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HEMODYNAMIC RESPONSE PATTERNING TO COGNITIVE AND COLD
STRESSORS: MECHANISMS & MODIFICATION WITH DIAZEPAM

City University of New York

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HEMODYNAMIC RESPONSE PATTERNING TO
COGNITIVE AND COLD STRESSORS:
MECHANISMS & MODIFICATION WITH DIAZEPAM

By

Bruce L. Wilson

A dissertation submitted to the Graduate Faculty in Psychology
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy, The City University of New York.

1985

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This manuscript has been read and accepted for the Graduate Faculty in Psychology in satisfaction of the dissertation requirement for the degree of Doctor of Philosophy.

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HEMODYNAMIC RESPONSE SPECIFICITY TO COGNITIVE AND COLD STRESSORS:
MECHANISMS & MODIFICATION WITH DIAZEPAM

by

Bruce L. Wilson

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This series of studies is based upon the premise that the behavioral topography of the heart cannot be adequately described with the traditional psychophysiological variables of heart rate and blood pressure. The technique of impedance cardiography was used to allow the examination of additional dimensions of cardiovascular behavior. These additional variables include: stroke volume, cardiac output, myocardial contractility, and total peripheral resistance. The first experiment was designed to replicate the findings of a pilot study which examined borderline hypertensive subjects using a within subjects design. The pilot data revealed that cognitive tasks and the cold pressor test produce similar changes in blood pressure through very different patterns of underlying hemodynamic activity. Twenty-four additional subjects were added to the analysis. The existence of differential hemodynamic patterning to these two stress conditions was confirmed. Analyses of variance for all variables were significant at or beyond the .01 level.

The second study investigated the role of increased peripheral resistance in the production of decreased stroke volume, cardiac output, and cardiac contractility during the cold pressor tests. The cognitive stress condition and a new physical stressor - sustained isometric contraction were administered to nine normotensive subjects. Isometric contraction was found to produce hemodynamic patterning similar

to that elicited by cold stress. All variables were significant at the .05 level. When the procedure was repeated with the same subjects, the stimulus specific patterns were found to be preserved.

In the third study fourteen normotensive subjects were randomly assigned to receive an anxiolytic compound, diazepam, or an active placebo. The drugs were administered in a single blind fashion prior to the administration of a second stress test procedure. The variables produced by impedance cardiography were able to discriminate the differential effects of the drug at or beyond the .02 level of significance. These findings support the use of a systems approach in the study of central nervous system control of cardiovascular behavior and demonstrate the utility of adopting new hemodynamic variables in behavioral research.

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PREVIOUS RESEARCH

The Autonomic Nervous System

Claude Bernard first proposed that the integration of the cardiovascular system is primarily under the control of the autonomic nervous system (1851). He demonstrated that stimulating nerves with electrical current could result in the contraction of smooth muscle as well as striated muscle. Ludwig and his colleagues later demonstrated that it is specifically the lower brainstem which is responsible for the control of blood pressure (1873). By observing the arterial blood pressure while progressively removing rostral brain tissue, they observed that blood pressure reductions occurred only following ablation of mid-pontine structures, and that maximal reductions were obtained by transecting the brainstem at the junction of the spinal cord.

In the traditional model of the autonomic nervous system (ANS), the sympathetic and parasympathetic subdivisions produce antagonistic visceral and glandular responses as a means of maintaining the body within a steady state. The anatomical features of the autonomic nervous system were elucidated by Gaskell who found that one of the subdivisions provided a relatively diffuse and undifferentiated pattern of visceral innervation (1886, 1916). Langley examined the physiology of this "involuntary" nervous system and proposed that it be called the "autonomic", or self-governing, nervous system. Langley applied the term "sympathetic" to the less differentiated

division, and named the other division "parasympathetic" (1905, 1921). Loewi demonstrated the inhibitory effect of acetylcholine (ACh) on cardiac activity, which established it as the parasympathetic post ganglionic transmitter. In 1933 Dale termed the parasympathetic nerves "cholinergic" (i.e., releasing ACh) and he called the sympathetic nerves "adrenergic" (i.e., releasing adrenalin). In 1946 von Euler demonstrated that it is norepinephrine which is the transmitter primarily responsible for the activating effect of sympathetic stimulation of the cardiovascular system.

Eppinger and Hess (1910/1917) were the first to propose the concept of "autonomic imbalance" to explain the role of the autonomic nervous system in physiological disorders such as hypertension, cardiac arrhythmias, and cardiac arrest. They reasoned that if normal functioning of the body were dependent upon a balance between the two autonomic divisions, then a shift in the direction of either influence could result in physiological disorders. On the basis of pharmacological studies, they concluded that some individuals demonstrate altered sympathetic or parasympathetic activity.

The notion of autonomic balance was further developed by Walter B. Cannon who proposed the concept of "homeostasis" to describe the role of the autonomic nervous system in stabilizing the body's "internal milieu" within tolerable limits (1929, 1932). Cannon also provided the time-honored description of the "fight or flight"

response as a widespread activation across a broad front of physiological systems. This response was said to be elicited by stimulus situations which are interpreted to be physically or psychologically threatening.

The Concept of Arousal or Activation

The concept of activation or arousal was proposed by Duffy to describe the intensity of behavior (1932a, 1934, 1941). Activation was said to range along a continuum from deep sleep to extreme excitation. This physiological activation or arousal was said to be measurable through such physiological indices as: heart rate, blood pressure, and electroencephalographic (EEG), electromyographic (EMG), or electrodermal (EDR) activity (1932b, 1951). Activation was found to occur in different patterns according to the stimulus conditions employed during the measuring process, but the key point is that activation only differs in degree across stimulus situations. Duffy did note that the various measures of activation were poorly correlated with each other. Duffy attributed these low correlations to response patterning produced by the different stimulus conditions, and to idiosyncratic "organic factors" (1957).

Darrow pointed out that the use of single variable indices of autonomic nervous system activity produces equivocal results (1943). Wenger tested the Eppinger and Hess notion of autonomic imbalance by using factor analytic techniques to analyze data from multiple physiological measures (1941, 1942). Wenger reasoned that chronic imbalances in autonomic functioning might

be detected by analyzing tonic levels of several variables under controlled conditions. From the various physiological measures (heart rate, blood pressure, skin conductance, etc.) a "score of autonomic balance" was derived. This estimate was obtained by transforming the raw data into T scores and entering them into a linear regression equation. Autonomic imbalances can be produced by a predominance of the sympathetic (adrenergic) or parasympathetic (cholinergic) nervous systems. A phasic dominance of the sympathetic division is a characteristic response produced during conditions of stress. Eventually Wenger identified several patterns of autonomic activity which described most subjects (1957). Low inter-measure correlations were interpreted as resulting from individual differences in patterns of autonomic activity (Wenger, 1966, 1972).

Response Specificity

The individual-specific type of response patterning was investigated by Lacey, who examined multiple physiological measures under many stimulus conditions (1950, 1952). These conditions included: mental arithmetic, oral word association, hyperventilation, and the cold pressor test. Lacey differentiated between tonic measures of "autonomic tension" and phasic measures of "autonomic lability" (i.e., change scores). Individual subjects were found to respond with the same idiosyncratic pattern, in terms of maximal response. Under each of the four stimulus conditions, all of the physiological changes were in the direction of sympathetic activation, but the responses differed only in terms of the magnitude of change

from pre-stimulus levels. Lacey used the term "response stereotypy" to refer to this tendency for subjects to respond with the same pattern of maximal response under various conditions.

In his studies of anxiety, Malmo utilized multiple physiological measures to serve as indices of behavioral arousal (1957, 1959). Malmo proposed the concept of "arousal" to be a continuum of behavioral intensity, and he clearly delineated it from a previous use of the same term by Lindsley (1952) to refer to EEG phenomena. Malmo also demonstrated that normal subjects and psychiatric patients could be discriminated by their rates of recovery from arousing conditions (Malmo, Shagress, & Davis, 1950). He hypothesized that it was the reticular activating system, described by Moruzzi and Magoun (1949), that was responsible for the different rates of recovery through failures in inhibitory processes following stimulation. Malmo also formulated the concept of "symptom specificity" to refer to his demonstration that patients tend to show maximal changes within the organ system involved in their disorder (Malmo & Shagress, 1949; Malmo et al, 1950). In reviewing contributions to psychophysiological research, Malmo pointed out the dangers of recording heart rate alone as a cardiovascular variable, since it is cardiac output (heart rate x stroke volume) which is the more important metabolic variable (1972).

The issue of autonomic response specificity was considerably clarified by Engel when he proposed a distinction between stimulus-

response specificity and individual-response specificity (Engel, 1960; Engel & Moos, 1967). He referred to the tendency with which an individual demonstrates characteristic responses to most stimuli as "individual specificity". Individual specificity thus refers to individual differences and is therefore similar to the concept of response stereotypy. The tendency for certain stimuli to produce characteristic responses within most subjects was termed "stimulus specificity". Stimulus specificity thus involves inter-subject consistency. Stimulus specificity is a primary factor in the determination of stimulus uniqueness (Engel, 1972).

Operant Conditioning of Cardiovascular Responses

Since the development of operant, or instrumental, conditioning procedures, there have been attempts to clarify the distinction between operant and classical, or Pavlovian, conditioning. Konorski and Miller postulated that operant conditioning is capable of producing effects only within the somatic, or skeletal-muscular, system and not upon autonomically mediated physiological functions (1937). Other researchers quickly adopted this view of the conditionability of autonomic responses (Schlosberg, 1937; Mowrer, 1938). There was not complete agreement on this issue, as evidenced by Skinner's reluctance to draw the same conclusion from his data (1937). Eventually, however, even Skinner appears to have accepted this theoretical position (1938, 1953).

This line of thinking appears to have been the accepted position, at least until the 1960's (Kimble, 1961). Reports began to appear in the literature during the 1960's which claimed to demonstrate the conditioning of autonomic responses (e.g., galvanic skin response, vasodilation, and heart rate) in humans (Kimmel, & Hill, 1960; Kimmel & Kimmel, 1963; Lisina, 1965; Shearn, 1961, 1962). Demonstration of operant conditioning of cardiac function in humans was extended by a study which showed that the variability of heart rate could be reduced through external feedback and verbal instructions (Honatiow & Lang, 1965). In another study it was demonstrated that information feedback and monetary reinforcement could be used to produce heart rate slowing (Engel & Hansen, 1966). Additional experiments with human subjects produced evidence that bi-directional control of heart rate could be demonstrated within the same session (Brenner & Hothersall, 1966; Levene, Engel, & Pearson, 1969).

The use of subhuman species in studies of autonomic conditioning is an effective way to handle the questions regarding "cognitive" mediation of autonomic responses. The use of curare to block skeletal muscle responses removes the additional questions of somatic mediation of those same responses. Trowill was the first to demonstrate learned cardiovascular responses using operant conditioning in the curarized rat (1967). By providing stimulation of the medial forebrain bundle he was able to demonstrate both increases and decreases in heart rate. Another study, by Miller and DiCara,

demonstrated that these heart rate responses could be shaped and controlled by a discriminative stimulus (1967). The use of intracranial stimulation in the curarized rat was found to be effective in producing learning in other autonomic responses such as vasodilation, vasoconstriction (DiCara and Miller, 1968a) and systolic blood pressure increases and decreases (DiCara and Miller, 1968b). To rule out the possibility that cardiovascular learning was specific to medial forebrain stimulation, an avoidance procedure was employed to replicate the operant conditioning of heart rate (DiCara and Miller, 1968c). Plumlee also used an avoidance procedure to produce increases in diastolic blood pressure in monkeys (1968).

Controversy soon arose over the role of cognitive and somatic mediation in the production of these presumed operant responses. Katkin and Murray (1968) reviewed the early literature and concluded that operant conditioning of autonomic responses had been demonstrated in curarized animals, but could not be shown to occur in humans. These authors reasoned that human subjects would need to be both curarized and unconscious in order to rule out possible mediating events. Other researchers responded in defense of operant autonomic conditioning and argued that the operant conditioning hypothesis was the strongest and most parsimonious explanation of the disputed findings (Crider, Schwartz, and Shindman, 1969). Other challenges to the operant conditioning position were provided by Obrist and his colleagues, who presented data concerning the issue of the interaction of cardiovascular and somatic, or skeleto-muscular systems (Obrist, Webb, Sutterer, and Howard, 1970).

In spite of these challenges and the difficulties experienced in replicating the curarization studies (Miller & Dworkin, 1974), it now seems clearly established that operant conditioning techniques can be used to modify autonomic responses. It is now time to examine operant conditioning of autonomic responses in a more detailed manner with respect to the conditionability of the various autonomic measures, and the rate, duration and magnitude of those measures (Black, Cott, & Pavloski, 1977). It appears that it is now prudent to examine the psychophysiological interrelationships between environmental stimuli, behavior, and the intact cardiovascular system.

The chair restrained baboon has been found to be an especially useful subject for this area of research. Harris and his colleagues have demonstrated the production of large magnitude, long duration changes in primate blood pressure with the use of biofeedback procedures (Harris, Gilliam, Findley, & Brady, 1973; Harris and Brady, 1977). These studies have provided an animal model of environmentally induced hypertension which is likely to be of great value in advancing our understanding of the pathophysiology of essential hypertension. More recently these investigators have urged that efforts now be directed towards improving our understanding of the neural and hormonal mechanisms involved in environmental and behavioral influences upon the intact, conscious organism (Harris, Goldstein, & Brady, 1977). However these authors also point out that the elucidation of these mechanisms must await the development of technology which can readily assess such factors as cardiac output and cardiac contractility (Goldstein, Harris, & Brady, 1978).

Cardiovascular parameters can change in: frequency, force, duration, rhythm, and magnitude. Typically no more than two of these dimensions are evaluated simultaneously within a single experiment. Psychophysiological studies and learning studies have typically been limited to an examination of heart rate and/or blood pressure when examining cardiovascular responses.

The success of early attempts to operantly condition autonomic activity gave rise to great expectations concerning the medical application of biofeedback to target specific physiological disorders. Some of the most convincing demonstrations of autonomic conditioning through operant reinforcement involved such cardiovascular variables as: heart rate, blood pressure, and tissue temperature (DiCara & Miller, 1968; Miller, 1969). Particular excitement was generated over the likelihood that behavioral techniques would be efficacious in the treatment of hypertension and other cardiovascular disorders.

Hemodynamics

The behavioral topography of the heart involves changes in rate, force, duration, periodicity, and magnitude. Biofeedback and psychophysiology have been somewhat limited by the available instrumentation for cardiovascular monitoring. Studies have typically used cardiometers to monitor heart rate and automated or manual sphygmomanometers for determining blood pressure. In a classic series of experiments Schwartz and his colleagues examined the ability to differentiate heart rate and blood pressure through

biofeedback techniques (1971, 1972, 1973). He demonstrated that the two parameters - heart rate and systolic blood pressure, could be trained to vary together, vary independently, or vary in opposite directions depending on the nature of the feedback signal provided. Schwartz has more recently suggested that it is now important for researchers to elucidate the mechanisms of cardiovascular responses to feedback for patterns of change. He also pointed out the need for additional information on cardiac activity such as: cardiac output, stroke volume, and myocardial contractility (1977).

It is clear that the behavior of the heart cannot be adequately described or represented by the use of heart rate and blood pressure alone. The hemodynamic patterning which occurs in response to various stimulus conditions has several theoretical and clinical implications. First, the use of biofeedback in the reduction of hypertensive blood pressure has produced mixed results (Blanchard & Young, 1974; Goldstein et al., 1982). Schwartz has proposed that one cause of failure of blood pressure feedback has been the failure to recognize the relationship the biofeedback signal to changes in other parameters (e.g., stroke volume, cardiac output, and myocardial contractility) (1977). In the same article Schwartz mentioned the possibility of one day obtaining noninvasive measures of these important hemodynamic variables. The logical extension of a new monitoring technique is the possibility of providing feedback from this new information about cardiac function. The consideration of changing patterns of activity among several hemodynamic variables taxes some existing models of biofeedback.

Systems Theory Paradigm

Psychological research, including biofeedback and psychophysiology, is based primarily on causative models and analytical techniques developed for the physical sciences (Cook & Campbell, 1979). Von Bertalanffy outlined the application of general systems theory in the behavioral sciences (1968a, 1968b). General systems was based largely on the mathematics of Wiener who developed the field of cybernetics (1948). Cybernetics is concerned with the self-regulation of systems through negative feedback loops. Cybernetics has been used extensively in such fields as engineering and biology, and it is an essential concept in the theory of biofeedback. Negative feedback is a process whereby the output of a system is modified by feeding back part of the output to the input of the system. Negative feedback loops in systems are thought to be automatically self-regulating. Mulholland provides a discussion of the relevance of cybernetics to biofeedback research (1977). The concept of homeostasis, developed by Cannon, was a major factor in the development of cybernetic concepts (von Bertalanffy, 1968b).

The characteristics of self-regulatory systems can be studied by perturbing the system and observing compensatory responses designed to restore equilibrium. The demonstration of specificity and patterning within the autonomic nervous system requires a revision of the concept of this system as diffuse, and undifferentiated (Miller, 1969; Schwartz, 1977). Systems theory thus would appear to provide a useful paradigm from which to study cardiovascular

patterning and interactions between the cardiovascular and central nervous systems. Ashby defined a system to be any set of variables chosen by the observer from the infinite set available. The observer therefore can create a picture of the system which may be quite different in nature from reality, depending on his/her selection of variables for study. It is a basic premise of this series of studies that the inclusion of additional hemodynamic variables will provide a different, and more accurate, picture of cardiovascular behavior in response to stress and other stimulus conditions.

Impedance Cardiography

Until the development of noninvasive, impedance-based measures of cardiac performance, researchers could examine such variables as stroke volume, cardiac output, and cardiac contractility only through invasive procedures. In the late 1960's, a noninvasive monitor of cardiac performance was developed for the National Aeronautics and Space Administration to study cardiac function during space flight (Kubicek, 1969). This technique employs a pair of surface electrodes to induce a radio-frequency (r-f) electromagnetic field across the chest cavity. A second pair of electrodes monitors changes in the impedance to the passage of this r-f current through the chest. The result is a pulsatile signal which is synchronous with the heartbeat. By calculating the first derivative, or rate of change (dZ/dt), of the impedance signal one can represent the change in velocity of the ejection of blood during systole.

Measurements can be made from well defined landmarks on the dZ/dt waveform and electrocardiogram (ECG). These landmarks have been shown to correspond to such cardiac events as valvular closing and the point of maximal ejection of blood from the left ventricle. The resulting measurements can then be entered into empirically validated formulae to produce estimates of: stroke volume, cardiac output, and cardiac contractility (Kubicek, Patterson, & Witsoe, 1970; Miller & Horvath, 1978). A list of the formulae, and their components, is presented in Appendix 1.

The measures derived from impedance cardiography have been compared to those obtained with such invasive procedures as: thermal dilution, dye dilution, and the Fick principle. These studies have shown there to be a very high correlation, often above .90, between the invasive and noninvasive estimates (Mohapatra, 1981). The correlations are generally highest in healthy populations. A major limitation of impedance cardiography to some clinical applications is its tendency to overestimate the stroke volume and cardiac output. A second limitation is its reduced accuracy in patients with significant cardiac pathology. The use of impedance cardiography in cardiology has been limited as a result of these problems. The potential value of impedance cardiography in psychophysiology has been presented by Miller and Horvath (1978). They made clear the value of the technique for noninvasive measurement of intra-subject change as is frequently the object of much psychophysiological

research. For this reason the procedure seems to hold considerable promise for the investigation of cardiovascular behavior.

Pilot Study Findings

In the pilot study for this proposed dissertation research, a group of active duty police officers, with borderline hypertension, were monitored while being subjected to two stress conditions - mental arithmetic and the cold pressor test. Measures of cardiovascular function were obtained from the impedance cardiograph, in addition to blood pressure and hand temperature. Analyses of variance performed on the pilot data are presented in Appendix 2.

The two stress conditions were found to produce equivalent changes in heart rate and blood pressure. The two stressors were found to produce an activation of all the more familiar measures: heart rate, blood pressure, and hand temperature. However, the measures obtained with impedance cardiography (stroke volume, cardiac output, and cardiac contractility) showed entirely different patterns during the two conditions. The results of post hoc comparisons of means are presented in Appendix 3. The examination of the heart from a systems oriented perspective emphasizes the homeostatic, or self-regulating nature of the cardiovascular system. This self-regulating behavior of the system is likely to place real constraints upon any changes that are produced by experimental manipulation. In attempts to elucidate the mechanisms of nervous system control of cardiovascular function, both stress and biofeedback procedures

have been frequently employed. The use of the impedance cardiography technique allows for the examination of the topography of cardiovascular responses in an important new way. The ultimate goal of the present research is to lay a foundation for the potential use of impedance cardiography to provide instantaneous feedback about cardiac function for the purpose of investigating the mechanisms of learned control of blood pressure and other cardiovascular variables.

Purpose of Dissertation

This series of studies is designed to replicate and extend this pilot data. The first study examines the reliability of the two hemodynamic patterns to the cognitive and cold stress conditions within the same borderline hypertensive subject population. The predicted hemodynamic response patterns to cognitive and cold stress conditions are displayed in Table 1. These predictions are based upon the mean values observed in the pilot study. The second experiment examines the generalizability of these findings across subject populations by examining the responses of normotensive subjects. The mechanism of increased peripheral resistance is also investigated in the second study by examining the ability of a different stressor, which produces increased peripheral resistance, to reproduce the original patterning to cold stress. The third study examines the effects of a benzodiazepine anxiolytic compound, diazepam, in modifying the response patterning to the cognitive and cold stressors.

TABLE 1

PREDICTED STIMULUS-SPECIFIC RESPONSES TO
COGNITIVE AND COLD STRESSORS

VARIABLE	DIRECTION (Change from Baseline)	
	Quiz	Cold
Systolic Blood Pressure	+	+
Diastolic Blood Pressure	+	+
Heart Rate	+	+
Stroke Volume	-	-
Cardiac Output	+	-
Cardiac Contractility	+	-
Systemic Resistance	+	+
Hand Temperature	-	-

METHOD

Dependent Measures

The psychophysiological measures which were obtained consist of heart rate, systolic and diastolic blood pressure, and hand temperature; as well as indices of: cardiac output, stroke volume, myocardial contractility, and total peripheral resistance. These indices were obtained from formulae which were developed for use with the derivative impedance cardiogram (Mohapatra, 1981). Thus in addition to the four traditional psychophysiological measures there are four new variables which reflect cardiac performance that are computed.

Cardiac output is the amount of blood which is pumped per unit of time and is expressed in terms of liters per minute. Stroke volume is the amount of blood, in milliliters, which is pumped with a single heartbeat. Cardiac output is the product of stroke volume times heart rate. Cardiac contractility is the vigor, or force, of the heart's contraction and it is indexed by the maximal instantaneous rate of change of the ventricular pressure curve (dP/dt) (Berne & Levy, 1981).

Cardiac output is pumped against the total peripheral resistance of the body, and those two factors jointly affect the arterial blood pressure. Peripheral skin temperature has been proposed as an index of peripheral resistance and increased hand and/or foot temperature is frequently the target of clinical biofeedback training for hypertension (Green, Green, & Norris, 1980).

Apparatus

Blood pressure in this series of studies was determined manually from the subject's dominant arm following standard procedures (Kaplan, 1978). Subjects were seated upright in a padded chair with the dominant arm elevated to about the level of the heart. The cuff was rapidly inflated during the final twenty seconds of each recording period. The systolic blood pressure was recorded as the point at which the first sounds of blood passing through the brachial artery are heard (Korotkoff phase I). The diastolic blood pressure was identified as the pressure at which the last sounds are heard (Korotkoff phase V). Only during the pilot study was blood pressure data collected with the use of an automated sphygmomanometer (Dimamap model 850). The decision to adopt the manual blood pressure procedure was due to the variability of the time involved to obtain the automated reading. It was difficult to coordinate the blood pressure determination with the end of the condition using the automated cuff. This problem was generally due to artifact rejection circuitry which was prone to trigger during the cold pressor test.

Peripheral skin temperature was determined with the use of an Autogenic Systems model 2000 skin temperature monitor. A thermistor was taped to the dorsal surface of the distal phalange of the middle digit on the nondominant hand. The thermistor was placed proximal to the fingernail with the thermistor lead secured to the finger at a second location in order to minimize movement. Readings were made to the nearest tenth of a degree Fahrenheit at the end of each condition.

The other hemodynamic variables were recorded with the use of an Instrumentation for Medicine model 400 impedance cardiograph. This device passes a 4 mA, 100 kHz, sinusoidal signal across electrodes encircling the subject's neck and thorax. A constant-current signal is passed across the chest cavity and the resulting voltage is detected by a second pair of electrodes placed between the two excitation electrodes. See figure 1 for a schematic illustration of this procedure. This voltage signal is synchronous with both the heartbeat and respiration. Changes in tissue volume and displacement within the thorax are responsible for the fluctuations in the impedance signal (Karnegis & Kubicek, 1970). The first derivative of the impedance signal (dZ/dt) is then computed and recorded on a chart recorder. By recording only during the same point in the respiratory cycle, respiration artifacts can be virtually eliminated (Miller & Horvath, 1978). All cardiograph recordings were obtained during respiratory apnea following a full exhalation.

The electrodes used by the impedance cardiograph are bands of aluminized mylar tape which encircle the subject's body. The first excitation electrode is placed high on the subject's neck and parallel with the floor. The second electrode is used for reception and is placed parallel to the first one, and at least 2.5 cm below it. The third electrode is also receptive and is placed parallel to the first two at the level of the xiphisternal joint at the base of the sternum. The fourth electrode is excitatory and it is placed at least two inches below electrode three, and parallel to it.

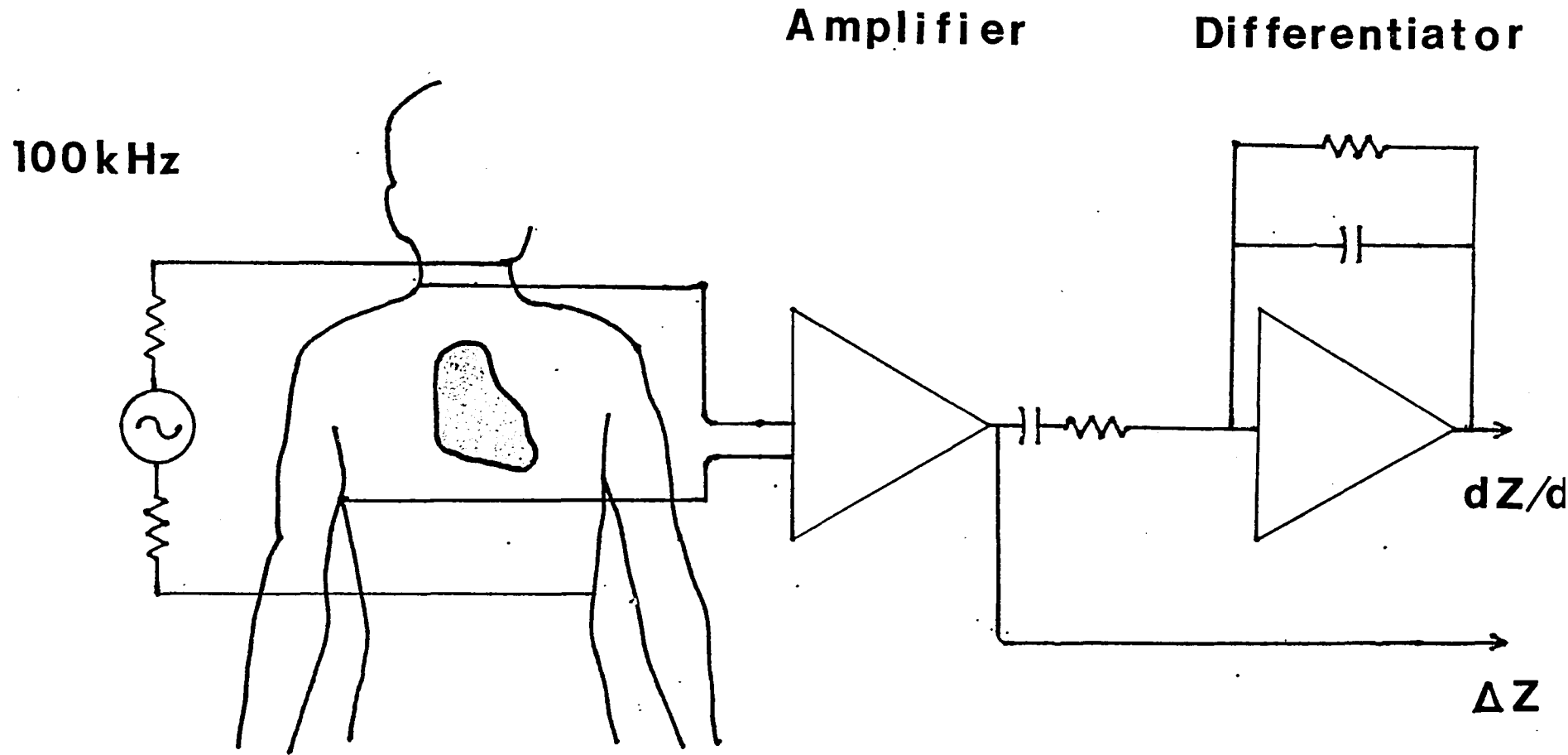


Figure 1. Schematic Diagram of Impedance Cardiograph

The dZ/dt signal and an electrocardiogram (ECG) were recorded on a thermal strip chart recorder at a chart speed of 50 mm/sec. Many of the records made during the first study were recorded at a speed of 25 mm/sec. to conserve materials. The two waveforms were manually scored to determine the following measures: interbeat interval, ventricular ejection time, maximal height of the dZ/dt waveform, and the interval between the R spike of the ECG tracing and the maximal height of dZ/dt (R-Z interval). The dZ/dt waveform, its relationship to the ECG, and the measurements involved in scoring the waveform are represented in Figure 2. The interbeat interval is measured between successive R spikes of the ECG. Ventricular ejection time is obtained by determining the time period between aortic valve opening and closure. Aortic valve opening coincides with the foot of the upstroke of the dZ/dt waveform, and valvular closure is indicated by the prominent notch which follows the dZ/dt peak. These two events also coincide with the first and second heart sounds, and may be determined with the use of a phonocardiogram.

The fact that some of the records in the first study were recorded at half-speed was unfortunate since changes in two important systolic time intervals become more difficult to determine (i.e., VET and the R-Z interval). The last three consecutive waveforms during each condition were measured and averaged for each condition. A calibration signal was recorded prior to and at the conclusion of each subject run.

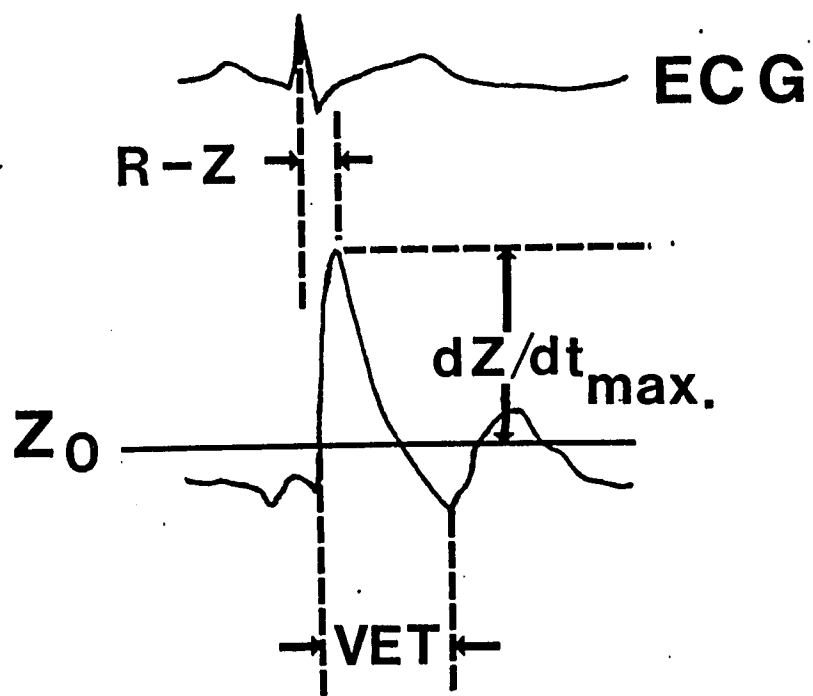


Figure 2. Measurements Taken from the Impedance Cardiogram

Measures taken from the impedance cardiograph waveforms were then entered into the appropriate formulae to estimate the hemodynamic parameters of heart rate, stroke volume, cardiac output, and myocardial contractility (Kubicek et al, 1966, 1970; Mohapatra, 1981). Heather's index of myocardial contractility was used for estimating contractile force (Heather, 1969). Total peripheral resistance was estimated by calculating the ratio of mean arterial blood pressure to cardiac output. Mean arterial blood pressure was estimated by adding one third of the pulse pressure (systolic minus diastolic) to the diastolic blood pressure (Berne & Levy, 1981). These formulae are displayed in Appendix 1.

Experiment 1

Design - This experiment is designed to replicate the pilot study and examine the response patterns produced by cognitive stress and the cold pressor test. A new cognitive task was employed in this study. This new task is a quiz of several cognitive abilities including: general knowledge, arithmetic skills, and reasoning. This task was developed for studying the effects of emotional stress on angina patients (Schiffer, Hartley, Schulman, & Abelmann, 1976). These investigators found the quiz to produce ECG changes similar to those induced by exercise stress. The quiz was preceded by an instructional set which explains that it is a test of mental ability and that the subject's score will be compared with other individuals his/her own age. The questions are then presented under time pressure by allowing only five seconds for responding.

The text of this quiz, and its instructional set, are presented in Appendix 4. Hemodynamic patterns which occur in response to the two stress conditions were examined to determine if either the cognitive or the cold pressor patterns had been replicated.

Subjects - Subjects were drawn from the same police department used in the original study (Stamford, Connecticut). Twenty four additional officers were recruited to participate in the "stress test". The average age of all 36 subjects was 36.1 years. No selection process was utilized other than screening individuals for existing or potential cardiac problems or symptoms of cardiovascular disease.

Procedure - The procedure which was followed was identical to that used in the pilot study with the exception of the new cognitive stressor. The experiment was conducted in a private room within the police station which was assigned to the project. The subjects sat upright in a padded conference chair throughout the entire procedure. Subjects were first interviewed to obtain demographic and medical history data while the various electrodes were being attached by a second experimenter. This hookup and interview process required approximately twenty minutes, which allowed for the subject's skin temperature to adapt to the ambient temperature of the experimental room which was maintained at approximately 70 degrees Fahrenheit. Before the start of the experiment the subjects were instructed in a respiratory pause on command procedure. Subjects were told

to hold their breath following a full, but not forced, exhalation. A trial cardiograph recording was made prior to the start of the experiment to ascertain that each subject understood the instructions and could produce the desired respiratory manipulation. A calibration signal was also recorded at the beginning and conclusion of each session.

The first four minutes of the stress test was a resting baseline period, during which the subjects were instructed to close their eyes and allow themselves to become as relaxed as possible. The quiz was administered next, and the two minute trial began as soon as the subject had heard ten questions or made three errors, whichever occurred first. A two minute recovery period followed the quiz condition. Subjects were instructed to immerse their dominant hand up to the wrist in a bucket of ice water for sixty seconds. The subjects were also monitored during a four minute recovery period, but that data was not evaluated at this time. The cognitive and cold stress conditions were not counterbalanced due to the extreme effects the cold stressor produces on hand temperature in the opposite limb. In the pilot study a two minute recovery period was sufficient for all other variables to return to approximate their original levels.

Experiment 2

Design - This experiment is designed to investigate the underlying mechanism of the hemodynamic patterning to cold stress by substituting a different physical stress condition which is known to increase blood pressure by increasing peripheral resistance. A period of sustained submaximal isometric contraction was used as the stressor, instead of the cold pressor test. Both stressors involve an increase in peripheral resistance, which is the presumed mechanism responsible for the blood pressure elevations produced during the cold pressor test. The experimental procedure was identical to that used in the first experiment in all other respects. As a test of the reliability of the hemodynamic patterns, a second stress test was administered to the same group of subjects.

Subjects - A single group of nine healthy volunteers were recruited for experiment 2. Subjects for this experiment were drawn from a healthy adult population of graduate students. The average age of subjects in the second study is 27.7 years, which is considerably younger than that drawn from the Connecticut police department. The use of younger subjects allows a test of the generalizability, across age, of the findings pertaining to the hemodynamic patterning resulting from the cognitive stress condition.

Procedure - The procedure for the second experiment was identical to that used in the first study except for the use of a new condition of physical stress. Subjects were first asked to demonstrate their

maximal grip strength with their dominant hand. Maximal grip strength was determined by having the subject squeeze a partially inflated blood pressure cuff which was rolled up to form a cylinder with a diameter of approximately three inches. The maximal pressure was read from the aneroid meter, and divided by three to obtain the target pressure to be maintained during the isometric contraction condition. They were then asked to maintain an isometric contraction at the target level for a period of two minutes. As in the first study the cognitive stress condition was presented first, followed by a recovery period then the isometric contraction condition. The baseline, self-relaxation, and recovery periods were lengthened to four minutes each to allow for maximal recovery to baseline levels following stress conditions. Physiological recording was conducted during the final twenty seconds of all conditions, including isometric contraction.

A second stress test was administered to the same subjects in an attempt to examine the reliability of the stimulus specific patterns. The second stress test was exactly the same as the first except that the questions administered during the quiz were divided into two lists. This allowed for the presentation of a different set of questions during the two stress tests. The recording period began with the presentation of the fourth question, regardless of the subject's performance. The second stress test was usually administered the same day in an effort to minimize variance due to differences in electrode placement.

Experiment 3

Design - The purpose of the third study is to examine the effects of a benzodiazepine anxiolytic compound on the hemodynamic patterning produced during the cognitive and cold pressor stress conditions. Subjects were randomly assigned to receive either diazepam, or an active placebo, immediately following the first stress test. A second stress test was administered after the drug had sufficient time to reach effective blood levels. Differences between the values obtained during the two stress tests were used as the data points.

Subjects - Fourteen healthy adult volunteer subjects were recruited for this experiment. The subjects were all healthy, normotensive students with ages ranging from 27 to 41. Half of the subjects were randomly assigned to receive the anxiolytic compound, while the other half were assigned to an active control group. All subjects were screened for possible medical contraindications to the use of the stress test or the two compounds.

Procedure - Each subject was administered two identical stress tests. The first stress test served as a baseline against which responses under the drug condition are compared. The stress tests were identical to that used in the first experiment. The quiz was divided into split-halves as in the second study. Following the first stress test each subject received the anxiolytic compound

or an active placebo. The anti-anxiety compound was diazepam, 10 mg. p.o. The active placebo was chlorpheniramine 8 mg. p.o. Chlorpheniramine was selected as the control compound due to its sedative effects which are similar to diazepam's at the dosages selected for this study. The second stress test was conducted an hour after the administration of the drug. No attempt was made to control for the time of administration of the drugs. The administration of pharmacologic compounds at a uniform time of day has been recommended to control for circadian periodicity when examining the behavioral effects of drugs (Stroebel, 1972). Subjects were told that they would receive a "Valium-like" compound, but they were not informed which drug was administered until after the second stress test procedure.

RESULTS

Experiment 1

The first experiment was designed to replicate the findings of stimulus specific hemodynamic patterns to the cognitive and cold pressor stress conditions. Subjects were exposed to both stressors in a repeated measures design identical to that used in the pilot study. The means for all cardiovascular variables under four conditions are displayed in Table 2. Each variable was subjected to a separate analysis of variance (ANOVA) procedure with four repeated measures. The results of these one-way ANOVA's are presented in Table 3. Each variable was found to demonstrate a highly significant main effect (conditions).

Duncan's New Multiple Range Test (1955) was used for the post hoc comparison of means. Three comparisons were conducted for each variable: 1) between the cognitive stressor and the baseline condition; 2) between cold pressor and baseline; and 3) between cognitive stress and cold stress. The results of these analyses are listed in Table 4.

The cold pressor test produced the predicted response in all cardiovascular variables, and all were found to be significant. Responses to the cognitive stressors were also all in the predicted direction. The changes produced by the cognitive stressor were all significant with three exceptions. Cardiac output, cardiac contractility, and systemic resistance were changed in the predicted

direction but failed to reach significance. When the two stress conditions were compared, all variables were found to be significantly different with the exception of hand temperature.

Both stress conditions produced significant increases in systolic and diastolic blood pressure, and heart rate. Both produced significant decreases in stroke volume and hand temperature. Cardiac output and cardiac contractility both changed in different directions under the two stress conditions, but the changes were not significant under the cognitive stress conditions. Systemic resistance increased under both stressors but the change during the cognitive stress condition was nonsignificant also.

In the pilot data, cardiac contractility was significantly increased and cardiac output was nonsignificant according to the one-way ANOVA (APPENDIX 1). Cardiac contractility lost significance when the sample size was increased by an additional twenty-four subjects. Since the cognitive task was changed it is the most obvious possible cause of this loss. However, there was also a change in the recording procedure which served to reduce the variability of the cardiac output, cardiac contractility, and systemic resistance estimates. During the testing of most of the additional twenty-four subjects the strip chart recorder was run at a chart speed of 25 mm/sec. for reasons of economy. Scoring such "half-speed" charts is more difficult when measuring along a temporal dimension such as in the R-Z interval used in the Heather index and in the

TABLE 2

EXPERIMENT ONE

MEAN VALUES OF HEMODYNAMIC VARIABLES BY CONDITION

VARIABLE	n	- - - - CONDITIONS - - - - -			
		BASE.	RELAX.	QUIZ	COLD
Systolic B P mm Hg	36	132.2	133.7	142.5	147.5
Diastolic B P mm Hg	36	84.8	84.7	88.4	94.9
Heart Rate B.P.M.	36	69.0	70.7	74.8	78.5
Stroke Volume ml	36	64.8	65.4	62.7	51.9
Cardiac Output l/min.	36	4.4	4.5	4.6	4.0
Contractility Heather's Index	36	13.9	13.5	14.0	11.0
Resistance MAP/CO	36	24.5	23.5	25.6	32.8
Hand Temperature Deg. F	36	90.2	90.7	88.6	87.8

TABLE 3

EXPERIMENT ONE

SINGLE FACTOR ANALYSES OF VARIANCE WITH REPEATED MEASURES

VARIABLE	ANOVA		
	F	df	p
Systolic Blood Pressure	31.14	3/105	.001
Diastolic Blood Pressure	18.63	3/105	.001
Heart Rate	24.37	3/105	.001
Stroke Volume	14.00	3/105	.001
Cardiac Output	5.74	3/105	.01
Cardiac Contractility	14.87	3/105	.001
Total Systemic Resistance	18.23	3/105	.001
Peripheral Skin Temperature	21.99	3/105	.001

Reference - Winer, B. J. Statistical principles in experimental design, 2nd ed. New York: McGraw-Hill, 1971, 261-305.

TABLE 4

EXPERIMENT ONE
DIRECTIONAL SPECIFICITY: POST-HOC TESTS

Variable	N	sig.		sig.	
		Change from Quiz	Baseline Cold	Quiz vs. Cold	Quiz vs. Cold
Systolic B P	36	+	.01	+	.01
Diastolic B P	36	+	.05	+	.01
Heart Rate	36	+	.01	+	.01
Stroke Volume	36	-	.01	-	.01
Cardiac Output	36	n.s.		-	.05
Contractility	36	n.s.		-	.01
Resistance	36	n.s.		=	.01
Temperature	36	-	.01	-	.01

Duncan's New Multiple Range Test

case of ventricular ejection time which is incorporated in the formulae for stroke volume, cardiac output, and thus in systemic resistance (MAP/CO).

An attempt was made to resolve the issue of the directional specificity during the cognitive stress condition by employing a nonparametric sign tests to examine the direction of change for each variable. These tests provided further support for the predicted changes in systolic and diastolic blood pressure, heart rate, and hand temperature. They left unanswered the question of directional specificity for cardiac output and cardiac contractility, and they failed to confirm the predictions for stroke volume and systemic resistance. The results of these tests are displayed in Table 5.

In a further attempt to resolve the issue concerning directional specificity with cardiac output and myocardial contractility was conducted by analyzing data form an additional data set. The measures obtained with the subjects from the remaining two experiments. Data from all twenty-three subjects during the quiz condition were examined to determine the direction of change with respect to baseline. In addition, t-tests for related measures were performed using the cognitive stress (quiz) and baseline conditions. The results are shown in Table 6.

Both tests agree, and they support the directional predictions for heart rate, cardiac output, and cardiac contractility. These three variables were found to be significantly affected by the cognitive stress condition. Only stroke volume failed to achieve significance in either the direction or the magnitude of change. Since the mental arithmetic task and the quiz both produced significant changes in the same direction it seems prudent to combine them for the purposes of this analysis under the label of cognitive stress conditions. Stroke volume is singularly distinguished in its failure to achieve significance under any of the three analyses (pilot, experiment 1 and the additional 23) using either sign tests or tests of differences between means. This failure suggests that there are significant individual differences in the way stroke volume responds during demanding cognitive tasks. These individual differences were not analyzed in this series of studies, but are similar to patterning seen during thermal biofeedback (Stanick, Wilson, & Steiner, in press). During handwarming, stroke volume shows reliable decreases, but heart rate increases for half of the subjects and decreases for the others.

The major finding of this experiment is that cognitive tasks and the cold pressor test produce specific hemodynamic response patterns which differ in both magnitude and direction. These patterns agree with all of the predicted changes with the sole exception of stroke volume, which consistently fails to reach significance in tests of either direction or magnitude.

TABLE 5

EXPERIMENT ONE
DIRECTIONAL SPECIFICITY - SIGN TESTS

VARIABLE	n	QUIZ		COLD	
		+/-	p	+/-	p
Systolic B P	36	+	.01	+	.05
Diastolic B P	36	+	.01	+	.05
Heart Rate	36	+	.01	+	.05
Stroke Volume	36	* n.s.		-	.05
Cardiac Output	36	n.s.		-	.01
Cardiac Contractility	36	n.s.		-	.01
Peripheral Resistance	36	n.s.		+	.01
Hand Temperature	36	-	.01	-	.01

* Equal numbers increased and decreased

TABLE 6

EXPERIMENT ONE

HEMODYNAMIC EFFECTS OF COGNITIVE STRESSOR:
SIGN TESTS AND t-TESTS FOR RELATED MEASURES

VARIABLE	n	DIRECTION		DIFFERENCE	
		+/-	p	t	p
Heart Rate	23	+	.01	3.11	.005
Stroke Volume	23	n.s.		0.82	n.s.
Cardiac Output	23	+	.05	1.90	.05
Cardiac Contractility	23	+	.01	2.78	.01

Compared to baseline conditions

A point of practical interest is that the use of the technique of impedance plethysmography allows for the non-invasive discrimination of these hemodynamic patterning with relatively few subjects. Both psychophysiological and biofeedback procedures frequently involve analyses of repeated measures, where relative change is of primary interest. The limitations of impedance cardiograph-derived overestimation of stroke volume is avoided in such cases. The use of small samples is of particular interest in studies which are either difficult or costly to conduct such as in biofeedback and clinical pharmacology. The next two experiments take advantage of the economy of the impedance cardiographic stress test by addressing their questions with sample sizes of less than ten.

One possible interpretation, but not the only one, of the mechanism by which the cold pressor test produces its dramatic hemodynamic effects is through the substantial increase in peripheral resistance. Increased peripheral resistance of this magnitude would be expected to increase total systemic resistance and therefore produce blood pressure elevations. With blood pressure already increased, further increases in stroke volume or cardiac output could push the arterial pressure to dangerously high levels. Since heart rate is increased along with blood pressure decreases in cardiac contractility could reduce stroke volume and cardiac output by ejecting a smaller portion of the blood contained within the ventricle (ejection fraction). This hypothesis is addressed in the next study which involves the use of a different procedure

to increase peripheral resistance in an attempt to replicate the directional changes produced by the cold pressor test.

Experiment 2

The second experiment was designed to investigate the role of increased peripheral resistance in the production of the hemodynamic response patterns to the physical stress condition (i.e., cold pressor test). The same repeated measures design used in experiment one was employed for this purpose, but with a different physical stressor (i.e., isometric contraction). A second purpose of experiment two is to examine the reliability of these stimulus specific response patterns across repeated administrations of identical stress tests. The means of the cardiovascular variables under five conditions of the stress test are displayed in Table 7. Data from both stress tests are included in this table. Separate one-way ANOVA's for repeated measures are presented in Table 8. Separate ANOVA's were conducted for each stress test. Most variables with the exception of cardiac output and hand temperature achieved significance in one or both stress tests.

The sign test was employed to determine which aspects of the predicted hemodynamic response pattern were produced by sustained isometric contraction. The results are presented in Table 9. All cardiovascular variables were found to demonstrate changes in the predicted direction with the sole exception of stroke volume.

TABLE 7

EXPERIMENT TWO

MEAN VALUES OF HEMODYNAMIC VARIABLES BY CONDITION

VARIABLES	TEST	CONDITIONS				
		Base.	Relax.	Quiz	Recov.	Isomet.
Systolic B P mm Hg	1	114.5	113.1	124.2	114.1	125.2
	2	108.6	110.4	120.9	109.9	121.8
Diastolic B P mm Hg	1	68.4	69.3	75.2	68.6	82.3
	2	64.7	64.7	69.8	66.1	82.1
Heart Rate BPM	1	65.6	66.2	70.6	68.1	72.8
	2	64.4	64.1	69.9	65.2	70.1
Stroke Volume ml	1	110.5	111.4	113.8	112.4	96.5
	2	101.6	100.9	97.3	103.1	88.3
Cardiac Output L/min.	1	7.3	7.2	8.1	7.5	6.9
	2	6.5	6.4	6.8	6.7	6.3
Contractility Heather Index	1	19.4	19.8	23.1	20.4	18.1
	2	18.2	18.4	19.5	19.2	17.1
Resistance MAP/CO	1	12.4	12.3	12.8	12.0	15.0
	2	13.2	13.5	14.4	13.4	16.3
Temperature deg. F	1	82.7	83.0	82.8	83.0	82.2
	2	81.8	82.6	81.3	80.6	80.6

TABLE 8

EXPERIMENT TWO

SINGLE FACTOR ANALYSIS OF VARIANCE WITH REPEATED MEASURES

VARIABLE	TEST	F	df	p
Systolic Blood Pressure	1	18.75	3/24	.001
	2	12.10	3/24	.001
Diastolic Blood Pressure	1	10.81	3/24	.001
	2	21.52	3/24	.001
Heart Rate	1	2.06	3/24	n.s.
	2	8.88	3/24	.001
Stroke Volume	1	5.54	3/24	.005
	2	3.10	3/24	.05
Cardiac Output	1	2.56	3/24	n.s.
	2	1.24	3/24	n.s.
Cardiac Contractility	1	4.45	3/24	.025
	2	1.79	3/24	n.s.
Total Systemic Resistance	1	1.22	3/24	n.s.
	2	4.36	3/24	.025
Hand Temperature	1	0.88	3/24	n.s.
	2	2.26	3/24	n.s.

TABLE 9

EXPERIMENT TWO

HEMODYNAMIC EFFECTS OF SUSTAINED SUBMAXIMAL
ISOMETRIC CONTRACTION - SIGN TESTS

VARIABLE	n	+/-	p
Systolic Blood Pressure	9	+	.01
Diastolic Blood Pressure	9	+	.01
Heart Rate	9	+	.05
Stroke Volume	9	-	.05
Cardiac Output	9	-	.05
Cardiac Contractility	9	-	.05
Total Peripheral Resistance	9	+	.05
Hand Temperature	9	-	.05

TABLE 10

EXPERIMENT TWO

HEMODYNAMIC EFFECTS OF ISOMETRIC CONTRACTION:
t-TESTS FOR RELATED MEASURES

VARIABLE	ISOMETRIC vs BASE.			QUIZ vs ISOMETRIC		
	t	df	p	t	df	p
Systolic B P	4.62	8	.005	0.41	8	n.s.
Diastolic B P	4.92	8	.005	2.07	8	.05
Heart Rate	2.51	8	.025	.084	8	n.s.
Stroke Volume	3.07	8	.01	3.11	8	.01
Cardiac Output	0.93	8	n.s.	2.17	8	.05
Contractility	0.15	8	n.s.	2.43	8	.025
Resistance	2.65	8	.025	2.60	8	.025
Hand Temperature	0.39	8	n.s.	0.94	8	n.s.

T-tests for related measures were used to determine if the magnitude of change produced by isometric contraction is significant. The differences between the isometric and baseline conditions and those between the isometric and quiz conditions were examined. The results are contained in Table 10. The isometric contraction condition produced significant changes in all variables with the exception of cardiac output, cardiac contractility, and hand temperature. When values obtained during the quiz are compared with those produced during isometric contraction are compared, hand temperature, heart rate, and systolic blood pressure are the only variables which fail to reach significance.

The major finding of this study is that a different stress condition, which also produces increased peripheral resistance, is able to replicate the hemodynamic pattern produced by the cold pressor test. Again it is stroke volume which proves to be the sole exception by demonstrating a non-significant increase during the isometric contraction.

A second finding of this study is that the hemodynamic patterning is reliable, since repeated testing results in a relatively small regression toward the mean effect. T-tests for related measures were employed to determine the reliability of the response patterning across repeated administrations of identical stress tests. The results of these tests are presented in Table 11. These decreases

which were observed during isometric contraction were found to be non-significant. Differences between baseline conditions were significant only for systolic blood pressure, stroke volume, and cardiac output. The greatest differences between values obtained during the two stress tests occurred during the cognitive task. Significant differences were seen in stroke volume, cardiac output, cardiac contractility, and total systemic resistance during the cognitive stress condition.

An additional point which can be made from these data is that hemodynamic stimulus-specificity can be observed in a younger, normotensive population than that used in the first study. This suggests that those earlier findings can be generalized to healthy subjects which are generally more readily available for psychophysiological and biofeedback research.

Experiment 3

The third study was designed to examine the effects of an anxiolytic compound (i.e., diazepam) upon the hemodynamic patterns produced by the cognitive and cold stress conditions. A repeated measures design identical to the first study was employed. Subjects were randomly assigned to receive either the anxiolytic compound or a control compound with sedative properties (i.e., chlorpheniramine). The drugs were administered in a single blind fashion following an initial stress test. An identical stress test was administered following a time period sufficient to allow the drugs to reach

effective blood levels. Following the second stress test subjects were asked if they thought they had received the diazepam or the placebo. They were unable to discriminate which compound had been administered. The mean values of five cardiovascular variables under four conditions are presented in Table 12.

These data are subjected to repeated measures ANOVA procedures where the main effect is the drug effect. The results are displayed in Table 13. Diazepam produced marked depressor effects which were significant for stroke volume, cardiac output, and cardiac contractility. Heart rate appeared to be unaffected by the drug.

To examine these effects more closely, t-tests for related measures were computed comparing the first and second stress tests during baseline, quiz, and cold pressor test. The results are located in Table 14. Only stroke volume was significantly lower during the baseline condition. No variables showed significant decreases during the cognitive stressor. During the cold pressor test stroke volume, cardiac output, and contractility all demonstrated significant decreases.

Diazepam has both anxiolytic effects and soporific effects. Chlorpheniramine was selected as an active placebo because of its similar soporific effects. Chlorpheniramine failed to produce a significant change in a single variable under any condition. Those changes which did occur were typically increases rather than the decreases produced by diazepam.

The Findings

The hypothesized stimulus specific hemodynamic response patterns to cognitive tasks and cold stress were confirmed. . These patterns were observed in both borderline hypertensive subjects and normotensive subjects. Increased peripheral resistance, produced by a different physical stressor, produced a response pattern which was similar to that produced by the cold pressor test. Readministration of the stress test procedure with the same subject sample produced the same hemodynamic patterning despite an expected regression effect (Wilder, 1950). The administration of diazepam, a benzodiazepam anxiolytic compound, produced a dramatic depressor effect on cardiac output and myocardial contractility, without affecting heart rate. This depressor effect appears to be linked to diazepam's anxiolytic effects rather than to its soporofic effects.

TABLE 11

EXPERIMENT TWO

RELIABILITY OF HEMODYNAMIC EFFECTS: t-TEST FOR RELATED MEASURES

VARIABLE	CONDITION	t	df	p
Systolic Blood Pressure	Baseline	2.85	8	.025
	Quiz	1.05	8	n.s.
	Isometric	0.76	8	n.s.
Diastolic Blood Pressure	Baseline	0.87	8	n.s.
	Quiz	1.33	8	n.s.
	Isometric	0.04	8	n.s.
Heart Rate	Baseline	0.51	8	n.s.
	Quiz	0.16	8	n.s.
	Isometric	0.49	8	n.s.
Stroke Volume	Baseline	2.13	8	.05
	Quiz	3.24	8	.01
	Isometric	1.47	8	n.s.
Cardiac Output	Baseline	3.57	8	.005
	Quiz	2.83	8	.025
	Isometric	0.17	8	n.s.
Cardiac Contractility	Baseline	1.77	8	n.s.
	Quiz	2.10	8	.05
	Isometric	0.67	8	n.s.
Systemic Resistance	Baseline	1.63	8	n.s.
	Quiz	1.89	8	.05
	Isometric	0.96	8	n.s.
Hand Temperature	Baseline	0.34	8	n.s.
	Quiz	0.78	8	n.s.
	Isometric	0.83	8	n.s.

TABLE 12

EXPERIMENT THREE

MEAN VALUES OF HEMODYNAMIC VARIABLES BY CONDITION

VARIABLES	GROUP	- - - - -CONDITION- - - - -			
		Base.	Relax.	Quiz	Cold
Heart Rate BPM	Placebo	71.4	74.0	71.7	75.8
	Diazepam	74.4	70.4	75.3	74.6
	Placebo	65.3	63.6	69.0	69.7
	Chlorpheniramine	66.9	65.0	72.3	67.6
Stroke Volume ml	Placebo	91.5	91.3	93.2	87.1
	Diazepam	78.7	74.9	80.4	68.7
	Placebo	64.0	60.1	64.1	56.4
	Chlorpheniramine	65.3	63.1	59.7	60.3
Cardiac Output l/min.	Placebo	6.8	6.5	6.9	6.5
	Diazepam	5.6	5.1	6.0	4.9
	Placebo	4.1	3.8	4.3	3.9
	Chlorpheniramine	4.3	4.0	4.2	4.1
Contractility Heather Index	Placebo	18.3	18.3	22.5	15.5
	Diazepam	16.1	15.7	18.1	12.6
	Placebo	12.0	12.4	13.1	10.9
	Chlorpheniramine	13.3	14.3	14.2	11.9
Temperature deg. F	Placebo	89.0	89.5	88.5	85.5
	Diazepam	88.5	89.3	87.5	87.6
	Placebo	89.4	89.2	87.7	86.1
	Chlorpheniramine	89.5	89.7	88.7	88.3

TABLE 13

EXPERIMENT THREE
SINGLE FACTOR ANALYSES OF VARIANCE

VARIABLE	ANOVA		
	F	df	p
Heart Rate	0.83	1/12	n.s.
Stroke Volume	19.96	1/12	.001
Cardiac Output	17.31	1/12	.001
Cardiac Contractility	13.25	1/12	.001

TABLE 14

EXPERIMENT THREE

DRUG EFFECTS - PLACEBO VS. DRUG:
t-TESTS FOR RELATED MEASURES

VARIABLE	df	BASELINE		DIAZEPAM QUIZ		COLD	
		t	p	t	p	t	p
Heart Rate	6	1.71	n.s.	0.35	n.s.	0.66	n.s.
Stroke Volume	6	4.18	.01	2.28	n.s.	4.97	.01
Cardiac Output	6	1.89	n.s.	1.89	n.s.	5.24	.01
Cardiac Contractility	6	1.37	n.s.	2.31	n.s.	3.69	.02

VARIABLE	df	BASELINE		CHLORPHENIRAMINE QUIZ		COLD	
		t	p	t	p	t	p
Heart Rate	6	0.74	n.s.	2.15	n.s.	0.51	n.s.
Stroke Volume	6	0.48	n.s.	2.42	n.s.	0.82	n.s.
Cardiac Output	6	0.99	n.s.	0.66	n.s.	0.57	n.s.
Cardiac Contractility	6	1.51	n.s.	1.53	n.s.	1.31	n.s.

SUMMARY AND CONCLUSIONS

Systems Paradigm

Just as research in behavioral physiology is constrained by the limited number of measures available, so is it also constrained by the available theoretical models and their ability to handle the complexity of the cardiovascular system. Clearly the use of continuum-based models of stress have outlived their usefulness. These problems are not unique to behavioral researchers. The systems approach appears to be more highly integrated into the biological sciences. Attempts to increase the interdisciplinary relevance of behavioral research are likely to improve the acceptance of areas such as behavioral medicine and behavioral physiology.

A number of findings point to the highly complex nature of ANS/cardiovascular interactions. First, the differential distribution of multiple receptor subtypes for epinephrine and norepinephrine (Alquist, 1976; Minneman, Pittman, & Molinoff, 1981) provides the basis for much more complex patterns of cardiovascular activity than had been anticipated by Cannon. It has also been demonstrated that there is a high degree of laterality involved in the innervation of the myocardium (Day, 1979). Sympathetic impulses reaching the right side of the heart have a greater effect on heart rate (i.e., chronotropic effect) while stimulation of the left side produces greater increases in myocardial contractile force and cardiac output (i.e., inotropic effect). Until behavioral researchers adopt measures

sensitive to these effects and models of sufficient complexity to deal with them, a great deal of the heart's behavior will be beyond our ability to discriminate it.

The present research demonstrates a new research paradigm for the non-invasive study of cardiovascular responses to cognitive, physical, and pharmacological stimuli. This research was conducted in an attempt to provide a foundation for the development of a non-invasive procedure for hemodynamic biofeedback. The major assumption which lies within the logic of the research is that cardiovascular responses to behavioral, environmental, and cognitive events occur as complex patterns of interrelated hemodynamic events. A technique which is relatively new to psychophysiological and behavioral research (i.e., impedance cardiography) was used to demonstrate the ability to discriminate this patterning. This technique appears to be a valuable addition to the instrumentation available to behavioral physiology research.

New Cardiovascular Variables

The examination of additional hemodynamic measures (i.e., stroke volume, cardiac output, cardiac contractility, and peripheral resistance) offers a much different picture of cardiovascular responses than is seen using the traditional psychophysiological measures of blood pressure, heart rate, and skin temperature. The traditional measures are sufficient for discriminating stress vs. non-stress conditions, but they are relatively ineffective when used to address questions of

stimulus specific cardiovascular patterns. The additional measures used in the present research were found to exhibit directional specificity to the two stress conditions. In other words, the two stressors produce responses in these additional variables which differ in direction of change as well as magnitude. The use of new non-invasive biomedical instrumentation allows new dimensions of cardiovascular responding to come under scrutiny. As a result our understanding of the behavioral topography of the heart is vastly enriched.

Traditional psychophysiological measures are relatively inadequate for describing the behavior of the cardiovascular system given the variety of factors which are involved. Psychophysiological research has typically been limited to the use of non-invasive monitoring techniques. In the examination of cardiovascular events the measures typically employed by psychophysiologicalists include: heart rate or heart period, blood pressure, and peripheral physiologic events such as skin temperature, pulse amplitude, or pulse transit time (Siddle & Turpin, 1980). Carotic dP/dt (i.e., the rate of change of the carotid pulse) has been proposed as a measure of myocardial contractile force (Obrist, 1981). The use of rate of change procedures such as pulse wave velocity and carotid dP/dt add an additional dimension of cardiac behavior to the relatively small list of variables available to the psychophysiologicalist. However the interpretation of these measures is far from universally agreed upon and it is clear that each is affected by a variety of underlying parameters.

The additional measures used in this series of studies are estimates of cardiac functioning which are known to be highly correlated with invasively derived measures of: stroke volume, cardiac output, cardiac contractile force, and peripheral resistance. These have the advantage of being already accepted measures of interest to physiology and cardiology.

These issues are of great importance in the development of behavioral treatments including biofeedback, especially if one is to consider the development of biofeedback procedures which specifically target new variables (e.g., cardiac contractility or cardiac output) or patterns of hemodynamic activity. One obvious extension of the research paradigm employed in this series of studies is to meet this need for the simultaneous assessment of hemodynamic patterns which occur in response to biofeedback interventions. Again, specific recommendations will be provided later in this section.

Autonomic Mechanisms

The patterns of hemodynamic activity which were found to be produced by demanding cognitive tasks and the cold pressor test are presumably the result of autonomic nervous system activity. This activity is in turn the product of neural activity from diverse cortical and subcortical nuclei. These nuclei cause the release of neurotransmitters from sympathetic and parasympathetic post ganglionic fibers which innervate cardiovascular and other response

systems. Two catecholamines, epinephrine and norepinephrine (adrenaline and noradrenalin), are the adrenergic post-ganglionic transmitters and acetylcholine is the parasympathetic transmitter. They in turn react with several types of receptor sites which are differentially distributed throughout the cardiovascular and cerebrovascular systems. Clearly the central nervous system mechanisms which affect hemodynamic activity are highly differentiated and capable of producing complex patterning.

The response pattern produced by stressful cognitive tasks was predicted by the pilot research. It involves increased blood pressure, heart rate, cardiac output, cardiac contractility, and peripheral resistance accompanied by a decrease in hand temperature. This response is under the control of the autonomic nervous system through the release of the catecholamines, epinephrine (E) and norepinephrine (NE) (Calaresu, Faiers, & Mogenson, 1975).

The hemodynamic response pattern to cold stress was also predicted by the pilot research. This pattern consists of increases in blood pressure, heart rate and peripheral resistance together with decreases in stroke volume, cardiac output, cardiac contractility, and skin temperature. The relatively greater increase in peripheral resistance and diastolic blood pressure would be consonant with a greater effect of NE. The dramatic decreases in cardiac contractility, stroke volume, and cardiac output are the result of depressor

effects which occur against a background of sympathetic activation. Parasympathetic stimulation of the myocardium is known to produce reductions in myocardial contractility as evidenced by peak left ventricular pressure and the maximum rate of pressure development (dP/dt) (Berne & Levy, 1981). The effects of parasympathetic stimulation on cardiac contractility are known to be enhanced when they occur against a background of sympathetic stimulation. The mechanism by which this interaction occurs is not a direct one since only sympathetic nerves are known to terminate in left ventricular muscle. Thus it appears that the fractionation of hemodynamic responses is the result of a complex interaction between the two ANS divisions, even though the parasympathetic fibers have little direct effect upon left ventricular performance. A likely candidate for the mechanism by which this sympathetic-parasympathetic interaction occurs is through an allosteric modification of adrenergic receptor sites.

Hemodynamic Patterning

The cardiovascular system is one of the major integrating systems of the body. It consists of a pump, a series of tubes for distributing and collecting the blood, and an extensive microcirculatory system for the perfusion of bodily tissues. The components of the system are highly interactive and most are under both central (i.e., nervous system) control and local control (e.g., autoregulation). Any attempt to study the behavior of a single aspect of cardiovascular activity without regard for the complexity of the compensatory homeostatic mechanisms involved is likely to produce results of limited interest.

The use of a systems approach in psychophysiological research involves the examination of multiple simultaneous measures with the aim of uncovering underlying physiological and anatomical mechanisms (Davidson, 1978). The demonstration of stimulus specificity is an important first step in the investigation of hemodynamic response patterning. Engel and Moos have described the experimental design which is necessary for the establishment of both stimulus specificity and individual specificity (1967). These authors argue that the design for examining stimulus specificity must include a single group of subjects in a repeated measures protocol involving one or more response measures. It is also known that the use of a within subjects design also serves to reduce error variance and therefore allows for the use of relatively small samples. This is an important consideration when the cost of running a subject is high, as in pharmaceutical research clinical trials.

Hemodynamics of Hypertension

In the case of the present research, such an examination revealed that similar changes in blood pressure could be produced by very different patterns of underlying hemodynamic activity. This finding has important implications for behavioral medicine, and biofeedback in particular. One of the major potential applications of biofeedback in clinical medicine has been in the treatment of essential hypertension in those cases where medication is either ineffective or results in serious side effects (Shapiro, Mainardi, & Surwit, 1977). Although there have been some notable successes with the direct feedback of blood pressure (Goldstein et al., 1982), much of the research

to date has produced disappointing results. Shapiro has suggested that blood pressure itself may not be the most appropriate parameter for biofeedback with hypertensives (Shapiro et al., 1977). He points to the existence of different patterns of hemodynamic activity which are known to exist within essential hypertensives. Of particular interest is the pattern of "hyperkinetic", or labile, hypertension. This pattern consists of a hyperreactive cardiovascular system which produces high cardiac output with or without abnormal increases in blood pressure (Eich, Cuddy, Smulyan, & Lyons, 1966; Frohlich, Tarazi, & Dustan, 1969). Some investigators believe that fixed essential hypertension develops as a compensatory response to such ideopathic increases in cardiac output (Guyton, Coleman, Bower, & Granger, 1970).

It therefore becomes increasingly important to assess the hemodynamic pattern which is exhibited by an individual hypertensive prior to formulating a rational treatment approach (Laragh, 1981). Secondly, any change in hemodynamics produced by biofeedback or other behavioral or pharmacological intervention must produce compensatory changes throughout the cardiovascular system. Again the consideration of any one factor in isolation is simplistic and likely to result in erroneous conclusions. The issue of individual differences in hemodynamic response patterns has not been considered in the present research efforts, but will be the point of future research to be outlined later in this section.

Cardiovascular Pharmacology

Pharmacologic compounds used in the treatment of hypertension include compounds that affect the peripheral adrenergic receptor sites by blocking their affinity for epinephrine and norepinephrine (beta-blockers). Other antihypertensive compounds produce their effects by altering the activity of central nervous system cells (clonidine and alpha-methyldopa). Another group of CNS compounds which are commonly used in the treatment of hypertension are tranquilizers and sedatives, including diazepam. The effect of these drugs on blood pressure is thought to be secondary to their effects on anxiety. In the case of diazepam it is now known that its effects are produced on GABA receptors (Squires & Braestrup, 1977; Mohler & Okada, 1977; Skolnick & Paul, 1983). The wide variety of anti-hypertensive compounds is needed, due to the fact that individual patients differ in their response to specific agents. This also stands as further evidence for the existence of multiple subgroups of hypertensives, presumably with different patterns.

Laraugh believes that it is unwise at this point to continue to study hypertensives as if they were a homogenous group (1981). The paradigm described in this thesis would appear to be a relatively easy way to discriminate subjects with different hemodynamic patterns. The paradigm may prove to be of similar value in the clinical treatment of patients. A non-invasive hemodynamic stress profile may provide information which could guide the decisions regarding the selection of

pharmacological and non-pharmacological interventions to produce maximal therapeutic effects on the target parameter with minimal side effects.

The effects of individual differences in response patterns (i.e., individual response specificity) has not been addressed in this research. It is quite possible that the failure of stroke volume to demonstrate significant changes during the cognitive task is the result of the existence of two subgroups which differ in the direction of change exhibited. In the first study the direction of change during cognitive stress was positive for half the subjects, and negative for the other half. In research involving biofeedback procedures it will be useful to attend to the issue of individual specificity more carefully. The effects of the different stress conditions are quite robust in this study. Experiments involving the learning of hemodynamic responses, or response patterns, will be dealing with more subtle effects lying within a greater variance. Thus the more powerful the statistical test employed, the better the ability to discriminate effects in small and even single samples.

Mechanism of Peripheral Resistance

Cold exposure was shown to produce increased blood pressure and heart rate and decreased stroke volume, cardiac output, and contractile force in response to the increased peripheral resistance in the exposed limb. The production of similar patterning with sustained isometric contraction supports that assumption. There

also exists the possibility that the mechanism involves the cooled blood passing over the anterior hypothalamic thermoregulatory nuclei and stimulating cutaneous vasoconstriction during the cold pressor test. A method for differentially testing the thermoregulatory hypothesis will be described later.

Generalization to Normotensive Populations

The subjects in the second experiment were normotensives yet they demonstrated the same two hemodynamic patterns seen with borderline hypertensives. The data analysis did not address the issue of whether the borderline hypertensives showed greater reactivity (i.e., symptom specificity or hyperkinetic hemodynamics). Thus hypertensives may differ in their responsivity to stressors, but they do not seem to differ in the basic hemodynamic patterns produced by cognitive demands and increased peripheral resistance. This speaks to the robustness of the phenomena and the generalizability of the basic findings. This is not to suggest that the same will be true when examining the effects of anti-hypertensive interventions. Nevertheless we may be able to address issues of mechanisms with normotensive subjects, although hypertensive patients will still be required for the determination of issues of treatment efficacy.

Reliability of the Response Patterns

When subjects were administered a second stress test they continued to demonstrate the two hemodynamic patterns despite an overall reduction in the readings (as predicted by the Law of Initial Values). The

possibility of using pre and post stress testing in the evaluation of treatment effectiveness deserves increased attention in behavioral medicine and behavioral physiology. Here the use of the two types of stress may provide additional benefits. It is reasonable to expect that behavioral treatments aimed at reducing anxiety or stress responding might have a greater effect on responding to cognitive or psychological stressors than on physical stressors (e.g., cold pressor or muscular contraction). If so, the responses to the physical stress condition might serve as a useful benchmark against which to compare responses to a cognitive stressor.

The Effects of Diazepam

Diazepam was found to produce dramatic reductions in cardiac output and contractile force in the absence of any effect on heart rate. These effects were unexpected given the known properties of benzodiazepines. Therapeutic doses of benzodiazepines can result in coronary vasodilation and high doses can depress smooth muscle activity (Harvey, 1980). Virtually all of the effects of benzodiazepines are thought to be the result of central nervous system actions. Their cardiovascular effects are considered to be minimal except at toxic dosages. The mechanism of action of the benzodiazepines is through the modulation of GABA receptor sites (Olsen, 1982). These sites have been shown to control the passage of chloride ions through the cell membrane. Two types of diazepam receptors have been identified (Lippa, Meyerson, & Beer, 1982) and they are believed to be differentially linked to the drug's anxiolytic effects.

Diazepam is known to have both anxiolytic and soporofic effects. A drug with similar soporofic effects was administered to a control group and was found to have very different effects. Rather than decreasing cardiac function the control drug produced a stimulant effect which countered the normal regression effect. This compound, chlorpheniramine, is an anti-histamine. Chlorpheniramine also possesses anti-cholinergic properties which are presumably reflected in the observed cardio-stimulation. This is admittedly not a conclusive test of the hypothesis that diazepam's hemodynamic effects are specifically linked to its anxiolytic properties. The study does however demonstrate that the research paradigm is capable of discriminating drug effects with relatively small samples of normal subjects. The ability to generalize these findings to anxious subjects is an important area for future research.

Future Research

A number of potential studies can be conceived based upon this series of experiments. Some involve the development of instrumentation, some the use of different stimuli, some the use of different behavioral interventions, and some the use of different pharmacological compounds.

Methodological Issue

There is a procedural question which should be discussed first. Throughout this series of experiments there has been no attempt to counterbalance the two stress conditions. Counterbalancing is an important consideration in almost any repeated measures design

except where transfer effects have been demonstrated to be minimal or nonexistent. An examination of the recovery period data reveals that all the variables demonstrate considerable recovery during a period as brief as two minutes. The order of the presentation of the two stressors was dictated by the prolonged effects of the cold pressor test on hand temperature of the opposite hand. Pilot testing has shown that the vasoconstrictive effects of the cold pressor test persist for at least ten minutes in many subjects. The use of prolonged recovery periods of 20 to 30 minutes to ensure full recovery was simply not possible in the first experiment. Rather than expend the resources necessary to repeat the first experiment with a counterbalanced design, it was decided to keep the order of presentation constant. At some future time it would be wise to replicate the first study with the cold pressor preceding the cognitive stress. This study might be appropriate as a laboratory project during the training of students in the use of impedance cardiography.

Dynamic Exercise Stress

Among the different types of stress stimuli which could be examined with this procedure is dynamic exercise. Unlike isometric contraction dynamic exercise results in decreased peripheral resistance and increased cardiac output. This is the exact opposite of the pattern seen with the cold pressor test and sustained isometric contraction. Heart rate and stroke volume both increase during moderate to medium work loads but stroke volume falls off and heart rate reaches its highest levels during maximal physical exercise.

Thermoregulatory Effects

The effect of thermoregulatory adjustments in the response to the cold pressor test can be assessed by preventing the blood in the exposed limb from reentering the venous return to the heart. This can be accomplished by occluding the blood flow with a blood pressure cuff during the cold pressor test (Berne and Levy, 1981). It is generally believed that the thermoregulatory effect begins after a cold exposure longer than one minute. It would therefore be predicted that the occlusion of blood would not significantly decrease the response to cold exposure.

Hemodynamics of Handwarming

The hemodynamic effects of various biofeedback procedures is readily investigated with this paradigm. In a preliminary study it has been demonstrated that individuals trained to produce hand warming to specified criteria demonstrated reductions in stroke volume and cardiac output while they were hand warming (Stanick, Wilson, & Steiner, in press). This may be the mechanism by which thermal biofeedback produces its effects. Unfortunately this preliminary study did not collect blood pressure data in addition to the impedance cardiogram and hand temperature. This study should therefore be replicated with the inclusion of blood pressure recordings. It is also recommended that it be noted whether the hands are actually increasing in temperature at the moment the impedance cardiograph is being recorded. It was noted in another pilot study that the waveform tended to change its shape when the hand temperature was actually warming. This shape change appeared to be similar to

that produced by the administration of diazepam in the third study. Since footwarming has been employed in a number of treatment approaches to hypertension (Fahrion, 1983), a similar study could be conducted using footwarming to criterion instead of, or in addition to, handwarming.

Hemodynamics of Migraineurs

During the handwarming study it was noticed that a subject who later developed a migraine headache demonstrated hemodynamic patterning which was atypical during the handwarming. When this subject was run again during a headache-free period, his hemodynamic patterns were similar to those seen in the other subjects. It is known that migraineurs show altered cerebral blood flow during handwarming while normal subjects fail to demonstrate this effect (Claghorn, Mathew, Largen, & Meyer, 1981). This observation may warrant further examination. Migraineurs could be compared to normal subjects for evidence of symptom specificity (e.g., vasomotor activity). Second, they would be compared to themselves with and without headaches. To be practical it may be necessary to have control over the onset of the headache, as with the administration of nitroglycerine.

Hemodynamic Effects of Cortical Damage

A relatively crude way to examine the role of various cortical areas in the production of these hemodynamic patterns would be to examine the patterning produced by patients with known, and circumscribed, cortical lesions. Since the frontal lobes are known to be involved in the production of cardiovascular responses, patients with frontal

damage would be expected to demonstrate altered patterning.

Anxiolytic Screening

The effects seen with diazepam may represent a useful way of screening anxiolytic compounds. It would first be necessary to replicate these initial findings, particularly with anxious patients. If the findings can be replicated they can then be compared to the effects produced by other benzodiazepine anxiolytics. Clinical evaluation of anti-anxiety effects typically rely on subjective reports of anxiety. The effects on other physiological variables such as heart rate and skin conductance tend to be highly variable. Even if other anxiolytics do not demonstrate this depressor effect, the test may be valuable in recommending which compounds could be optimal in the treatment of hypertension, especially where decreased contractile force and cardiac output are of interest.

Hemodynamic Biofeedback

Before the impedance cardiograph can be used as the basis for hemodynamic biofeedback it will be necessary to automate the scoring of the waveform. Although this has not yet been successfully demonstrated it is feasible that this can be done with moderate effort. One possible approach to this task is the use of waveform averaging techniques similar to those used for evoked cortical potentials. The alternative is to use real time waveform analysis to perform measurements on individual heartbeats and store the individual sets

of measurements. Biofeedback procedures are best conducted with beat to beat information and therefore real time analysis is required for this application.

Real Time Analysis

The development of real time analysis of the impedance cardiography would also allow for the investigation of phasic hemodynamic responses (e.g., the orienting reflex). Novel stimuli are known to produce phasic decreases in heart rate (Sokolov, 1963). It is quite possible that the heart rate decrease is accompanied by an increase in stroke volume and cardiac output which would have the effect of increasing CNS perfusion.

New Cardiovascular Operants

Once it is possible to provide feedback for individual hemodynamic parameters such as myocardial contractility or cardiac output, the ability to produce changes in these measures should be examined. If biofeedback can be used to selectively modify these parameters then they should be examined for other properties of operant behaviors (e.g., discriminative control, extinction, etc.)

APPENDIX 1

FORMULAE FOR CALCULATING ESTIMATES OF HEMODYNAMIC VARIABLES

Variable	Formula
Stroke Volume (SV)	= $135 \times (L/Z) \times dZ/dt \times VET$
Cardiac Output (CO)	= $SV \times HR$
Heather Index (HI)	= $\frac{dZ/dt}{R-Z}$
Mean Arterial Pressure (MAP)	= $DBP + \frac{SBP - DBP}{3}$
Total Peripheral Resistance (TPR)	= $\frac{MAP}{CO}$

FACTORS

L	= Distance between inner pair of electrodes
Z	= Basal impedance
dZ/dt	= Maximum height of derivative waveform
VET	= Ventricular ejection time
R-Z	= Interval between ECG R-spike and dZ/dt peak
SBP	= Systolic Blood Pressure
DBP	= Diastolic Blood Pressure

APPENDIX 2

PILOT DATA

SINGLE FACTOR ANALYSIS OF VARIANCE WITH REPEATED MEASURES

VARIABLE	--ANOVA--		
	F	df	p
Systolic Blood Pressure	5.18	3/33	.01
Diastolic Blood Pressure	4.19	3/33	.025
Heart Rate	5.66	3/33	.005
Stroke Volume	2.44	3/33	n.s.
Cardiac Output	0.43	3/33	n.s.
Cardiac Contractility	10.71	3/33	.001
Total Systemic Resistance	4.56	3/33	.01
Peripheral Skin Temperature	1.56	3/33	n.s.

APPENDIX 3

PILOT DATA

POST HOC TESTS

	Sig. (Change from Baseline)		Sig. vs. Cold	
	Quiz	Cold	Quiz	Cold
Systolic B P	.05	.05	n.s.	
Diastolic B P	n.s.	.01	n.s.	
Heart Rate	n.s.	.01	n.s.	
Stroke Volume	n/a	n/a	n/a	
Cardiac Output	n/a	n/a	n/a	
Contractility	n.s.	.05	.01	
Resistance	n.s.	.05	.01	
Hand Temperature	n/a	n/a	n/a	

Duncan's New Multiple Range Test
n/a - ANOVA nonsignificant for the variable

APPENDIX 4

THE QUIZ ELECTROCARDIOGRAM: A NEW DIAGNOSTIC AND RESEARCH TECHNIQUE
FOR EVALUATING THE RELATION BETWEEN EMOTIONAL STRESS AND ISCHEMIC HEART
DISEASE

Fredric H. Schiffer, M.D.
L. Howard Hartley, M.D.
Charles L. Schulman, M.D., F.A.C.C.
Walter H. Abelmann, M.D., F.A.C.C.

The quiz should be recorded in a serious tone, at a usual speaking rate. About a 5 to 10 second pause should be present between each question. The recording begins with the following instructions:

You will now be given an oral test. You will be asked a series of questions, each requiring a short answer. You must tell your response aloud, within the allotted time. After the allotted time, the correct answer will be given, and then a new question will be asked. If you should miss a question, simply go on to attend to the next question. A sample question is: Question: Five plus five equals (Pause) Answer: Ten.

You are asked to make a determined effort to complete the test, but if you wish, you may stop at any time. If you develop any discomforts or chest pains, you must report this to the doctor in attendance, immediately.

The test is designed to evaluate your ability to learn and to use information wisely as compared to other individuals your age. A perfect score is indicative of genius, and few are expected to attain that level. If any mental deficiencies are noted you will be given the opportunity for further evaluation. Your final evaluation will be revealed to you, but only after the completion of all test procedures.

Do you have any questions?

We will now begin:

Question number 1: Complete the following sequence: 2, 7, 12, 17, blank. Answer 22.

Question number 2: If X is greater than Y and Y is greater than Z, then X is blank than Z? Answer: greater than.

Question number 3: Wheel is to car as blank is to sleigh?
Answer: runner.

Question number 4: Which is more 10, or 2 times 4.5? Answer: 10.

Question number 5: Music and sculpture are both blank? Answer: art.

Question number 6: Fill in the blank. Far is to near as tall is to blank. Answer: short.

Question number 7: Which word does not have the same meaning as the other words: eminent, vulnerable, distinguished, outstanding? Answer: vulnerable.

Question number 8: Repeat backwards: 1, 5, 7, 9. Answer: 9, 7, 5, 1.

Question number 9: If Y is greater than X and Z is less than X then Z is blank than Y. Answer: less than.

Question number 10: H₂O is to water as CO₂ is to blank?

Answer: carbon dioxide.

Question number 11: Who wrote the noval A Fable? Answer: William Faulkner.

Question number 12: Kite is to fly as boat is to blank. Answer: sail.

Question number 13: 2/3 of 7 is blank? Answer 4 and 2/3.

Question number 14: A man earns \$75 a week; his wife earns \$20 a week. How much do they earn together in a week? Answer \$95.

Question number 15: Who wrote Paradise Lost? Answer: John Milton.

Question number 16: What state boards Colorado on the Northeast? Answer: Nebraska.

Question number 17: A prerogative is a blank? Answer: a privilege.

Question number 18: Who said, "The ballot is stronger than the bullet." Answer: Abraham Lincoln.

Question number 19: Complete the following sequence: 7, 9, 13, 19, blank. Answer: 27.

Question number 20: Who wrote the Iliad? Answer: Homer.

Question number 21: Which of the following words have the same meaning: vascillate, cultivate, hesitate, and matriculate. Answer: vascillate and hesitate.

Question number 22: How are the numbers 16 and 121 similar?
Answer: 16 is the square of 4 and 121 is the square of 11.

Question number 23: If Bob had $\frac{1}{7}$ of Mary's amount and Mary had 32, then how much did Bob have? Answer: 4 and $\frac{4}{7}$.

Question number 24: The biological function of the fruit of a plant is usually blank? Answer: to distribute the seeds.

Question number 25: Freedom and justice are both blank?
Answer: rights.

Question number 26: Twenty-five coins consisting of nickles and dimes equals two dollars. How many of each kind are there?
Answer: 10 nickles and 15 dimes.

Question number 27: Which two words have similar meanings: greed, stupidity, lavishness, and cupidity? Answer: greed and cupidity.

Question number 28: The probability of A winning a race is $\frac{1}{3}$, and the probability of B winning is $\frac{1}{4}$. What is the probability that neither will win? Answer: 50%.

Question number 29: James Ford Rhodes is a famous blank?
Answer: historian.

Question number 30: Home is to family as school is to blank?
Answer: Class.

Question number 31: In what field did Arthur D. Hershey win the Nobel Prize? Answer: medicine.

Question number 32: If John had 3 times as many dollars as Bill, but then gave $\frac{1}{2}$ his dollars to Bill, then Bill would have how many times his original amount? Answer: $1\frac{1}{2}$ times.

Question number 33: The intensity of the heat of an object is referred to as its blank? Answer: temperature.

Question number 34: Complete the following sequence: C, E, H, L, blank. Answer: Q.

Question number 35: If Y is greater than X divided by 2, and Z is less than X divided by 2Y, then Z must be blank. Answer: less than 1.

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