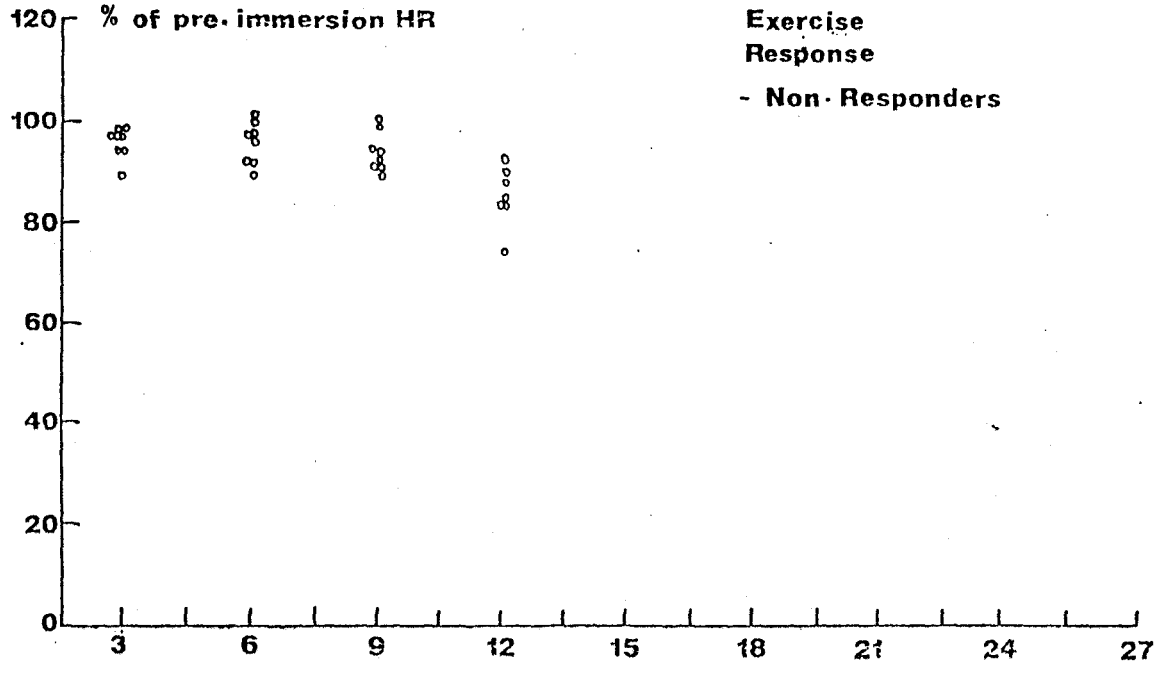
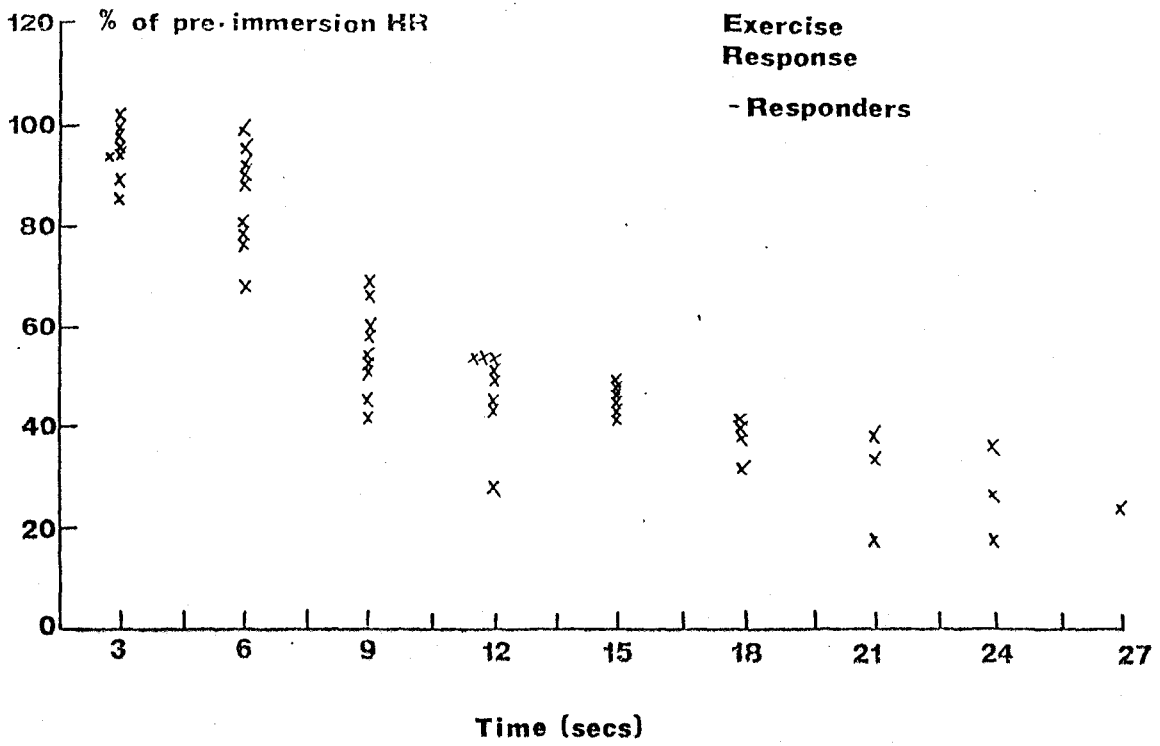
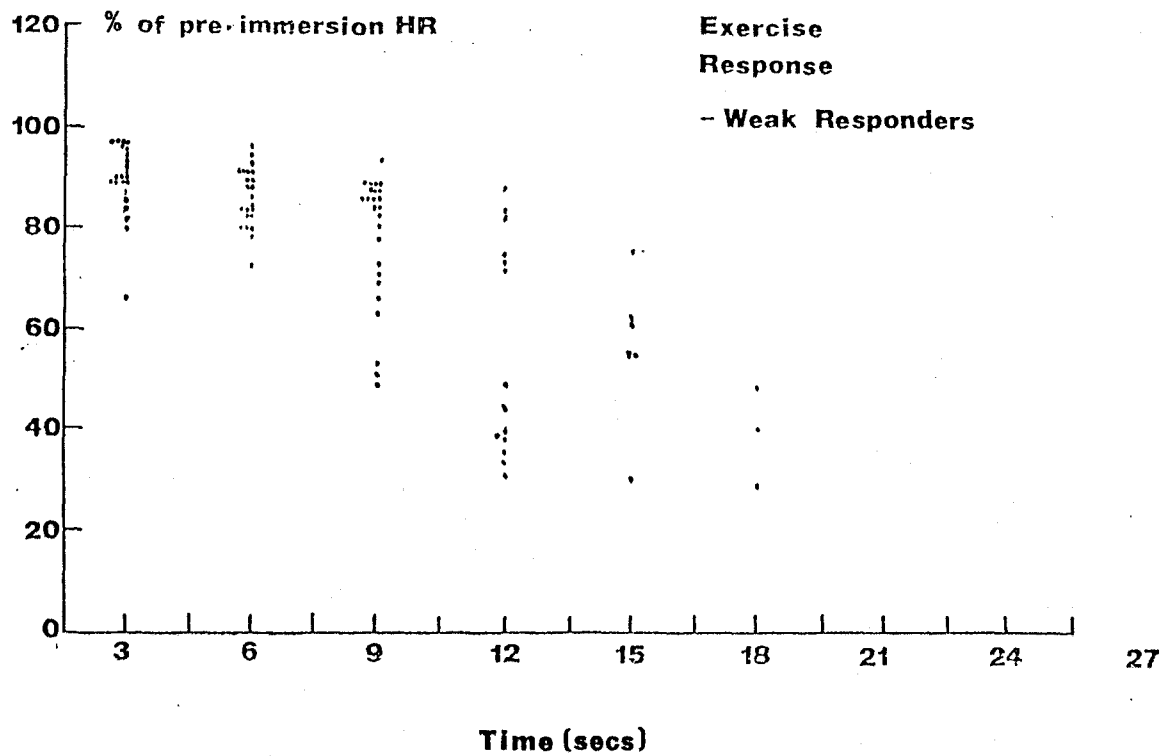
APPENDIX 'A'



Changes in Heart Rate Shown as Percentages of Pre-Immersion Values and Plotted over the Duration of Exercise Facial Immersion for Each Trial of Each Non- Responder.



Changes in Heart Rate Shown as Percentages of Pre-Immersion Values and Plotted over the Duration of Exercise Facial Immersion for Each Trial of Each Responder.



Changes in Heart Rate Shown as Percentages of Pre-Immersion Values and Plotted over the Duration of Exercise Facial Immersion for Each Trial of Each Weak Responder.

APPENDIX 'B'

CONSENT FORM

Heart Rate and Blood Pressure Changes during Resting Facial Immersion, Facial Immersion Combined with Exercise, Forced Expiration and Isometric Exercise.

I, _____, consent to take part in a student project that will examine the effects of facial immersion during rest and moderate exercise, forced expiration and isometric exercise with a handgrip dynamometer on my heart rate and blood pressure. The purpose of the study is to compare the relationship between heart rate and blood pressure in those people who demonstrate a strong heart rate response and those who demonstrate a weak heart response to exercise facial immersion.

Gina Reid, the principal investigator, has explained to me that three electrodes will be attached to my chest for the measurement of heart rate. An experienced physician will insert a fine wire 1 to 2 mm upstream in an artery in my arm in order to measure blood pressure.

The insertion of the wire may result in slight bruising, but this should disappear in a day or two. I understand that there is a very small risk of arterial thrombosis (clotting) and occlusion. This risk is minimized by the short duration of the study and the use of an anti-clotting agent, herapin.

I understand that I can withdraw from this study at any time, even after signing this form.

_____	_____	_____
Name (print)	Signature	Date

_____	_____	_____
Witness (print)	Signature	Date

I have explained the nature of the study to the subject and believe he/she has understood it.

_____	_____	_____
Name (print)	Signature	Date

APPENDIX 'C'

ISOMETRIC EXERCISE - NONINVASIVE STUDY

Slopes and intercepts for the regression lines which describe the systolic blood pressure response

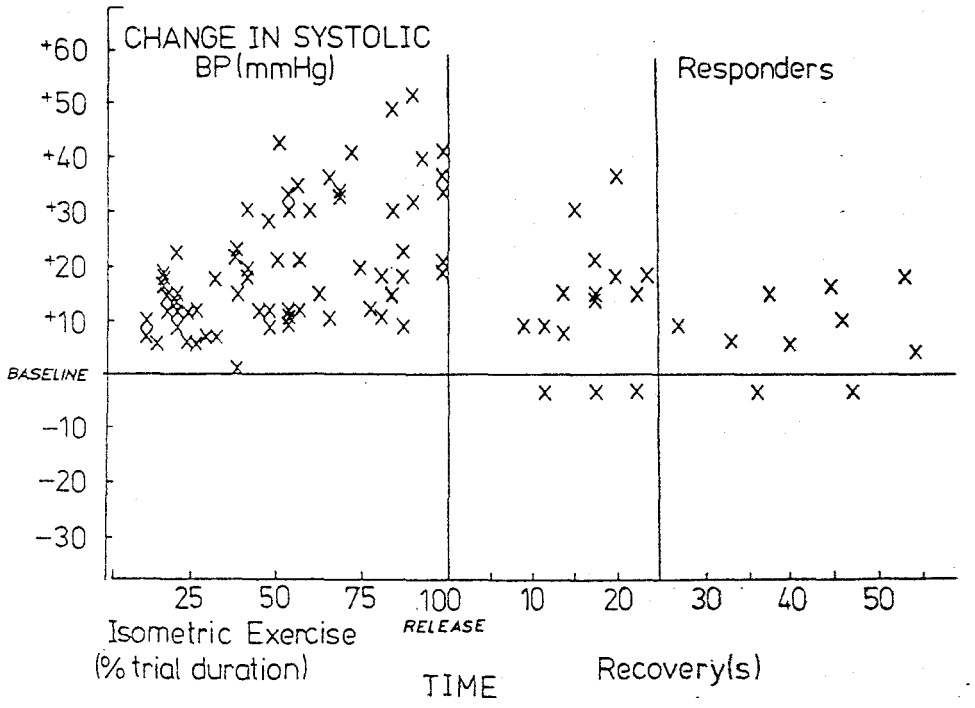
	Duration of the isometric trial		Immediately before release through 25s		26 to 55 s post-release	
	Slope	Intercept	Slope	Intercept	Slope	Intercept
Responders	1.031	4.158	.878	-42.102	- .144	16.043
	.809	8.074	- .333	44.333	-	-
	.836	10.368	- 5.000	304.000	.272	- 13.303
	.559	7.453	.563	- 19.875	- .128	16.779
	.332	2.620	.888	- 40.755	1.333	-105.667
	.282	5.293	- .426	23.246	.036	- 1.031
Non-Responders	.975	5.058	- 2.250	138.250	-1.453	129.430
	.743	- 6.006	- .500	16.000	.435	- 37.413
	1.100	- 5.856	- 1.145	84.565	-	-
	.890	3.284	10.000	- 550.667	- .327	30.097
	1.027	5.432	- .138	15.207	.300	- 17.700
	.946	.938	- .554	43.237	.316	- 22.582
Weak Responders	.728	21.159	- .211	29.105	- .250	27.500
	1.059	- 2.002	- 1.413	93.109	.333	- 27.000
	.374	- 4.854	- 1.625	78.750	- .394	17.346
	.397	18.232	- .507	45.214	.248	- 14.208
	.523	12.798	.931	- 38.052	- .311	22.802
	1.956	- .648	- 1.633	132.715	.172	1.699
	1.140	16.186	- 1.931	136.615	- .185	27.395
	.639	3.340	- 1.667	98.333	.161	- 15.649
	.775	6.588	- 1.071	81.357	.333	- 8.000
	.790	6.684	- 1.167	79.500	- .405	34.856
	- .633	26.156	- 7.000	425.000	-	-
	.729	5.629	- 1.436	91.392	.234	- 11.681
	.462	10.215	- .731	51.654	.216	- 5.744
	.175	13.135	- .393	33.236	- .344	33.973
	.909	17.125	- 1.946	129.859	- .283	32.380
	1.455	6.523	- 1.679	126.330	- .113	30.082
	.767	16.047	- .385	17.679	1.000	- 84.000
	- .014	.479	- .750	48.800	- .003	3.269
	-5.214	102.762	-34.500	1930.500	.055	- 3.715
	1.164	3.698	- 1.792	115.747	- .201	26.263
	1.566	6.304	2.250	- 125.917	-1.654	166.692
	.770	5.765	- 1.267	88.786	- .011	8.570
	1.313	11.719	- .730	90.697	.505	- 15.280
	.890	10.203	- 1.307	99.206	- .276	36.207
	.715	11.792	- 1.130	81.767	- .045	13.127
	.219	8.779	- .579	33.368	.258	- 13.028
	.660	8.514	- 1.320	87.415	.527	- 33.810

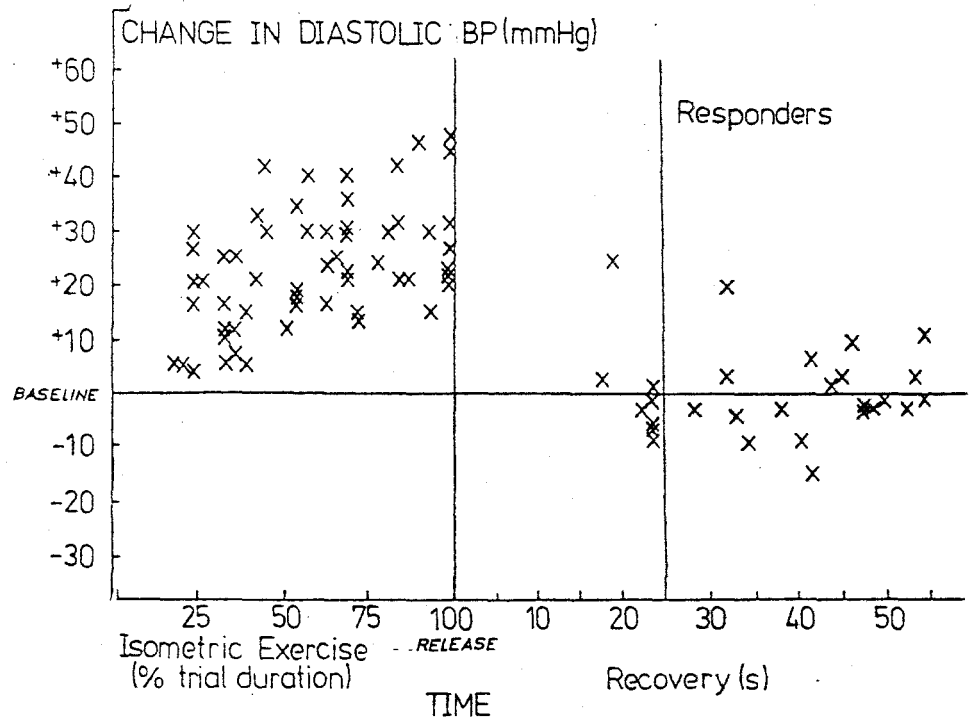
ISOMETRIC EXERCISE - NONINVASIVE STUDY

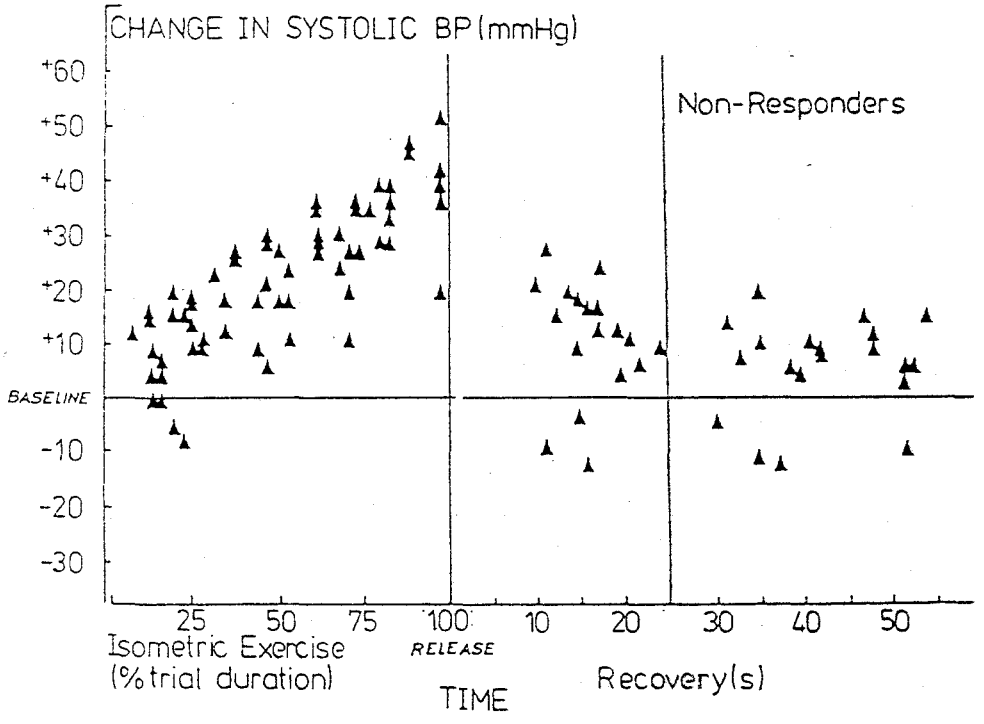
Slopes and intercepts for the regression lines which describe the diastolic blood pressure response

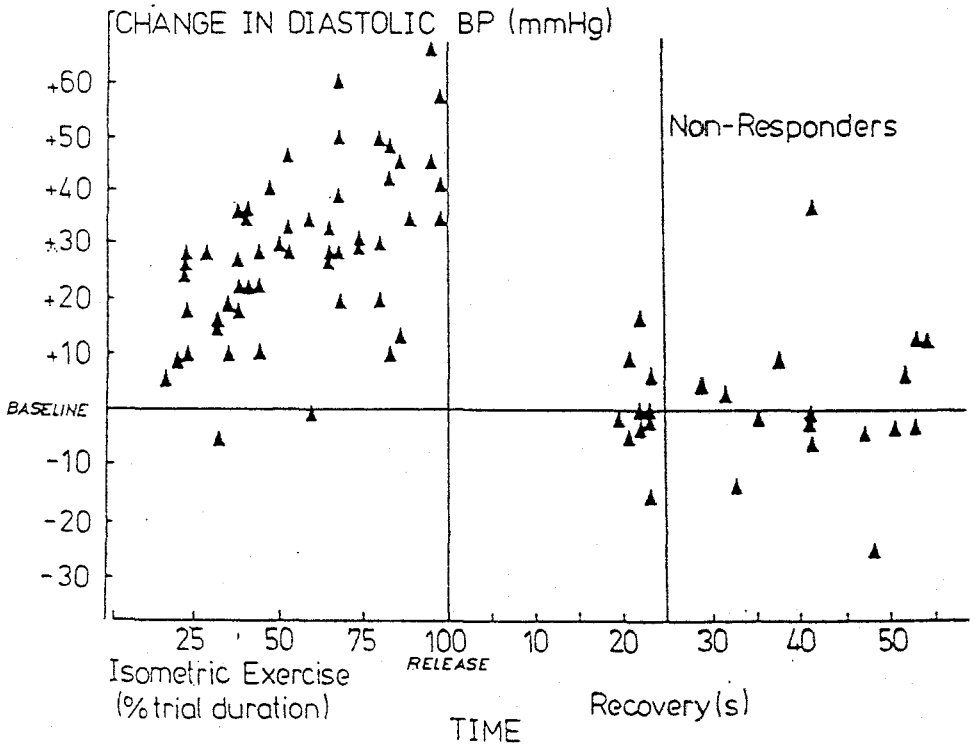
	Duration of the isometric trial		Immediately before release through 25s		26 to 55 s post-release	
	Slope	Intercept	Slope	Intercept	Slope	Intercept
Responders	.084	22.927	- 1.209	70.837	- .455	40.692
	.971	1.445	-	-	1.916	-164.143
	.930	13.510	- 7.667	475.333	.127	- 10.438
	.899	5.549	-	-	1.750	-139.167
	.467	2.788	1.000	- 66.000	2.333	-211.667
	.424	4.912	-	-	- .046	1.682
Non Responders	.064	19.705	-55.000	3305.000	.139	- 6.810
	- .597	31.868	2.889	- 198.000	- .578	35.191
	- .756	64.509	-	-	- .414	29.753
	- .296	36.721	- .934	69.265	- .025	5.727
	- .270	31.749	-	-	- .180	28.692
	- .407	38.480	-	-	- .194	14.456
Weak Responders	.936	21.663	- 2.439	148.339	.638	- 55.514
	.180	8.068	-	-	-	-
	.582	5.887	- 1.379	78.353	-.368	29.526
	.232	27.837	-	-	1.990	-157.551
	.425	18.808	- 1.535	95.192	.074	- 7.361
	1.476	- 5.114	- 2.741	172.148	- .380	20.045
	.803	24.451	-	-	-4.571	318.571
	.461	11.959	-	-	.341	- 25.050
	.597	15.890	-	-	-3.577	263.731
	.998	- 10.868	-	-	- .164	8.366
	- 1.333	84.000	-	-	3.154	-253.615
	.302	9.093	- 1.385	71.746	.076	- 9.594
	.533	30.231	-	-	.390	- 35.733
	.302	9.137	-	-	- .643	46.714
	.506	30.880	- 1.727	113.636	1.008	- 67.388
	1.241	2.051	2.929	- 191.833	1.075	- 96.315
	.494	14.272	-	-	- .260	29.915
	.122	17.757	- 1.213	74.153	-	-
	5.750	- 101.833	5.500	- 339.500	-	-
	.601	21.263	- 1.849	120.196	- .121	8.000
	.793	9.425	-	-	- .671	49.890
	.268	15.749	- 1.074	68.956	- .077	15.385
	.133	17.919	-	-	-	-
	.580	12.389	-	-	.622	- 49.568
	.107	17.498	- 1.250	74.567	-	-
	.159	19.619	- .333	26.333	.142	- 3.821
	.416	12.262	- 1.092	65.728	.336	- 29.277

APPENDIX 'D'


CHANGE IN SYSTOLIC BP (mmHg)
Responders
+60
+50
+40
+30
+20
+10
BASELINE
-10
-20
-30
25
50
75
100
RELEASE
10
20
30
40
50
Isometric Exercise (% trial duration)
TIME
Recovery (s)


CHANGE IN DIASTOLIC BP (mmHg)
Responders
+60
+50
+40
+30
+20
+10
BASELINE
-10
-20
-30
25
50
75
100
RELEASE
10
20
30
40
50
Isometric Exercise (% trial duration)
TIME
Recovery (s)


CHANGE IN SYSTOLIC BP (mmHg)
+60
+50
+40
+30
+20
+10
BASELINE
-10
-20
-30
Non-Responders
25
50
75
100
10
20
30
40
50
Isometric Exercise
(% trial duration)
RELEASE
Recovery (s)
TIME


CHANGE IN DIASTOLIC BP (mmHg)
+60
+50
+40
+30
+20
+10
BASELINE
-10
-20
-30
Non-Responders
25
50
75
100
10
20
30
40
50
Isometric Exercise
(% trial duration)
RELEASE
Recovery (s)
TIME

APPENDIX 'E'

PRELIMINARY INVASIVE STUDY

1. Methods

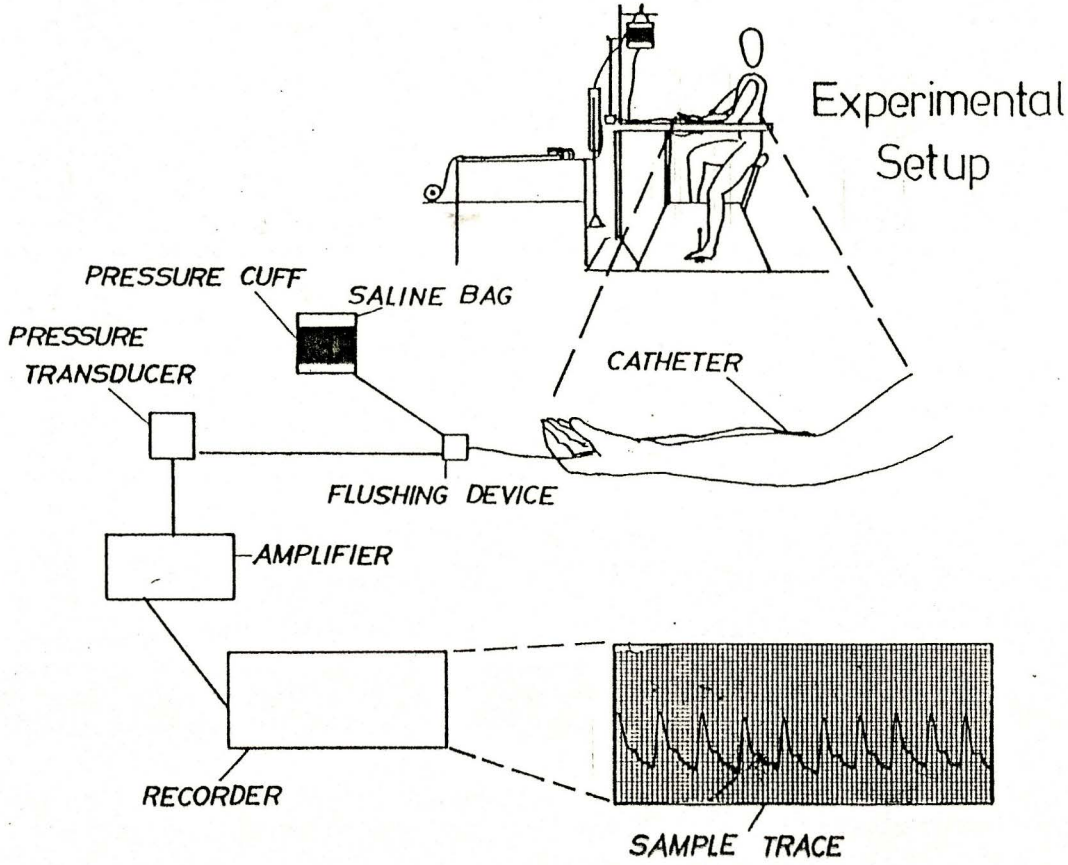
1.1 Design

Two responders and two non-responders to breath-hold facial immersion participated in an invasive study. A catheter was placed in the brachial artery of the nondominant arm for direct measurement of arterial blood pressure. Subjects then repeated two trials each of resting facial immersion, exercise facial immersion, Valsalva manoeuvre and isometric handgrip exercise. The heart rate, systolic blood pressure and diastolic blood pressure responses to isometric exercise found in the two groups were compared with the noninvasive data. Measures recorded during breath-hold facial immersions (both rest and exercise) and during recovery from the Valsalva manoeuvre were used to examine the responsiveness of the RR interval to changes in pulse and mean arterial pressure in these subjects.

1.2 Direct measurement of arterial blood pressure (Figure A)

The subjects involved in the invasive study were informed of the purpose of the study and risks involved (see Informed Consent Form - Appendix B). A physician then placed an Angiocath intra-arterial catheter 1 to 2 cm upstream in the brachial artery of the subject's nondominant arm. The remote chance of arterial thrombosis was minimized through the addition of heparin

Figure A. The experimental setup for the direct measurement of arterial blood pressure.


Experimental
Setup
PRESSURE CUFF
SALINE BAG
PRESSURE
TRANSDUCER
CATHETER
FLUSHING DEVICE
AMPLIFIER
RECORDER
SAMPLE TRACE

to the saline solution.

Subjects were seated on an Elema constant workload cycle ergometer (Type EM 370-1, model #314) throughout the testing period. The catheterized arm rested on a table at sternal level. The pressure transducer (Bell and Howell, model #4-327-I) was suspended at the same height as the catheter.

The pressure signals were amplified with a Hewlett-Packard carrier amplifier (model #8805A) and then inscribed on a Hewlett-Packard 8 channel series recorder (model #7700). A standard sphygmomanometer was used to calibrate the transducer. The pressure cuff was wrapped around the saline bag. Pressure changes were sustained and therefore used only in the calculation of diastolic measures. Cuff measures of blood pressure were also taken before the trials, at different points throughout the trials and during recovery from the trials. Since difficulties were encountered with critical damping of the system, a correction factor was applied to the actual trace values of pulse pressure based on cuff measures of systolic and diastolic blood pressure. The recorder ran at a paper speed of $10\ mm.s^{-1}$.

1.3 Data analysis

The blood pressure traces recorded during the facial immersions and during the recovery from forced expiration were used to examine the responsiveness of the RR interval to pressure

stimuli. Two regression coefficients were calculated for each trial for each subject. One related changes in RR interval to levels of pulse pressure and the other to levels of mean arterial pressure. The RR interval immediately preceding the first recovery measure included in the analysis of the Valsalva manoeuvre data was considered to represent the baseline level. All RR interval measures used in the Valsalva manoeuvre analysis were then entered as a change from this value. Measures used in the calculation of the regression coefficients from the resting and exercise facial immersion data represented the change from pretest levels.

Pulse pressure was taken as the difference between each diastolic measure and the succeeding systolic pressure. The calculation of mean arterial pressure paired each diastolic pressure with the preceding systolic value. One third of the difference between these two measures was added to the diastolic pressure. Pretest measures (RR interval, mean arterial blood pressure and pulse pressure) were calculated as the average of five consecutive measures recorded 10 s before each trial.

Each pressure measure was entered into the regression analysis with the second RR interval following. Regressions were only performed on the sections of the facial immersion traces where RR intervals were equal to or larger than at rest. As well, periods where the RR interval showed a gradual decrease or remained constant for more than 10 beats were excluded. A third

requirement was that the blood pressure measure of interest was at least 5 mmHg above the resting level. The series of measures used in the calculation of regression coefficients for the Valsalva manoeuvres began with the first elongated RR interval during recovery. All pairs of blood pressure measures and RR interval from that point in the trace up to the point where blood pressure had reached a peak level and then decreased by a value greater than 10 mmHg were included. A drop in blood pressure of this size during the first 7 s was ignored if the blood pressure returned to within 10 mmHg of the highest value.

Direct measures recorded during the isometric handgrip trials were analyzed over the first two time intervals used in the noninvasive trials (Table 1 p. 57). The dependent variables were the change in heart rate, the change in systolic blood pressure and the change in diastolic blood pressure from baseline levels. Measures were taken from the blood pressure traces at eight points during the isometric exercise and after each 5 s of recovery. Values for systolic blood pressure, diastolic blood pressure and RR interval were averaged over three consecutive pulse waves. The average RR interal was then converted to a measure of heart rate in beats per minute. Each dependent variable was again analyzed separately over each time interval through a repeated measures analysis of variance (BMDP-2V). The orthogonal option of this statistical program was used to identify quadratic components of the responses over these

sections of the graphs.

2. Results

Mean values for pretest mean arterial pressure were 104 ± 2 (resting facial immersion) and 100 ± 3 (forced expiration) mmHg. Subjects began the isometric trials with a mean systolic pressure of 126 ± 5 mmHg and a mean diastolic blood pressure of 88 ± 4 mmHg. Mean pretest heart rates recorded during rest were 86 ± 5 (isometric exercise), 80 ± 7 (resting facial immersion) and 84 ± 5 (forced expiration) bpm. The steady-state exercise levels chosen for the noninvasive exercise breath-hold facial immersions brought heart rates to 128 ± 5 bpm and mean arterial pressure to 111 ± 3 mmHg.

2.1 Resting breath-hold facial immersion (Table A)

The number of data pairs from individual trials which met the criteria for the correlation analyses ranged from 0 to 19 (pulse pressure) and from 0 to 22 (mean arterial pressure). Correlation coefficients between the degree of elevation in pulse pressure and the msec change in RR interval during resting breath-hold facial immersion were all nonsignificant. As well, in only 2 of 8 trials were increases in mean arterial pressure significantly related ($p<.05$) to the increase in the second RR interval following.

TABLE A

BREATH-HOLD FACIAL IMMERSION PERFORMED DURING REST - INVASIVE STUDY

Regression and correlation coefficients for the degree of change in RR interval (msec) per mmHg increase in pulse pressure (A.) and per mmHg increase in mean arterial pressure (B.)

			TRIAL # 1				TRIAL # 2			
			# of data points	regression coefficient	correlation coefficient	significance level	# of data points	regression coefficient	correlation coefficient	significance level
A	Responders to breath-hold facial immersion	Subject # 3	5	5.2	.57	N.S.	11	12.1	.41	N.S.
		Subject # 4	0	-	-	-	0	-	-	-
	Non-Responders	Subject #37	0	-	-	-	3	0	0	N.S.
		Subject #39	15	4.4	.46	N.S.	19	1.7	.22	N.S.
B	Responders	Subject # 3	4	10.0	.67	N.S.	7	11.8	.37	N.S.
		Subject # 4	22	5.3	.66	***p<.001	0	-	-	-
	Non-Responders	Subject #37	12	13.2	.42	N.S.	19	21.4	.45	N.S.
		Subject #39	15	- 2.7	-.17	N.S.	20	4.1	.70	***p<.001

2.2 Breath-hold facial immersion performed during exercise (Table B)

Between 0 and 15 (pulse pressure) or 0 and 12 (mean arterial pressure) data pairs were available for the correlation analyses. Data from 7 of 8 facial immersions performed during exercise did not demonstrate a significant ($p<.05$) relationship between increses in pulse pressure and the response of the RR interval. A significant ($p<.05$) effect of increases in mean arterial pressure on the RR interval was only found in 2 of 8 trials.

2.3 Valsalva manoeuvre (Table C)

Only 3 to 8 data points from individual trails of the Valsalva manoeuvre met the criteria set for the analysis of the influence of pulse pressure on the RR interval (see Methods). Similarly, 3 to 9 data pairs were taken from the recovery trace for the measurement of the response of the RR interval to changes in mean arterial blood pressure. All correlation coefficients calculated from the heart rate and blood pressure responses to the Valsalva manoeuvre were nonsignificant.

2.4 Isometric handgrip exercise

The repeated measures analyses of variance were applied to the heart rate, systolic blood pressure and diastolic blood pressure data collected during the isometric handgrip trials.

TABLE B

BREATH-HOLD FACIAL IMMERSION PERFORMED DURING EXERCISE - INVASIVE STUDY

Regression and correlation coefficients for the degree of change in RR interval (msec) per mmHg increase in pulse pressure (A.) and per mmHg increase in mean arterial pressure (B.)

			TRIAL # 1				TRIAL # 2			
			# of data points	regression coefficient	correlation coefficient	significance level	# of data points	regression coefficient	correlation coefficient	significance level
A	Responders to breath-hold facial immersion	Subject # 3	7	34.	.82	*p<.05	15	-32.8	-.49	N.S.
		Subject # 4	9	9.7	.62	N.S.	12	6.2	.49	N.S.
	Non-Responders	Subject #37	0	-	-	-	0	-	-	-
		Subject #39	8	- 1.4	-.14	N.S.	7	7.0	.72	N.S.
B	Responders	Subject # 3	7	12.1	.81	*p<.05	3	-46.7	-.97	N.S.
		Subject # 4	9	16.2	.64	N.S.	12	11.4	.78	***p<.001
	Non-Responders	Subject #37	0	-	-	-	4	0	.000	N.S.
		Subject #39	8	4.0	.29	N.S.	7	- 3.1	-.40	N.S.

TABLE C

VALSALVA MANOEUVRE - INVASIVE STUDY

Regression and correlation coefficients for the degree of change in RR interval (msec) per mmHg increase in pulse pressure (A.) and per mmHg increase in mean arterial pressure (B.)

			TRIAL # 1				TRIAL # 2			
			# of data points	regression coefficient	correlation coefficient	significance level	# of data points	regression coefficient	correlation coefficient	significance level
A	Responders to breath-hold facial immersion	Subject # 3	8	- 6.9	- .20	N.S.	8	3.0	.15	N.S.
		Subject # 4	3	-13.6	- .93	N.S.	4	-5.8	-.51	N.S.
	Non-Responders	Subject #37	7	12.2	.68	N.S.	6	13.8	.68	N.S.
		Subject #39	3	1.3	.30	N.S.	4	7.5	.58	N.S.
B	Responders	Subject # 3	6	28.5	.71	N.S.	8	3.7	.29	N.S.
		Subject # 4	3	34.2	.86	N.S.	9	-5.2	-.14	N.S.
	Non-Responders 9	Subject #37	5	- 8.8	-.53	N.S.	6	-10.6	-.33	N.S.
		Subject #39	3	3.3	.55	N.S.	4	10.	.21	N.S.

Over each time interval these measures demonstrated a significant ($p<.05$) linear change over time. In addition, significant ($p<.05$) quadratic components were found in the change in the dependent variables over the recovery time period. Groups did not differ in the linear or quadratic components of change over time.

The two responders demonstrated a greater degree of change in systolic blood pressure from the pretest level than the two non-responders at each time point examined during isometric exercise (Figure B). This was indicated through a significant group effect ($F[1,2]=30.65$, $p<.05$) and a nonsignificant time by group interaction. A stronger diastolic blood pressure response (group effect -- $F[1,2]=64.65$, $p<.05$); time/group interaction -- N.S.) was also found during isometric exercise in the responders (Figure C). A marginal group effect ($F[1,2]=16.84$, $p<.06$) and a nonsignificant time by group interaction suggests that with a larger number of subjects measures of change in diastolic blood pressure from pretest levels may be found to be higher in the responders over the initial 25 s of recovery. No differences were found between responders and non-responders in the heart rate response to isometric exercise.

Figure B. Changes in systolic pressure ($X \pm SE$) during isometric handgrip exercise. Measures of change in systolic blood pressure during the isometric trials were higher in the responders than in the non-responders to breath-hold facial immersion (analysis of variance -- group effect $p<.05$, time/group interaction N.S.). However, recovery values were not different in the two groups (analysis of variance -- group effect N.S., time/group interaction N.S.) and the mean levels plotted represent data collapsed over groups.

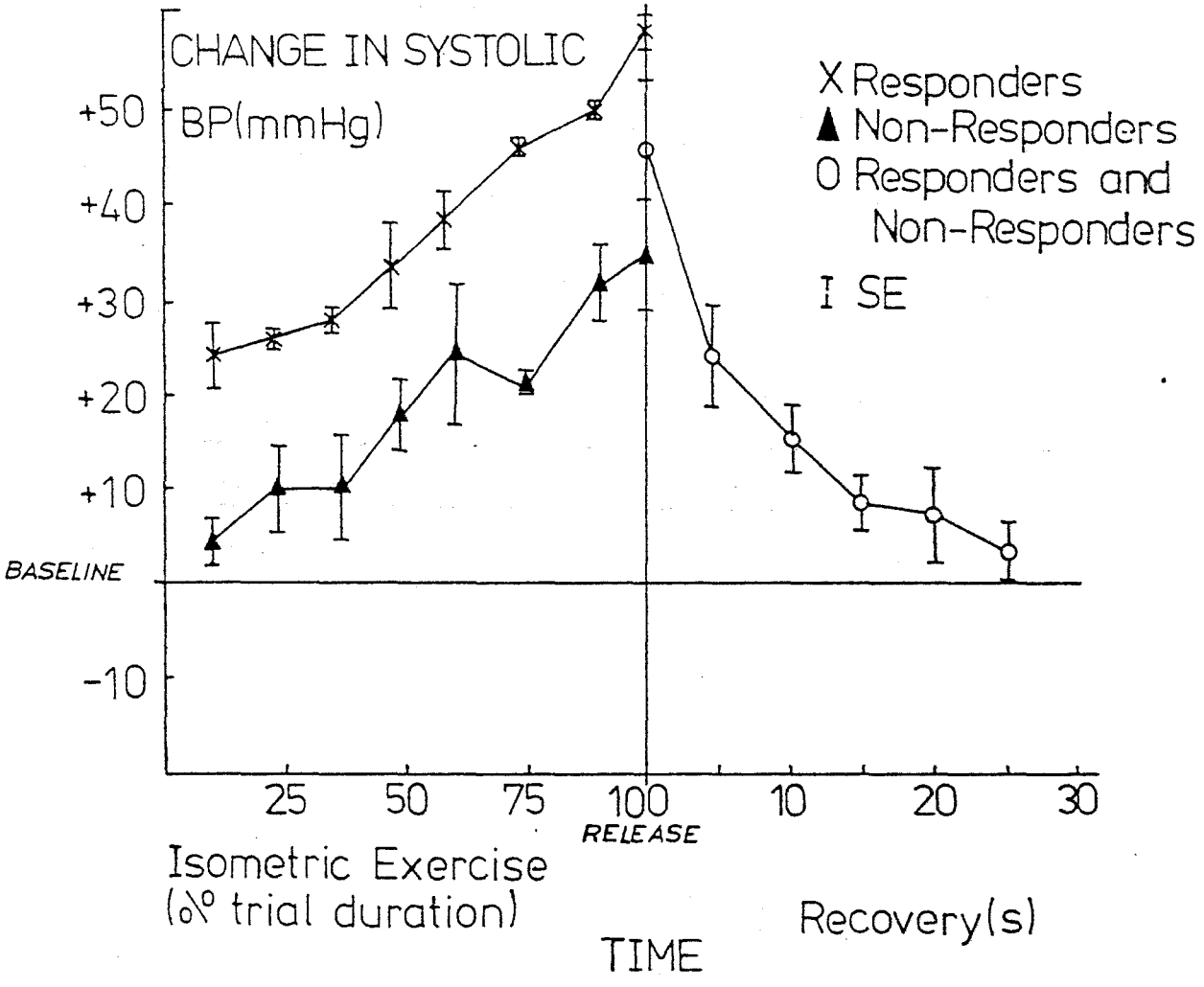

CHANGE IN SYSTOLIC
BP(mmHg)
+50
+40
+30
+20
+10
BASELINE
-10
X Responders
▲ Non-Responders
O Responders and
Non-Responders
I SE
25
50
75
100
RELEASE
10
20
30
Isometric Exercise
(∂° trial duration)
Recovery(s)
TIME

Figure C. Changes in diastolic blood pressure (X ± SE) in response to isometric handgrip exercise. These values were higher in the responders than in the non-responders to breath-hold facial immersion during the isometric trials (analysis of variance -- group effect $p<.05$, time/group interaction N.S.). A similar but nonsignificant trend appeared over the first 25 s of recovery (analysis of variance -- marginal group effect $p<.06$, time/group interaction N.S.).

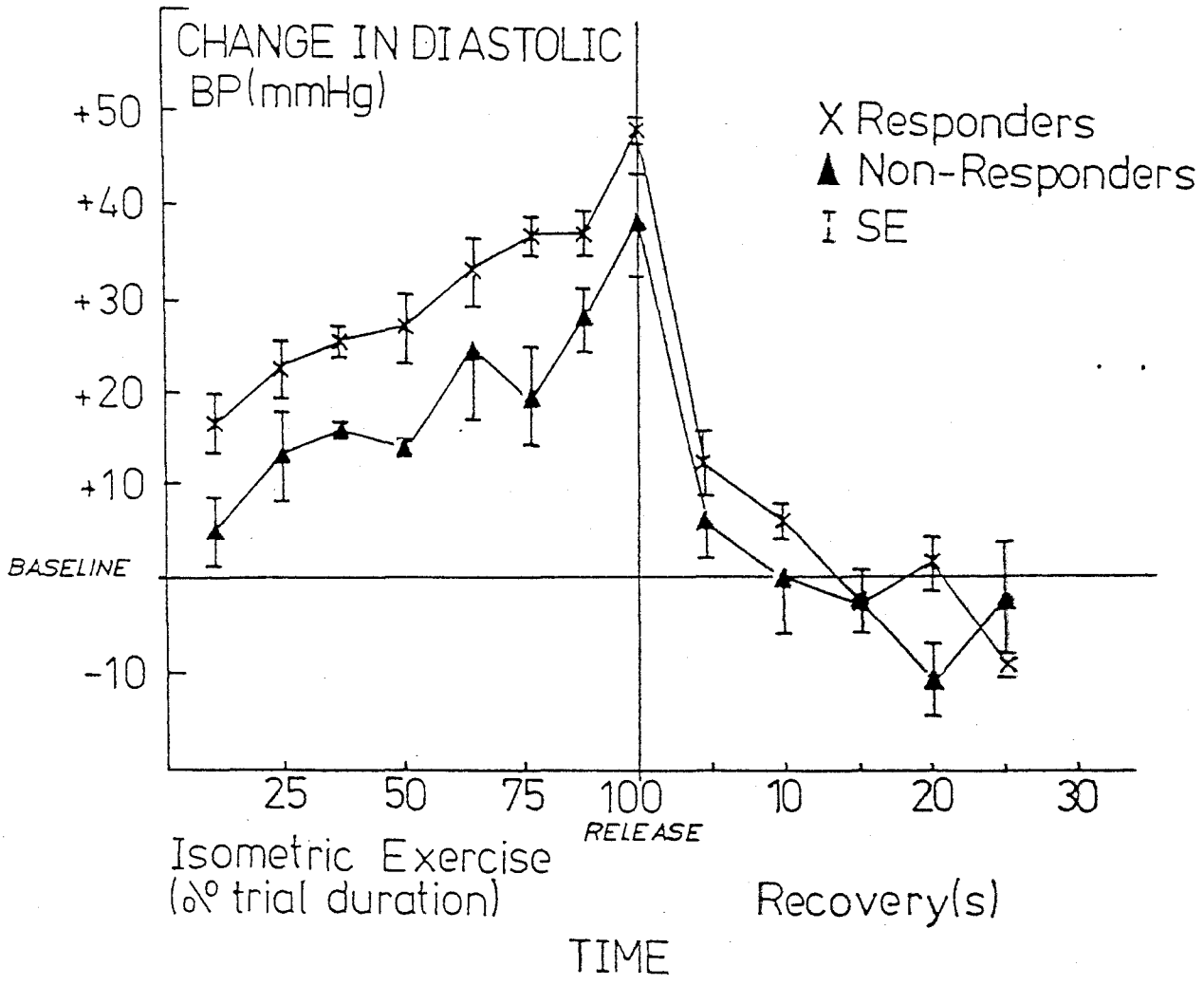

CHANGE IN DIASTOLIC BP(mmHg)
+50
+40
+30
+20
+10
BASELINE
-10
X Responders
▲ Non-Responders
I SE
25
50
75
100
RELEASE
10
20
30
Isometric Exercise
(∆° trial duration)
Recovery(s)
TIME

Figure D. The brachial arterial pressure response to forced expiration in subject DA (non-responder).

Figure E. The brachial arterial pressure response to breath-hold facial immersion performed during rest in subject DA (non-responder).

Figure F. The brachial arterial pressure response to breath-hold facial immersion performed during mild steady-state cycling in subject DM (non-responder).

Figure G. The brachial arterial pressure response to breath-hold facial immersion performed during mild steady-state cycling in subject BL (responder).

FIGURE *D*

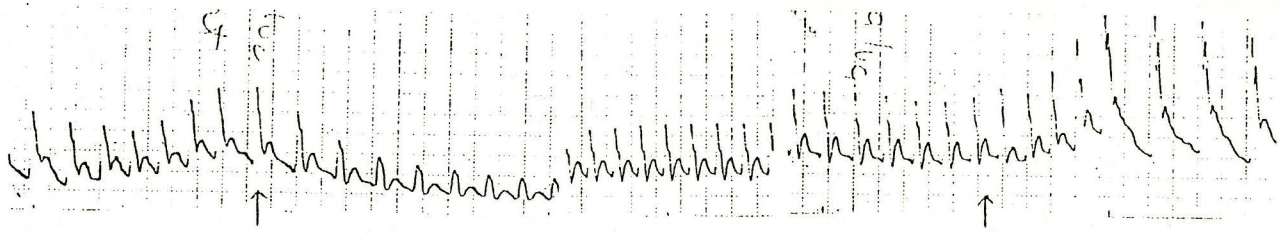


FIGURE *E*

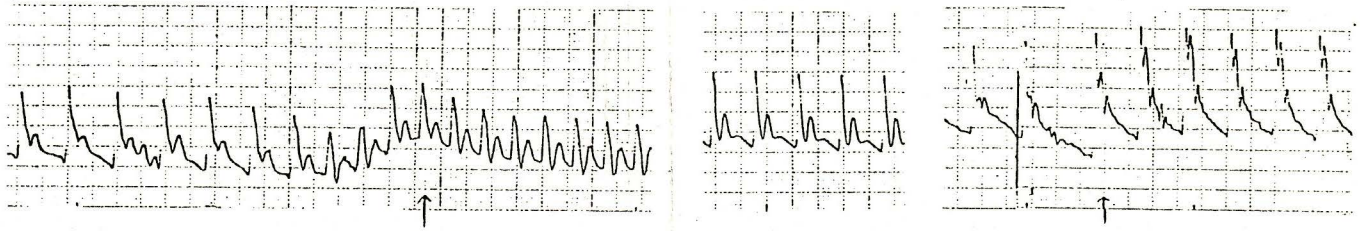


FIGURE *F*

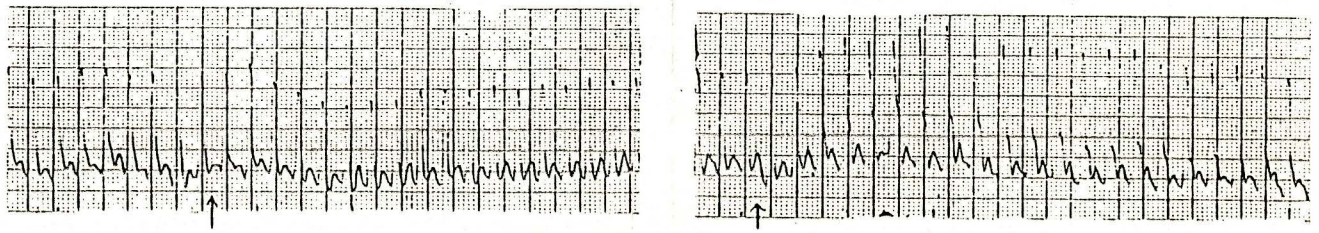


FIGURE *G*